Online assisted psychological therapy for targeted populations with inflammatory bowel disease.

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Abstract

Introduction: Inflammatory bowel disease (IBD) is a chronic condition affecting over 300,000 people in the UK. Despite a high level of comorbid mental disorders, most patients do not receive psychological help. As a result of scarce healthcare resources in IBD, technology is increasingly being recognised as a useful tool to manage anxiety and depression associated with IBD. However, there is no online psychotherapy programme for patients with IBD and comorbid anxiety and/or depression available in the UK.

Aim: The aim of this thesis was to develop a prototype online psychological intervention for patients with IBD and comorbid anxiety and/or depression.

Methods: The development of the prototype followed the Medical Research Council (MRC) framework for complex interventions (the development phase). Firstly, theoretical evidence on the effectiveness of online psychological therapy in gastrointestinal diseases was gathered in a systematic review. Secondly, a qualitative study investigated patients' with IBD and comorbid anxiety and/or depression and their service providers' views about lived experiences with IBD and about an online psychological intervention. Finally, the recommendation for the online psychological intervention for this population was provided.

Results: The evidence on the usefulness of online psychological interventions in gastroenterology, and IBD specifically, is scarce. There is a need for more robust trials of psychotherapy in IBD, particularly in patients with IBD and anxiety and/or depression. Patients had positive attitude towards online psychological intervention, while health professionals were unsure about patients' participation in the intervention. Based on the theoretical evidence and the qualitative study findings the recommendations for the future interventions were developed.

Conclusions: This PhD project demonstrated the need for an online psychological intervention for patients with IBD and comorbid anxiety and/or depression. The intervention based on the prototype could be tested in a future trial. The productive collaborations between patients, stakeholders and researchers in co-designing of an online psychological intervention are essential during the development, evaluation and implementation of the intervention.

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Author's declaration

I declare that this thesis is a presentation of original work, and I am the sole author. This work has not previously been presented for an award at this, or any other, University. All sources are acknowledged as References. The protocol for the qualitative study in this thesis was submitted as an assignment for the qualitative health research module. The credits for it were not received, as it was a part of MPhil training required for the completion of this thesis. The material of the protocol was used in this work.

Parts of this thesis have been disseminated in the following formats:

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> Patients' and health professionals' views about online psychological interventions (PI) for Inflammatory bowel disease (IBD): a qualitative exploratory study.

1 Chapter 1: Introduction

This chapter provides an introduction to, the rationale for, and the overview of the thesis.

1.1 Background

Gastrointestinal (GI) diseases are a substantial burden for the health service providers and society as a whole across Europe and the UK (Farthing et al., 2014; Williams et al., 2007). Patients affected by the symptoms of these diseases have reduced health-related quality of life (HQOL) (Williams et al., 2007). Despite individual and population impact caused by GI disorders, they receive small financial and policy support (Farthing et al., 2014).

Disorders of brain-gut interaction (DBGI), formerly known as functional GI disorders (the terms will be used interchangeably) (Drossman and Hasler, 2016), and organic GI diseases such as inflammatory bowel disease (IBD) are the most common forms of GI disease (Langshaw et al., 2018), although the pathophysiological mechanisms of these disorders are still poorly understood (Farthing et al., 2014). Nevertheless, the gut-brain-microbiota links are important in pathogenesis and pathophysiology of GI disorders (Martin et al., 2018).

IBD is a GI illness with an incidence increasing globally (Ng et al., 2017). There is a high rate of comorbid anxiety and depression in patients with IBD (Mikocka-Walus et al., 2016b). Despite the evidence of bidirectional links between the gut and brain in IBD (Gracie et al., 2018), there is a lack of clear evidence on the effectiveness of psychotherapy for IBD (Timmer et al., 2011). There is some tentative evidence of higher effectiveness in selected subgroups of IBD patients (e.g. patients who have a high baseline IBD activity; have been recently diagnosed; are young; and with comorbid psychological distress) than in unselected IBD cohorts (Mikocka-Walus, 2015; Gracie et al., 2017; Timmer et al., 2011).

This thesis explores psychotherapy in the targeted population of IBD patients with comorbid anxiety and/or depression by analysing the existing literature and developing and evaluating a prototype of an online psychotherapy programme. This has involved identification/development of the appropriate theory and consultation with the end-users to adapt the online intervention to their needs regarding its content and design, with the aim of improving the acceptability of the intervention during the implementation.

1.2 IBD definition

IBD is a chronic idiopathic condition, which involves inflammation of the gastrointestinal tract (Fusunyan and Sanderson, 1998). IBD is used as a combined term for three disease subtypes: ulcerative colitis (UC), Crohn's disease (CD) and indeterminate colitis (IC). Predominantly, CD affects the ileocecal area of the GI tract (Mills and Stamos, 2007). However, it can affect any segment of the GI tract from the mouth to the anus, in contrast to UC, which affects the rectum and colon mucosa (Mills and Stamos, 2007). IC is an IBD subtype that, based on diagnostic tests, has both CD and UC characteristics (Malaty et al., 2013; Burakoff, 2004; Satsangi et al., 2006). The strong similarity in pathophysiology and treatment approaches of these autoimmune inflammatory heterogeneous diseases had led to the development of the integrated classification system and the common name of IBD (Silverberg et al., 2005; Spekhorst et al., 2014).

The definition of IBD only became widely used at the end of the last and the beginning of the present century, whereas the term ulcerative colitis was first used in the middle of the 19th century (Mulder et al., 2014) and the term Crohn’s disease was initially used in 1932 (Crohn, Ginzburg and Oppenheimer, 1932). Nevertheless, IBD has affected humans for thousands of years (Mulder et al., 2014).

1.3 Incidence and prevalence

IBD is highly prevalent, affecting 2.5 to 3 million people in Europe (Burisch et al., 2013b). The numbers of those affected by IBD people in the UK differ according to different sources but it is likely that over 300,000 people live with this disease in the country (The IBD Standards Group, 2013; NICE, 2014; The IBD UK, 2019). The distribution of IBD types among different age and sex groups and in different countries varies greatly (Cosnes et al., 2011). The highest incidence of CD is in those 20 to 30 years old and of UC, in those 30 to 40 years old (Cosnes et al., 2011), with occurrence of CD 20% to 30% more frequent in females and occurrence of UC 10% more frequent in males (Cosnes et al., 2011). However, this distribution is different for children, where CD is more prevalent in boys and UC in girls, with the trend changing during the teenage years (Cosnes et al., 2011). Approximately a fifth of all IBD cases are paediatric, with more frequent occurrence of the CD subtype in this population and across most countries (Cosnes et al., 2011).

The prevalence of IC is higher in children compared to adults (Carvalho et al., 2006). The majority of IBD cases that were initially considered as IC ultimately will be diagnosed with UC or CD, however between one and 10% of IBD patients will retain the IC diagnosis (Burakoff, 2004; Meucci et al., 1999; Nuij et al., 2013; Ng et al., 2013; Buderus et al., 2015).

It has been shown that IBD is more likely to affect urban populations compared to rural populations and individuals of higher rather than lower socioeconomic status (M'Koma, 2013). There is evidence that migration to urban and developed areas from the low IBD incidence regions before adolescence considerably increases the risk of IBD (M'Koma, 2013). The incidence of IBD is increasing significantly in developing countries and countries where it was traditionally low, for instance, Japan (Ng et al., 2017; Cosnes et al., 2011).

1.4 Aetiology and epidemiology of IBD

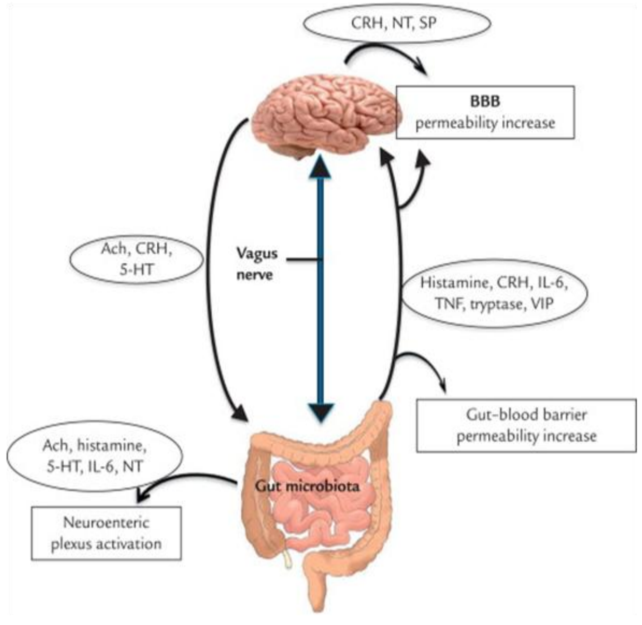
Although IBD's aetiology is unknown, microbial, dietary, genetic, infectious and other environmental factors influence the occurrence of the diseases (Molodecky and Kaplan, 2010; Asakura et al., 2008; Luther et al., 2010; Jostins et al., 2012; Loftus, 2004; Jess et al., 2005; Karlinger et al., 2000), with only a few systematic reviews conducted on the aetiology of IBD to date (Penagini et al., 2016; Klement et al., 2004).

1.4.1 Gut-brain-microbiota axis

The interaction between the brain and the digestive system was explored by the Russian scientist Pavlov in the nineteenth century. Pavlov demonstrated that the brain affects the functioning of the gut (Tansey, 2006). Since then, this area of research has been developing rapidly, particularly in the last few decades as a result of the breakthrough in: microbial gut-brain bidirectional signalling (Rhee, Pothoulakis and

Mayer, 2009; Mayer, 2011), neuroimaging (Tillisch and Labus, 2014), intestinal microbiology and host-microbial interactions (Bron, de Vos and Kleerebezem, 2006; Collins and Bercik, 2009; Martin et al., 2007), and enteric neuroscience (Gershon, 1999; Furness, 2006; Mayer, 2007). Increasing evidence suggests that the gut also influences the brain functions (Heijtz et al., 2011; Neufeld et al., 2011; Gareau et al., 2011), predominantly its behaviour and emotional processing (Burokas et al., 2016; Borre et al., 2014; Al Omran and Aziz, 2014; Clarke et al., 2014).

The interactions between the digestive tract and the central nervous system occur through various pathways Figure 1) (Petra et al., 2015), including the enteric nervous system (ENS), the neuroendocrine system and the humoral immune system (Carabotti et al., 2015; Powell, Walker and Talley, 2017; Evrensel and Ceylan, 2015; Mayer and Tillisch, 2011; Petra et al., 2015). This bidirectional communication between the brain and the gut forms the gut-brain axis (GBA) (Burokas et al., 2016; Carabotti et al., 2015; Powell et al., 2017). This well-known term is now being redefined as a gut-brain-microbiota axis as a result of the discovery that microbiota also influences brain functioning (Montiel-Castro et al., 2013; Carabotti et al., 2015; Cryan and O'Mahony, 2011). Furthermore, the gut microbiome influences the outcomes and the effect of treatment in IBD (Zuo and Ng, 2018).



"Gut microbiota can release molecules that may activate the neuroenteric plexus and stimulate brain production of neuropeptides, as well as increase gut–blood barrier and blood–brain barrier (BBB) permeability. The brain releases molecules that stimulate the neuroenteric plexus and gut function. The vagus nerve sends orthodromic and antidromic. CRH = corticotropin-releasing hormone; NT = neurotensin; SP = substance P; Ach = acetylcholine; IL-6 = interleukin 6; TNF = tumor necrosis factor; VIP = vasoactive intestinal peptide; 5-HT = 5-hydroxytryptamine"(Petra et al., 2015)

Figure 1 from (Petra et al., 2015): "Diagrammatic representation of the microbiota–gut–brain (MGB) axis highlighting the proposed bidirectional communications." (Petra et al., 2015).

The gut-brain-microbiota axis provides new insights into treatment directions of gastrointestinal diseases (Martin et al., 2018). Emerging from this insight, it has been found that modifying stress and mood with the assistance of psychological interventions may lead to better management of GI disease (Tabibian, 2013; Roditi and Robinson, 2011).

1.5 Symptoms of IBD

The symptoms of IBD vary depending on the severity and localisation of inflammation but most commonly include: diarrhoea, tiredness and fatigue, unintended weight loss, abdominal pain, blood in stool, minor fever, reduced appetite, mouth ulcers and anaemia (The IBD Standards Group, 2013; Waljee et al., 2009; Baumgart and Sandborn, 2007). Despite having common symptoms, CD and UC also have some distinguishing symptomatic features.

Depending on the localisation of inflammation and ulceration of the inner lining of rectum and colon, UC's subtypes include:

- Proctitis characterised by rectal bleeding, mucus in the stools, tenesmus (an urge to pass a stool without being able to due to empty bowel), occasional severe constipation.
- Proctosigmoiditis whose symptoms are similar to that of proctitis, but constipation is less likely.
- Left-sided (distal) colitis characterised by bloody diarrhoea with mucus, left-hand side abdomen pain, and tenesmus.
- Extensive pancolitis characterised by frequent bloody diarrhoea with mucus; sometimes fever, lethargy, tenesmus, abdominal discomfort and abdominal pain, cramps.

Rarely, gases trapped in the bowel due to severe inflammation could cause toxic megacolon with a high temperature and abdominal pain (Waugh et al., 2013; Panaccione, 2013).

Symptoms of CD depend on the localisation of the lesions. The most common are crampy severe pain, diarrhoea, nausea, vomiting and weight loss. Less common, CD can affect the upper gastrointestinal tract such as oesophagus, stomach or duodenum, causing pain, nausea with/without vomiting, loss of appetite, weight loss and anaemia. CD occasionally affects the mouth, causing swollen lips and mouth fissures or mouth ulcers due to nutrition deficiency during flare-ups. There are specific types of CD present in distinct ways:

- Patients with ileal CD have abdominal pain in the right side, with possible intestinal obstruction and watery diarrhoea without blood or mucous, and weight loss.
- In Crohn's disease with colonic localisation, patients have UC-like symptoms (bloody diarrhoea with mucus, tenesmus) often with perianal symptoms. However, many patients have symptoms of ileocolic CD, and a small number of CD patients have isolated perianal disease (Waugh et al., 2013; Panaccione, 2013).
- Perianal symptoms manifest in: skin tags (small fleshy growths around the anus); haemorrhoids (swollen blood vessels in or around the anus and rectum); fissures (tears or splits in the lining of the anal canal); abscesses around the anus causing a fever or leading to a fistula; fistulas (narrow passages or tunnels between the anal canal and the skin surface around the anus, leaking pus or sometimes faecal matter from skin openings); anal fissures, anal ulcers, anorectal carcinoma (de Zoeten et al., 2013; Ingle and Loftus, 2007).

During the healing process in CD, the scars (strictures) form in the bowel tissue, causing obstruction with cramping abdominal pain, nausea, vomiting and constipation (Turnage and Bergen, 1998). Other complications include perforations of the bowel, causing severe abdominal pain, fever, nausea, vomiting and occasional a passage of the faecal matter through that perforation (Lahat and Chowers, 2007). At times an abnormal tunnel between a different internal organ or opening to the skin surface (particularly around the anus) called a fistula can be formed (Marzo et al., 2015).

Symptoms that affect the entire body, for instance, tachycardia, weight loss, anorexia and high body temperature are more common in CD, however, could be present in severe cases of UC as well (Tontini et al., 2015; Waugh et al., 2013).

1.5.1 Extra-intestinal symptoms (EISs)

EISs are a manifestation of IBD in the systems other than the gastrointestinal tract. The EISs can occur prior to the IBD diagnosis and in some cases could impair patient's health more than the IBD itself (Jang, Kang and Choe, 2019). The chance of EISs increases with the disease duration and is higher in CD compared to UC (between 24%-40% and 26%-31%, respectively) and even higher (47%) for colonic localisation of CD (Tontini et al., 2015). The most commonly manifested EISs are in the dermatological (most often erythema nodosum and pyoderma gangrenosum) and musculoskeletal (most often enteropathic arthritis) systems (Levine and Burakoff, 2011). However, the consequences for the hepatobiliary system in the form of primary sclerosing cholangitis (PSC) are the most serious (Levine and Burakoff, 2011). PSC is a long-term progressive precancerous disease of the liver and gallbladder with the incidence in men double that of women (Tontini et al., 2015). Patients with IBD also report eye problems in the form of episcleritis, have thinning bones, kidney stones and gallstones, thrombosis of deep veins and anaemia (Levine and Burakoff, 2011). The probability of EISs is higher in CD, with the exception of PSC whose probability is twice as high in UC and which occurs in 2 to 4% of patients with UC (Tontini et al., 2015).

1.6 Psychological burden

In addition to the presence of the aforementioned symptoms, many patients have a high level of comorbid anxiety and depression (Mikocka-Walus et al., 2016b).

1.6.1 Anxiety

1.6.1.1 Epidemiology of anxiety

Anxiety is the most prevalent mental health disorder affecting approximately 264 million (3.6%) people globally (WHO, 2017). This disorder can affect people of any age with lower prevalence amongst the older population (Ritchie and Roser, 2019; WHO, 2017). Anxiety affects 4.2% of the UK population and accounts for over 200 thousand Total Years Lived with Disability (YLD) (WHO, 2017).

1.6.1.2 Diagnosis and symptoms of anxiety

According to DSM-5, anxiety disorders are a combined term used for disorders with typical features of excessive fear and anxiety (American Psychiatric Association, 2013). Anxiety is an anticipation of the future internal or external danger without evident

object or cause, while fear is an emotional reaction to a real or perceived danger (American Psychiatric Association, 2013). Short-term stress is not considered as a mental health problem, while long-term anxiety that interferes with everyday life indicating the severity of the symptoms (American Psychiatric Association, 2013).
According to the WHO (ICD-10), there are two classes of anxiety disorders:

- phobic anxiety disorders, which include social phobia, agoraphobia, specific (isolated) phobias, which are restricted to very particular situations, other phobic anxiety disorders and unspecified phobic anxiety disorder that often coexist with depression;
- other anxiety disorders (generalized anxiety disorder, depressive disorder and mixed anxiety, panic disorder, other specified and mixed anxiety disorders, anxiety disorder and unspecified disorders) (WHO, 2004).

The most common types of anxiety disorders are Generalized Anxiety Disorder, Panic Disorder, Post-Traumatic Stress Disorder (PTSD) and Social Phobia (or Social Anxiety Disorder) (American Psychiatric Association, 2013).

Often anxiety is accompanied by somatic symptoms, the most typical of them include feelings of nervousness, rapid breathing or struggling to breathe, pain in the chest, sweating, hand tremor, trembling, muscular tension, sweating, tachycardia, light-headedness, feelings of unreality (depersonalisation or derealisation), blushing, nausea and choking sensations (American Psychiatric Association, 2013).

1.6.1.3 Risk factors for the development of anxiety

Anxiety is more common among females (63%) compared to males (Ritchie and Roser, 2019; WHO, 2017). Genetic predisposition, childhood trauma and environmental factors play a role in the development of anxiety (Dabkowska and Dabkowska-Mika, 2015; Hettema, Neale and Kendler, 2001). People with disabilities, with physical illness, who are smokers, who are from lower socioeconomic groups and young offenders are also predisposed to anxiety (Department of Health, 2011b). A recent systematic review and meta-analysis concluded that anxiety and depression are not merely highly comorbid but are the risk factors for each other, with anxiety predisposing more to depression than depression to anxiety (Jacobson and Newman, 2017).

1.6.2 Depression

1.6.2.1 Epidemiology of depression

Depression affects around 300 to 350 million (4.4%) people globally and is the leading cause of disability worldwide relating to YLD (WHO, 2017). It is estimated that in two decades, depression will be the primary source of disease burden globally (WHO, 2012). The prevalence rates of depressive disorders vary by age with a peak in the older populations (WHO, 2017). Depression affects 4.5% of the UK population and accounts for 454 789 YLD (WHO, 2017) contributing to the vast economic productivity loss (Trautmann, Rehm and Wittchen, 2016; Bloom et al., 2012).

1.6.2.2 Diagnosis and symptoms of depression

Depression (depressive disorders) include disruptive mood dysregulation disorder, major depressive disorder (including major depressive episode), persistent depressive disorder (dysthymia), premenstrual dysphoric disorder, substance/medication-induced depressive disorder, depressive disorder due to another medical condition, other specified depressive disorder, and unspecified depressive disorder (American Psychiatric Association, 2013).

The most commonly reported symptoms of depression are decreased energy levels, considerable tiredness, sadness, low mood, loss of interest and ability to enjoy, disrupted sleep, loss of interest in sex, lessened self-esteem and self-confidence, feeling of guilt/worthlessness (American Psychiatric Association, 2013). These symptoms are persistent and often interfere with normal functioning and capacity of the person and, in some severe cases, they could lead to suicidal thoughts and acts (American Psychiatric Association, 2013). Besides the presence of those symptoms, depression frequently has negative impacts on QOL, social, family, sexual and professional life of sufferers (Holubova et al., 2016; González-Blanch et al., 2018).

Depression severity is categorised into mild, moderate or severe. Patients with mild and moderate depression, despite considerable suffering, are capable of continuing with normal functions, whereas severe depression has marked, persistent (at least six months) and distressing symptoms of low self-esteem, guilt, and worthlessness with somatic symptoms and potentially suicidal thoughts and acts (WHO, 2004).

1.6.2.3 Risk factors for the development of depression

Genetic and environmental factors play a role in the development of depression (Sullivan, Neale and Kendler, 2000). The prevalence of depression among females is higher (5.1%) than in males (3.6%) (WHO, 2017). The risk of developing depression is increased by several factors including female gender, low socioeconomic status, unemployment, low social support, several traumatic life events, somatic illness and substance misuse, childhood adversities, family history of depression, pregnancy (WHO, 2017; Kessler et al., 2010; Bennett et al., 2004). A systematic review and meta-analysis (n=20,678 participants at follow-up) concluded that female gender, disability, bereavement, disturbance in sleep, and previous depression are the risk factors for developing depression in older populations (Cole and Dendukuri, 2003). Whereas for adolescents, according to longitudinal data (n=1322), the risk factors are female gender, increases in smoking and decreases in social support (Galambos, Leadbeater and Barker, 2004).

Depression and anxiety have a great financial impact on society and individuals (McCrone et al., 2008). However, the WHO survey (n=51,547 participants) from 21 countries highlighted that fewer than half of those who suffer from major depression receive effective treatment (Thornicroft et al., 2017).

1.6.3 Coping

To deal with anxiety and depression, people develop coping mechanisms — thoughts and behaviours employed to deal with stressful situations, called coping (Folkman and Moskowitz, 2004). There are several ways to classify coping strategies described by different authors depending on the methods of assessment (Riera-López de Aguileta et al.). The most frequently used categories are: emotion-oriented, task-oriented, and avoidance-oriented coping (Endler and Parker, 1990). Lazarus and Folkman (1984) distinguished two types of coping: coping directed at managing or changing the problem that is the source of the distress called problem-focused, and coping directed at managing the emotional response to the problem known as emotion-focused (Lazarus and Folkman, 1984). However, Skinner et al. (2003) highlighted the importance of distinguishing healthy coping from harmful coping and considered the following typologies of coping: adaptive against maladaptive, or healthy against unhealthy, or constructive against harmful, or challenge against the threat (Skinner et al., 2003).

1.7 Quality of life in IBD

In addition to the presence of physical and psychological symptoms, IBD often has substantial negative impacts on the person's quality of life (QoL), physical, social, educational, occupational, and other functioning (Gay et al., 2011). Evidence from a series of systematic reviews and meta-analyses highlighted that people suffering from IBD have poorer QOL compared to healthy people (Knowles et al., 2018a) and QoL is poorer during disease relapses and possibly is poorer for individuals with CD compared to UC (Knowles et al., 2018a; Knowles et al., 2018b).

According to the World Health Organization (WHO), QOL "assesses individuals' perceptions of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns" (WHO, 1995, p. 1403). Health-related quality of life (HRQoL) is considered a subcategory of QOL (Torrance, 1987). HRQoL examines a perceived physical and mental health state of individuals and its impact on QOL (Yin et al., 2016). As stated by the constitution of the WHO, "health is a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity" (WHO, 1947, p. 13). These three terms (QOL, HRQoL and health) are often used interchangeably by the health professionals and researchers (Post, 2014). In this thesis, both terms QOL and HRQoL have been used, as studies discussed here used them both and both are applicable to the experience of living with IBD.

1.8 Cost of IBD

IBD is costly, this is a chronic condition with an early onset which requires lifelong treatment, including medication, hospitalisation and surgery, leading to substantial direct medical cost (Petryszyn and Witczak, 2016). However, these account for only part of the healthcare costs on a societal level, namely reduced productivity in the workplace, sickness absence rates, decreased employment and possibly retiring before the pension age due to a disability, resulting in high indirect cost (Petryszyn and Witczak, 2016).

Although the costs of IBD are vast, at both the individual and societal levels, there are significant challenges in the assessment, monitoring and treatment of IBD patients (M'Koma, 2013). Even in developed countries, there is a considerable socio-economic impact of IBD, about a fifth of individuals affected by IBD in Europe are accessing their disability pension, up to a quarter have problems with employment, and about half go on sick leave (Burisch et al., 2013a).

IBD patients themselves sustain large out-of-pocket costs (Sin et al., 2015; Park, Bhattacharya and Park, 2014; Campbell et al., 2017). In the UK, 33% of patients aged 40 and above with long-term chronic conditions, including IBD, do not collect medications due to the cost of charged prescriptions (Crohn's and Colitis UK, 2018b). This factor contributes to medication non-adherence and, as a consequence, lower QoL, reduced functional abilities, increased use of medical resources such as hospitalisation risk, increased health services use and spending on health care (Crohn's and Colitis UK, 2018b). York Health Economics Consortium (YHEC) has found that over £200 million might be saved over the next decade if the prescription charges for IBD patients were to be cancelled (YHEC, 2018). Therefore, this study recommended looking for other possible options of care and optimal treatment strategies to reduce IBD healthcare costs.

1.9 Diagnosis of IBD

Diagnosis of IBD is established on clinical examination and diagnostic tests (endoscopy, colonoscopy, histological criteria, radiology, and MRI type imaging and laboratory analysis) (Plevy et al., 2013; Gee and Harisinghani, 2011). The gold standard for diagnosing IBD is ileocolonoscopy with biopsy and histological analysis of the tissue (Passos, Chaves and Chaves-Junior, 2018).

As an additional diagnostic instrument, the disease activity could be tested with widely used non-invasive inflammatory biomarkers (Tontini et al., 2015). However, they could not be used to forecast the course of the disease, differentiate IBD subtypes or response to treatment. C-reactive protein (CRP), faecal calprotectin (FC), stool lactoferrin (SL), ferritin, platelets ESR, albumin and fibrinogen, are universally used markers (Tontini et al., 2015; Rokkas, Portincasa and Koutroubakis, 2018; Mosli et al., 2015).

Late diagnosis dramatically increases the risk of disease complications and surgical procedures for IBD patients (Lee et al., 2017). Increased awareness about IBD is likely to translate into more patient self-referrals to primary care and earlier diagnosis of IBD by health professionals (Angelberger et al., 2009).

1.9.1 Current approaches to IBD treatment

The World Health Organisation (WHO) has recommended the integrated model of patient care as the current best practice and provided a process-based definition of health care integration: “Integration is a coherent set of methods and models on the funding, administrative, organisational, service delivery and clinical levels designed to create connectivity, alignment and collaboration within and between the cure and care sectors. The goal of these methods and models is to enhance the quality of care and quality of life, consumer satisfaction and system efficiency for people by cutting across multiple services, providers and settings. Where the result of such multi-pronged efforts to promote integration leads to benefits for people, the outcome can be called integrated care” (WHO, 2016, p. 3; Kodner and Spreeuwenberg, 2002).

Holistic care is a part of integrated care and is described as a model of care that considers and treats the person as a whole: mind, body, and spirit, considers a person's environmental circumstances and encourages the patient's participation in the treatment process (Zamanzadeh et al., 2015; Papadimitriou, 2017). A recent systematic review (n=50 papers, of them: 5 qualitative studies, 40 theoretical articles, 4 book chapters and 1 thesis) found that three, often interchangeably used but not synonymous terms, "whole person", “biopsychosocial” and “holistic care” stress the importance of a complex integrated care approach (Thomas et al., 2018). Nevertheless, the holistic care term has a broader meaning than the biopsychosocial care (Thomas et al., 2018). An interaction between psychological (stress, thoughts, emotions, behaviours), biological (genes) and social (family relationships, social support, cultural impact) factors influence health and disease (Wade and Halligan, 2017). They underlie the principles of a biopsychosocial model (Papadimitriou, 2017) which often has been applied to understand gastrointestinal diseases, IBD in particular, because of the bidirectional link between the brain and gut through the gut-brain-microbiota axis (Grover, Herfarth and Drossman, 2009; Long and Drossman, 2010). Thus, IBD treatment approaches should be based on the consideration of the biopsychosocial model (Rakovec-Felser, 2011; Lee et al., 2018; Casati and Toner, 2000; Mikocka-Walus et al., 2012b). However, to date the biomedical approach to IBD treatment is still used at times instead of the biopsychosocial, as current treatment models in IBD do not involve regular allied health input or psychological care (Mikocka-Walus et al., 2014), with the accessibility of psychological help for IBD patients limited (Bennebroek Evertsz et al., 2012).

The concept of QOL is increasingly being recognised for its importance within IBD, consequently achieving remission, maintaining remission, and improving HRQoL are becoming key goals of IBD treatment (Orlando et al., 2013; Dubinsky, 2017).

The treatment approach to IBD has recently focused not only on managing flares (Orlando et al., 2013; Dubinsky, 2017; Loftus, 2011; Kemp et al., 2018) but on early intervention and preventing permanent damage to the bowel structure (Pariente et al., 2011). An early IBD treatment is vital in the prevention of this damage (Peyrin-Biroulet et al., 2010).

IBD treatment consists of long ongoing pharmacological (drug) therapy, surgical treatment, dietary, and psychological support (psychotherapy) (Wilhelm and Love, 2017; RCP, 2014; Kaenkumchorn and Kesavan, 2019; Green et al., 2019). Many patients become unresponsive to drug therapy, which is the fundamental therapy in IBD and require surgery (Wilhelm and Love, 2017). Establishing the IBD subtype is essential for the choice of treatment tactics, especially when choosing a surgical intervention (Mills and Stamos, 2007).

1.9.1.1 Specialist care

Despite an increase in the number of IBD nurses in the UK, according to the UK IBD audit, only 4 in 10 services met the required number of IBD nurses to deliver the appropriate level of care and approximately 1 in 10 services did not have IBD nurses in the care team (RCP, 2014). IBD nurses work overtime and struggle meeting service requirements (Crohn's and Colitis UK, 2018a).

Almost a quarter of IBD services have no provision of a dietitian (RCP, 2014). Some IBD service providers also do not have routing support or comprehensive pathways to other services, for example to, pharmacology (just under three quarters have a referral) or rheumatology (over quarter patients have a referral) (RCP, 2014). Nevertheless, over 90% of services had some multidisciplinary team of the clinician involved in managing complicated cases of IBD (RCP, 2014). However, only 40% of them were formalised with regular meetings (RCP, 2014). Patients with a relapse of IBD were not able to be seen within the required time (5 days) (RCP, 2014). Only around half of the providers had a clear transition from paediatric to adult clinics, and even fewer of them had an explicit transition policy (RCP, 2014).

1.9.2 Pharmacological treatment

The pharmacotherapy selection depends on the localisation of inflammation, the course of the disease, complications, side effects and other factors (Kemp et al., 2018). Predominantly, treatment is directed at the reduction of inflammation or to manage infection (abscesses, fistulas, post-surgery) (Nitzan et al., 2016; Matsuoka et al., 2018). There are five main classes of drugs used for the treatment of IBD: Aminosalicylates, Corticosteroids, Immunosuppressants, Biological therapies and Antibiotics (Matsuoka et al., 2018). Recently, there is an increased interest in antidepressants in the treatment of comorbid psychological disorders as well as IBD itself, which have a possible positive effect on disease course (Hall et al., 2018; Daghaghzadeh et al., 2015; Macer, Prady and Mikocka-Walus, 2017).

1.9.3 Psychological treatment in IBD

While a significant proportion of IBD patients suffer from depression and/or anxiety, (Byrne et al., 2017), the standard IBD care in the UK does not include screening for anxiety and depression. This is important as these mental disorders are associated with the clinical recurrence of IBD (Mikocka-Walus et al., 2016c). Only 53% of services could refer IBD patients for psychological support when needed, and only 12% of services could refer them to a psychologist or counsellor with particular IBD knowledge (RCP, 2014).

Presently, psychological care in IBD includes psychotherapeutic (psychotherapies) and psychopharmacological (central neuromodulators which include antipsychotics, antidepressants, and other central nervous system−targeted medications) treatments (Van Assche et al., 2013; Van Assche et al., 2010; Drossman et al., 2018).

As part of pharmacological treatment, antidepressants have been used effectively for some gastroenterological diseases (Ford et al., 2014; Xiong et al., 2018) and used as adjuvant therapy in IBD (Mikocka-Walus et al., 2007b), with positive outcomes (Macer et al., 2017). A systematic review also suggested that gastrointestinal symptoms, disease activity, anxiety and depression in IBD could be reduced using psychotherapy and antidepressants (Tarricone et al., 2017). Furthermore, IBD patients appear to have a positive attitude toward antidepressants (Mikocka-Walus et al., 2012a) and express desire to have access to psychological support (Fourie, Jackson and Aveyard, 2018). Moreover, certain groups of antidepressants are protective against the development of IBD, as concluded in a retrospective cohort study of 6 million patients followed over an average of 6.7 years (Gracie and Ford, 2019). However, a systematic review and meta-analysis (n=188 participants) concluded that the efficacy and safety of antidepressants in IBD are unclear and needs further investigation (Mikocka-Walus et al., 2019).

Psychological therapies (also referred to as psychotherapy or talk therapy or talking therapy) have different mechanisms of action depending on its type and can improve coping, help dealing with the trauma, bereavement, somatic illness and some mental disorders and as a result improve well-being (American Psychiatric Association, 2019; Zimbardo, 1995). Psychotherapy can be used in combination with medication or on its own (American Psychiatric Association, 2019). Psychotherapy is used in individual, family, couple or group format for people of various ages, including children (American Psychiatric Association, 2019). The length and duration of sessions vary, from weeks to months or years, but is determined by agreement between the patient and therapist and the type of psychotherapy. Usually, sessions take place once a week between 30 and 50 minutes and between 12 to 16 sessions to achieve considerable clinical improvement (American Psychiatric Association, 2019). The typical duration of the most commonly used psychotherapies, such as CBTs being between 2 and 4 months of one per week session (Beck and Beck, 2011).

There are several different types of psychotherapies with some appearing more effective than others for specific problems or disorders (American Psychiatric Association, 2019). According to NICE (2011), evidence-based psychological interventions for the treatment of mental disorders are: Cognitive Behaviour Therapy (CBT), Interpersonal Psychotherapy (IPT), Narrative therapy, Family therapy and family-based interventions, Mindfulness-Based Cognitive Therapy (MBCT), Acceptance and Commitment Therapy (ACT), Solution-Focused Brief Therapy (SFBT), Dialectical Behaviour Therapy (DBT), Schema-focused therapy, Psychodynamic psychotherapy, Emotion-focused therapy, Hypnotherapy, Self-help, and Psychoeducation (Australian Psychological Society, 2010; NICE, 2011). The trained mental health care professionals, such as psychiatrists, mental health nurses and psychologists can deliver these therapies (Zimbardo, 1995).

CBT is a therapy directed towards changing dysfunctional (unhelpful or inaccurate) thoughts or behaviours (Beck and Beck, 2011). Results of a systematic review and meta-analysis, highlight that CBT is very effective in treating social anxiety (Powers, Sigmarsson and Emmelkamp, 2008; Mayo-Wilson et al., 2014) and reduces symptoms of generalised anxiety disorder and depression (Tyrer et al., 2014). Moreover, psychotherapies, particularly CBT, seem to be effective in the short-term for treating depression and QOL in IBD (Gracie et al., 2017). Considering that CBT is the most studied psychotherapy to date and shown to be more effective in treating depression and anxiety and in improving these symptoms and QOL in IBD patients compared to the other psychological interventions, this thesis focused on CBT but looked for the evidence of the effectiveness of psychotherapy in general.

A qualitative study on patients' views about psychotherapy in IBD conducted in Australia concluded that psychotherapy in patients with IBD with mental health problems is underutilised, even though patients have good access to psychological services in this country (Mikocka-Walus, 2013). The author suggested this could be due to the lack of direct referral pathways between gastroenterologists and mental health providers and lack of in-house psychology services within gastroenterology clinics (Mikocka-Walus, 2013). There is an inadequate level of psychological support for patients with IBD, particularly from psychologists specialising in IBD (NICE, 2014). Thus, the implementation of the integrated care model could improve the provision of psychological services for IBD patients.

Psychological therapies can be delivered through different modes, in-person, telephone-assisted, or online assisted (Mozer, Franklin and Rose, 2008; Backhaus et al., 2012; Jackson, 2016; Beck and Beck, 2011).

1.9.4 Online psychological interventions (PI) in mental and physical health

In recent years, the use of online interventions in health has increased rapidly, including mental health applications (e-therapy, computerised CBT (cCBT), internet CBT, virtual reality-based interventions) (Hill et al., 2017; Maples-Keller et al., 2017; Fodor et al., 2018). Implementation of the digital tools into healthcare is a response to high demand for services and to provide cost-effective interventions that are accessible and flexible (Hollis et al., 2015). Online interventions include a self-management/self-directed component, involving activities that patients use themselves without guidance from clinicians (Grady and Gough, 2014) to empower them to manage their own disease (Hollis et al., 2015).

Online interventions are widely implemented in the US and Australia due to the size of the countries and distances that need to be overcome by some patients to access the services (Hill et al., 2017). The UK falls behind despite recent government projects directed on the promotion of online interventions in mental health (Hunt, Koteyko and Gunter, 2015a; Department of Health, 2011a; Department of Health, 2017). Implementation of online interventions in mental health is essential in the UK where the demand for mental health services is higher than the National Health Service (NHS) can provide (Hill et al., 2017). There is an urgent need to find novel approaches in the provision of value for money services (Hill et al., 2017).

Online PIs are accessible and cost-effective (Hill et al., 2017). There is good evidence that psychotherapy delivered online (therapist-assisted) is effective in the treatment of anxiety/depression (Andersson et al., 2014; Beiwinkel et al., 2017; Johansson et al., 2019) and considered to have the same cost-effectiveness as treatment as usual for depression in primary care settings (Holst et al., 2018). However, there is modest use of online interventions for depression in primary care according to an online survey (n=1044) (Breedvelt et al., 2019). Over 90% of responders (general practitioners (GPs)) in this study were unaware about recent online interventions for mental health or did not have any training on how to implement them in primary care (Breedvelt et al., 2019). Introducing training about the online interventions into a clinical curriculum could ease the decision on the choice and recommendation of the intervention and improve the effectiveness of the intervention delivery (Breedvelt et al., 2019).

Online psychotherapy offers a new, accessible mode of delivery and may be a solution to the lack of psychotherapeutic resources in gastroenterological services (Mikocka-Walus, 2013).

1.9.5 Rationale: Previous research, gaps in the literature and future direction

Psychotherapies are effective in the management of mild to moderate levels of anxiety and depression in patients with long-term physical conditions, as suggested in a recent systematic review (Thabrew et al., 2018). To date, studies have mainly focused on the efficacy of psychotherapy in unselected patients with IBD (i.e. anyone with IBD), but a recent trial showed that cognitive behavioural therapy (CBT) could significantly improve QOL in specific groups of participants: who have poor mental health, have been recently diagnosed, are young and have high baseline IBD activity (Mikocka-Walus et al., 2015). A recent systematic review and meta-analysis demonstrated only a short-term beneficial effect of psychological interventions, CBT in particular, on depression scores and quality of life and no beneficial effect on disease activity or other mental health outcomes in unselected patients with IBD (Gracie et al., 2017). However, the authors recommended further investigation of the efficacy of these interventions in specific subgroups of patients with IBD. PIs are possibly beneficial for subgroups of these patients including patients with IBD with comorbid psychological distress (Gracie et al., 2017), where PIs could be effective for the management of anxiety and/or depression in this population in addition to the influence on IBD through the gut-brain-microbiota axis. Furthermore, psychological interventions are effective in managing other gastrointestinal conditions such as irritable bowel syndrome (IBS) (Ford et al., 2014; Lackner et al., 2018). Given that the link between brain and gut in patients with IBD via the gut-brain axis is comparable to patients with IBS (Gracie et al., 2018); psychological interventions are also promising in IBD. However, to date, there is no online psychological intervention available for patients with IBD in the UK, and there is no study assessing this population's views on online psychological interventions for patients with IBD and comorbid anxiety and/or depression. Thus, the focus of this thesis is the population of patients with IBD and comorbid anxiety and/or depression.

1.9.6 Aims

1.9.6.1 Overall project aim

This PhD project's aim was to develop a prototype of an online psychological intervention for patients with IBD and comorbid anxiety and/or depression applicable to the UK environment.

The Medical Research Council (MRC) framework for complex interventions (Figure 2) was used as a guide for the development phase of the current online PI intervention (Craig et al., 2013).

The MRC framework recommends identifying an evidence base, developing theory and modelling process and outcomes during the development phase prior to the feasibility or piloting stages (Craig et al., 2013).

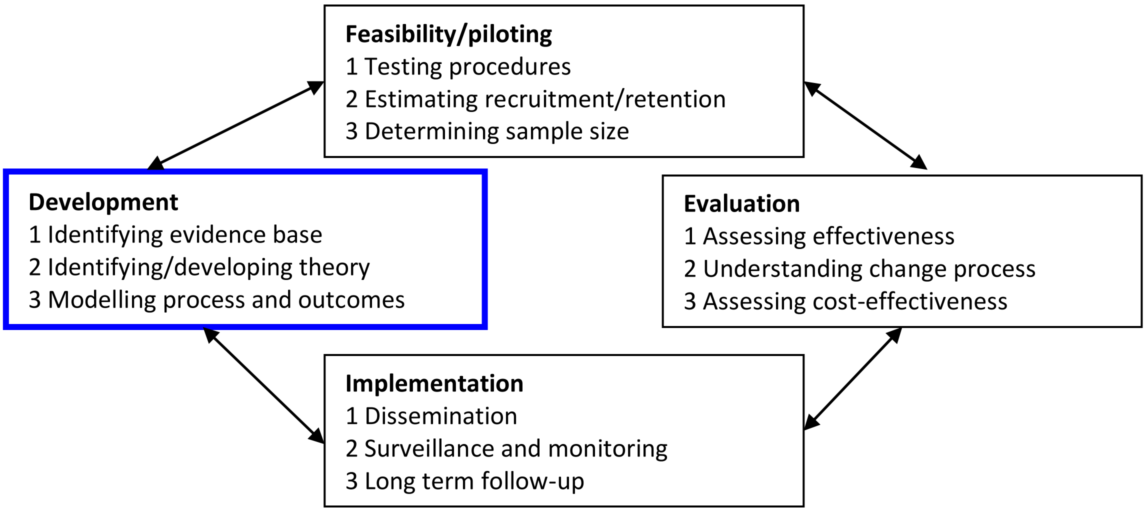


Figure 2 MRC framework of complex interventions (Craig et al., 2013).

Medical Research Council (MRC) framework corresponds with Pagliari's framework (Figure 3). Some of the elements of the concept evaluation and the prototype stage of Pagliari's framework were also considered during the development of the current online psychological intervention.

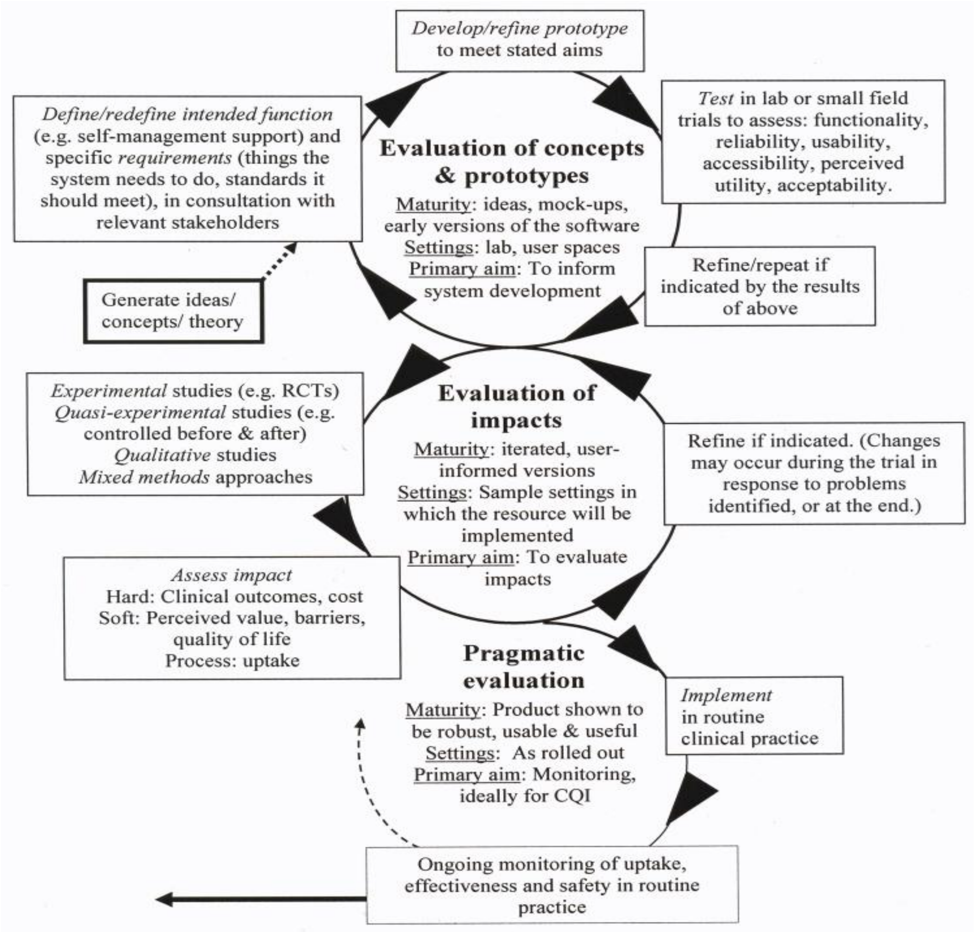


Figure 3 An idealised framework for evaluating emergent e-Health resources at different stages of development and implementation (Pagliari, 2007).

The specific aims and sections of the thesis presented below reflect the MRC framework informing the present work.

1.9.6.2 Specific aims

To achieve the overall aim, the project has three specific aims:

1. To gather theoretical evidence on the effectiveness of the online psychological therapy in gastrointestinal diseases.
2. To investigate patients' with IBD and comorbid anxiety and/or depression and their service providers' views about the lived experiences with IBD.
3. To investigate participants' views about online psychological intervention and provide the recommendation for the online psychological intervention for patients with IBD and comorbid anxiety and/or depression.

1.9.7 Thesis sections

To address the study aims, informed by the MRC framework, the dissertation has the following chapters:

1) Chapter 1 provides an overview of the literature on current IBD aetiology, epidemiology and treatment concepts to clarify previous research in the field and identify gaps in the literature;

2) Chapter 2 presents a systematic review and meta-analysis to demonstrate how online psychological interventions affect mental and physical outcomes in gastrointestinal diseases. Since little data on the effectiveness of online psychological interventions for IBD only were available, a broader gastrointestinal context was used.

3) Chapter 3 supports the theoretical evidence discussed in Chapter 2 by reporting on a primary qualitative exploratory study to investigate patients' and health professionals' views about the lived experience of patients with IBD and comorbid anxiety and/or depression;

4) Chapter 4 presented the main qualitative data on online psychological interventions for IBD. Chapter 4 also presents the modelling prototype of the online psychological intervention for patients with IBD and comorbid anxiety and/or depression based on evidence gathered throughout the whole PhD project;

5) Chapter 5 summarises the work accomplished during this project, its outcomes and limitations and discusses its implications for future research, practice and policy.

2 Chapter 2: Systematic review: Do online psychological interventions improve mental and physical outcomes in gastrointestinal disorders, including irritable bowel syndrome and inflammatory bowel disease?

This chapter intends to provide a detailed background to understanding the role of psychological therapy in gastrointestinal conditions. There was little data available on the online psychological intervention in IBD only. Therefore, taking into account a similar mechanism of bidirectional communication between brain and gut through brain-gut-biota axis (Gracie et al., 2018), it was decided to investigate the effectiveness of the online PI from the general GI diseases context.

2.1 Introduction

GI diseases affect any part of the digestive tract, the liver, biliary tract, and the pancreas (Martin, 2016). International Statistical Classification of Diseases and Related Health Problems (10th revision) classifies the diseases of the digestive system as diseases of oral cavity; salivary glands and jaws, diseases of oesophagus; stomach and duodenum; hernia; diseases of appendix; noninfective enteritis and colitis; other diseases of intestines; diseases of liver; disorders of gallbladder; biliary tract and pancreas; diseases of peritoneum; other diseases of the digestive system (World Health Organization, 2006). For this systematic review, the terms gastrointestinal diseases or gastrointestinal disorders will predominantly be used and will refer only to the chronic organic and functional diseases of the gastrointestinal tract, excluding neoplasm, acute and infectious diseases.

Diseases of the gastrointestinal tract, liver, and pancreas are a significant social, healthcare and financial burden for the society (Peery et al., 2015; Peery et al., 2012; Russo et al., 2004; Pinho et al., 2015; Guarner et al., 2008; NIH, 2017). The prevalence of depression and anxiety has been found to be high in patients with GI disorders at over 30% (Kabra and Nadkarni, 2013; Zhang et al., 2016), but this has been found to vary amongst different GI diseases between around 10 - 40% (Xiao-Jing et al., 2012; Tribbick et al., 2015; Mikocka-Walus et al., 2007a; Fuller-Thomson and Sulman, 2006; Goodwin and Stein, 2002; Mussell et al., 2008; Walker et al., 1992). It has been estimated that during disease relapses the rate of symptoms of anxiety and depression can be as high as 80% (Whitehead, Palsson and Jones, 2002; Nahon et al., 2012). Despite the high prevalence, psychological symptoms accompanying GI conditions often remain undiagnosed (Xiao-Jing et al., 2012; Bennebroek Evertsz et al., 2012). Studies show that certain stressful life events can worsen the symptoms of digestive system disorders, such as peptic ulcer, functional GI disorders (FGiDs), IBD and gastro-oesophageal reflux disease (Mayer, 2000; Drossman et al., 1990; Blanchard et al., 2008; Folks and Kinney, 1992). At the same time, the aggravation of the symptoms of the GI disease can be attributed to the worsening of co-morbid psychological disorders (Graff, Walker and Bernstein, 2009; Mu, Yang and Zhu, 2016; Mikocka-Walus et al., 2007a). An internet survey (n = 1,181) showed that the majority of patients with IBD were stressed and reported symptoms of depression and over half of the patients admitted that their social life was affected by the disease (Viazis, 2013). Another cross-sectional study (n = 136) showed that relapsing IBD patients with higher levels of stress had lower HRQoL than IBD patients without high perceived stress (Tabibian, 2013). The study also documented an association between higher levels of stress and lower adherence to medication and work productivity. A higher rate of absence from school or work, lower HRQoL, and high healthcare costs were also noted in the population suffering from functional gastrointestinal disorders (FGiDs) (Drossman et al., 1993).

Evidence suggests that the management of GI disease can be achieved by decreasing stress with support from psychological interventions (Tabibian, 2013; Roditi and Robinson, 2011), which in turn improves HRQoL and medication adherence.

Psychological interventions (psychotherapy) have been used with good effects in chronic diseases (McCombie et al., 2015; Bennett et al., 2015; Kew et al., 2016; Klainin-Yobas et al., 2016) and they have shown promising results in patients with GI diseases (Lackner et al., 2004; Rutten et al., 2013; Knowles, Monshat and Castle, 2013; Goodhand, Wahed and Rampton, 2009; McCombie, Mulder and Gearry, 2013; von Wietersheim and Kessler, 2006; Zijdenbos, 2009; Ford et al., 2014; Timmer et al., 2011). The use of psychotherapy is limited for GI conditions, and one of the reasons suggested for this are the limited resources available in these populations (Mikocka-Walus et al., 2013; Bennebroek Evertsz et al., 2012).

To overcome this barrier and to increase the accessibility of the psychotherapies, distant or remote self-management directed at the psychological aspects of the disease has been the focus of research over recent years. Self-treatment, self-management or self-help supported by a clinician or another health professional (i.e. guided self-help) have been found useful in treatment of phobias, panic disorder, anxiety, obsessive-compulsive disorder and subclinical levels of depression (Newman et al., 2011) and have better outcomes and higher completion rates compared to non-assisted, pure self-help (Ghosh, Marks and Carr, 1988; Klein, Richards and Austin, 2006).

A systematic review shows that most self-management programmes, including self-management interventions to reduce anxiety or depression, have beneficial effects on HRQoL in patients with IBD (Tu, 2015). Self-management interventions can be delivered with the assistance of printed materials, such as manuals, guides, and books. In two recent studies, patients with FGiDs and Crohn's disease found cognitive behavioural self-help workbooks helpful, which was demonstrated in the improvement of HRQoL, visceral sensitivity, GI symptom severity, and the reduction in the use of the medical services (Hunt, 2014; Hunt et al., 2015b).

In recent years the communication between patients and clinicians increasingly occur via electronic devices, which help to provide distant clinical health care, a phenomenon called telemedicine (Marks, Shaw and Parkin, 1998). Some authors use the term telemedicine, telehealth, e-health, internet-based, computerised, online interchangeably, and others think that e-health is a broad term including all others (Kabene, 2010). In the European Union, the term e-health is widely accepted and has been defined as "[…] the application of information and communications technologies (ICT) across the whole range of functions that affect healthcare, from diagnosis to follow-up" (Silber, 2003, p. 7). The term online refers to the use of a computer or other electronic devices connected to the Internet, such as a smartphone, iPad or tablet, but internet-based, internet-delivered, e-health, and computerised terms are often used as synonyms.

In general, there is a controversy on the effectiveness of online CBT to manage mental disorders, with the two recent systematic reviews presenting contradictory findings (Hedman, Ljotsson and Lindefors, 2012; Kaltenthaler, 2002). In the first systematic review, the quality of the included studies varied from poor to moderate and included studies up to 2001 (Kaltenthaler, 2002). In the systematic review by Hedman et al., (2012) studies up to 2012 were included, with higher quality studies and a greater number of included studies. This systematic review has not formally pooled studies into a meta-analysis or done a between-group analysis, a within-group analysis, which they provided is not an optimal approach, and the valid conclusion cannot be drawn based on this (Bland and Altman, 2011). A subsequent large trial (n=691), which compared two types of computerised CBT with usual general practitioner (GP) care, showed that online CBT does not significantly improve depression outcomes (Gilbody et al., 2015). However, a subsequent trial by the same team found that the addition of telephone support can enhance the short-term effectiveness of online CBT in depression and other psychological symptoms (Brabyn et al., 2016).

In the last few years, several studies have been conducted on the effectiveness of ICBT in physical illness (Sharp, Holly and Broomfield, 2013; McCombie et al., 2015). A systematic review demonstrated that online self-help interventions could decrease distress and improve the management of chronic diseases (Beatty, 2013). A more recent systematic review shows only a moderate effect of online CBT in the treatment of psychological distress in patients with physical illness (McCombie et al., 2015). This evidence led to the conclusion that more robust and well-performed RCTs are needed to conclude on the effectiveness of online psychological interventions in chronic diseases.

The use of e-health in gastroenterology is increasing due to the rising demand, limited healthcare resources (Knowles and Mikocka-Walus, 2014) and its cost-effectiveness (Jackson et al., 2016; Hedman et al., 2012). This mode of intervention delivery is also well received by patients (Con et al., 2016; Tonkin-Crine, 2013). A cross-sectional (n=102) survey of IBD patients shows that they prefer to take part in online rather than face-to-face (F2F) interventions (McCombie, Gearry and Mulder, 2014), though the generalisability of this study is questionable, as it included populations recruited from outpatient clinics only. Despite all these advantages, online interventions are associated with high attrition rates (Jackson et al., 2016) and thus blended designs such as therapist-assisted therapies have been proposed to improve the retention of participants (Mikocka-Walus et al., 2016a).

In summary, a systematic review by Knowles and Mikocka-Walus (2014) on e-health interventions in gastroenterology shows that online disease management improves quality of life (QoL) up to one year of follow up, enhances adherence to medications, improves knowledge about the disease and reduces bowel symptoms and healthcare costs. This systematic review was the first of its kind, but despite being well-performed and discussing the strengths and limitations of the included studies, it did not use a formal critical appraisal tool. A more recent systematic review by Jackson et al. (2016) confirmed the results of the previous review by Knowles and Mikocka-Walus (2014). Both reviews searched a limited number of databases (three by Jackson et al., and three by Knowles and Mikocka-Walus), looked at the whole range of e-health interventions and included studies that did not consider psychological aspects of the disease. Jackson et al. (2016) reviewed e-health use in IBD only. Therefore, given the increasing popularity of online psychotherapies and their potential to offer accessible and cheap psychotherapy, and the lack of recent systematic reviews on online psychological interventions in gastrointestinal diseases (the last conducted by Knowles and Mikocka-Walus (2014) with searches conducted in EBSCOhost Medline, CINAHL, and PsycINFO), this systematic review was proposed. The current review was adapted from the previous reviews in a number of ways: 1) it offered a comprehensive search strategy, with a broad definition of the search terms, 2) it used a wider range of databases, 3) it applied a formal risk of bias tool for randomised controlled trials, 4) it formally pooled studies in a meta-analysis; and 5) it included studies up to February 2017.

Aims of this review:

This review aimed to establish whether online psychological interventions improve mental and physical health outcomes in gastrointestinal diseases.

2.2 Methods

PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) checklist was used for the reporting of this systematic review and meta-analyses (see Appendix 10) (Moher et al., 2009). The protocol of this systematic review was registered in PROSPERO (CRD 42016052321).

2.2.1 Inclusion and exclusion criteria

2.2.1.1 Types of studies

2.2.1.1.1 Inclusion criteria:

Randomised, quasi-randomised and non-randomised controlled trials of psychological interventions in children and adults with gastrointestinal diseases

2.2.1.1.2 Exclusion criteria:

Conference abstracts
Observational studies, including all non-controlled experimental designs
Secondary studies (e.g. reviews, guidelines, commentaries)
Studies that did not have a comparison group
Studies for which a full text was not available
Studies that were not published in English that could not be translated

2.2.1.2 Types of participants

2.2.1.2.1 Inclusion criteria

Studies referring to adult and/or paediatric populations with gastrointestinal diseases diagnosed using any well-established criteria (e.g. ROME criteria for FGiDs, Montreal classification for Crohn's disease) and where disease course is monitored using well-established scales or tests (e.g. CDAI, faecal calprotectin, colonoscopy, gastroscopy, endoscopy, sigmoidoscopy, enteroscopy, sigmoidoscopy, enteroscopy, abdominal ultrasound, esophagogastroduodenoscopy, surgery, Percutaneous Endoscopic Gastrostomy (PEG), CT enterography, barium enema, surgery; blood parameters (C-reactive protein (CRP), Haemoglobin (Hb), platelet, White Cell Count (WCC), haematocrit).

Studies examining rates of anxiety, depression, stress and coping in patients with gastrointestinal diseases (based on validated screening scales such as the Hospital Anxiety and Depression Scale (HADS), the Perceived Stress Scale (PSS) or COPE).

Studies examining health-related quality of life (based on validated screening scales such as the IBDQ or WHO-QOL).

2.2.1.2.2 Exclusion criteria

Studies examining tumour, infectious and acute diseases of the gastrointestinal tract.

2.2.1.3 Types of exposure

2.2.1.3.1 Inclusion criteria

Studies investigating all types of online psychological interventions in GI diseases patients.

No restriction on the type of medication used for gastrointestinal symptoms.

2.2.1.3.2 Exclusion criteria

Studies focusing on other psychological variables such as personality.

2.2.1.4 Types of comparator

Any comparison group (e.g. patients receiving standard care or on the waiting list, or receiving alternative therapies).

2.2.1.5 Types of outcomes

2.2.1.5.1 Inclusion criteria

Primary outcomes

The remission rate (or only mild symptoms) in patients with gastrointestinal diseases. For the FGiDs, for instance, IBS, the severity of symptoms.

Secondary outcomes

Rates of anxiety and depression and/or mean levels of anxiety and depression (symptoms or diagnosis, reported separately) co-existent with gastrointestinal diseases;

Levels of stress;

Levels of coping;

Levels of HRQoL;

Any related outcomes (e.g. reduced time off work or school, sick leave, hospitalisation (frequency and length), pain, adverse events, trial withdrawal and attrition).

2.2.1.5.2 Exclusion criteria

Studies that did not report the outcomes of interest
Studies using mood scales with no independent anxiety or depression scale/dimension
Studies with non-validated outcome measures

2.2.2 Data sources

A systematic and comprehensive literature search of the following databases was conducted:

CINAHL Plus (EBSCO),
Ovid MEDLINE(R) Epub Ahead of Print
In-Process & Other Non-Indexed Citations
Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present
EMBASE (Ovid)
Health Management Information Consortium (HMIC) (Ovid)
PsycINFO (Ovid)
British Nursing Index (BNI) (ProQuest)
Cochrane Library (Wiley) including a specialised register of the IBD/FBD Group
MEDLINE (PubMed)
WHO International Clinical Trial Registry, ClinicalTrials.gov
Reference lists of all papers included in the review on the 19th of February 2017.

The search strategy was extensive with no restrictions on publication date or language to avoid language bias and to identify all available relevant papers.

2.2.3 Search strategy

The search was developed in MEDLINE using population and intervention terms to broaden the search. To make it more precise, the terms of the mode of delivery of the intervention were used, for instance, online, e-health, and telemedicine. Then, it was adapted to the other databases. The full search strategy can be found in Appendix 1-8.

To adapt the search to the other databases, the headings from MEDLINE were replaced with alternative terms. If a substitute heading could not be found, they were searched as a term in the title and/or abstract. If the exploded heading in the other databases included some of the subheadings, which were searched as a heading in MEDLINE, then this term was not used as a separate heading in the other database to avoid repetition and vice versa. If the exploded term in Medline had more subheadings, then they were searched additionally, for example, "Color therapy/ or Crisis intervention/ or Horticultural therapy/ or Psychoanalysis/ or Sleep therapy/" headings were added into the Embase search, i.e. they were included in the exp. term ‘Psychotherapy’ in MEDLINE, but they were not included in the exp. term ‘psychotherapy’ in Embase. This was also tested with the assistance of the function "OR" and "NOT", to make sure that there were no additional articles missed. Another example of how the search was adapted is that in Embase the heading ‘patient-centred care’ did not exist, but the heading ‘patient care’ was too broad to explore. Therefore this term was used only to search in the title and/or abstract.

In some databases, the search was more difficult to adapt. For example, in PubMed the attempt to apply a similar approach as to the search in MEDLINE produced a large number of unrelated articles as there are no adjacency/proximity operators in PubMed; therefore, it was decided to search only the MeSH Major Topic field. The list of all the papers (n = 1457) in the IBD/ FGiDs Group Specialized Register (Non Medline Records) were examined and double-checked if none of the related articles was missing, using the search capabilities of PDF Reader (Ctrl + F), which is limited to the search for one key term. Then, the titles of prospective studies were extracted, and their abstracts were assessed for inclusion.

2.2.4 Study selection

All electronically identified papers were transferred to EndNote referencing software. For the ease of management of the data and sharing the data with the second reviewer, all the papers were transferred to Excel. This process required some changes to the formatting of the citation in EndNote. After the formatting was complete, it allowed identification of additional duplicates. The remaining duplicates were identified manually.

Additionally, the reference lists of included studies were searched applying the same principles and inclusion and exclusion criteria as above.

2.2.5 Data extraction and management

The systematic review was based on the recommended PRISMA statement guidelines (Moher et al., 2009). The selection process was performed independently by two reviewers to reduce the potential risk of bias. Disagreements were resolved by consensus or through discussion with a third reviewer. Extracted data included: authors, year of publication, country of origin, design, setting, participant characteristics (disease type, age, gender and disease activity status), sample size, intervention (type and duration), outcome measures, results for the main outcome measures and attrition.

2.2.6 Risk of bias assessment

The included studies were assessed for internal validity using The Cochrane Risk of Bias Tool for randomised controlled trials (Higgins et al., 2011) and ROBINS-I (a tool for assessing the risk of bias in non-randomised studies of interventions) (Sterne et al., 2016) for quasi-experimental and controlled non-randomised trials.

2.2.7 Data synthesis

2.2.7.1 Narrative synthesis

A structured narrative synthesis of the findings from the included studies was carried out to summarise, integrate and explain the findings. A systematic approach to synthesis was adopted to understand the results, regarding similarities and differences between and within the studies and develop a theory of how, why and for whom the intervention works (Centre for Reviews and Dissemination, 2008). The robustness of the evidence was assessed by considering the risk of bias, suitability of study design to the research objective, choice of outcome measure, statistical analysis, quality of reporting, and generalisability of findings (Ryan and Cochrane Consumers and Communication Review Group, 2013; Centre for Reviews and Dissemination, 2008).

2.2.7.2 Meta-analysis

The meta-analysis of the included studies (with the same type of outcome measures, similar methodologies, and homogenous samples) was performed using the random-effects model using Review Manager (RevMan-5) software. The analysis was completed according to the Cochrane Handbook statistical guidelines (Higgins and Green, 2011).

As the population in one of the studies differed in age from the rest of the sample (the sample of adolescents (Bonnert et al., 2017)), this study was not included in the meta-analysis, despite providing the same outcome measures as other studies.

If the study used more than one tool to measure the outcome of interest, the assessment by clinician rather than self-reported questionnaires were prioritised. Self-report questionnaires were used where assessment by a clinician was not available. To combine continuous data, weighted mean differences (MD) with 95% confidence intervals (CI) were used for the same validated rating scales and standardised mean differences (SMD) with 95% confidence intervals (CI) for different validated rating scales for measuring the outcomes. To combine in the meta-analysis the data often needed to be converted. If a study provided a standard error (SE) instead of standard deviation (SD), SE was converted into SD, using formula SD = SE x square root (sample size), if study provided mean and CI, SD were calculated from CI, using formula SD = square root (sample size) x (upper limit - lower limit)/3.92. If there were multiple interventions being explored then the results from all arms that received the intervention of interest were combined and treated as an intervention group, and all participants without online CBT intervention were regarded as a control group. The data from the arms receiving intervention were combined:

	Group 1 (e.g. males)	Group 2 (e.g. females)	Combined groups
Sample size	N_1	N_2	$N_1 + N_2$
Mean	M_1	M_2	$\frac{N_1M_1 + N_2M_2}{N_1 + N_2}$
SD	SD_1	SD_2	$\sqrt{\frac{(N_1 - 1)SD_1^2 + (N_2 - 1)SD_2^2 + \frac{N_1N_2}{N_1 + N_2}(M_1^2 + M_2^2 - 2M_1M_2)}{N_1 + N_2 - 1}}$

The calculated total mean and SD for the intervention group and SD for the control group presented in Table 1.

The studies were pooled together in the meta-analyses at four points of follow up: post-intervention assessment, 3-month follow-up, 6-month follow-up, and 12 and over month follow-up for each outcome measure if the data was available. Studies with an adult population were combined separately to that of the adolescent or child populations. Data from waitlist design studies were only included until the point at which the control group received the intervention as after this point they no longer retained a comparator arm meeting the inclusion criteria.

To combine a mixture of change from the baseline and raw outcome scores in the same meta-analysis, the mean difference was used as an effect measure. At the same time, if these studies used different scales to measure outcome, the meta-analysis was not performed, since a standardised mean difference would be the most appropriate measure of effect.

Study heterogeneity was assessed with Cochran's Q (chi-square) and measured with the I-squared (I^2) statistics (Bland, 2015). The Cochran's Q usually stands for the weighted sum of the squared differences between observed effects for the studies and the pooled effect estimate, each divided by the variance of the study effect. This statistic gives a chi-squared test with degrees of freedom equals a number of studies – 1. However, Cochran Q test has low power to detect the heterogeneity with a small number of studies or, on the other hand, too much power with a large number of studies included in the meta-analysis. This test gives a test of significance for heterogeneity, but it does not measure it (Higgins et al., 2003). Conversely, an index of heterogeneity I^2 does not essentially determined by the number of studies included in the meta-analysis and represents the percentage of the total variation across studies due to variation between studies rather than chance, $I^2 = 100\% \times (Q-df)/Q$ (Higgins et al., 2002; Higgins et al., 2003). Therefore, both the Cochran's Q (chi-square) and the I-squared (I^2) were used to measure the heterogeneity. The level of significance for heterogeneity was $p < 0.10$. An I-squared value of 25% was considered as low, 50% as moderate, and 75% as high heterogeneity (Higgins et al., 2003).

2.3 Results

2.3.1 Results of the search

A total 2,627 references were identified, of them: 284 were from CINAHL Plus (EBSCO), 387 Ovid MEDLINE(R), 1,206 EMBASE (Ovid), 2 HMIC (Ovid), 56 PsycINFO (Ovid), 166 British Nursing Index (BNI) (ProQuest), 91 (80 trials, 6 Cochrane SR, 1 other Reviews, 1 Technology Assessments, 2 Economic Evaluations, 1 Methods Study) Cochrane Library (Wiley), 435 PubMed, 0 from the register of the IBD and functional bowel disorders (FBD) group, WHO International Clinical Trial Registry, ClinicalTrials.gov and from reference lists of all included in the review papers.

Overall, 567 duplicates were identified, 400 with the assistance of EndNote and an additional 36 after the changes to the styles of the references in the EndNote library were made. Further, 131 duplicates were found manually during the process of screening titles and abstracts.

The majority of the retrieved papers were excluded during the stage of screening titles and abstracts based on the irrelevance of the material to the research question or duplication, retaining only possibly relevant studies. Then, the full texts of these papers were accessed and only the articles that met the inclusion criteria retained. There were 22 full-text articles assessed for eligibility, and 11 were included in the current systematic review. Figure 4 summarises the search and the retrieval process.

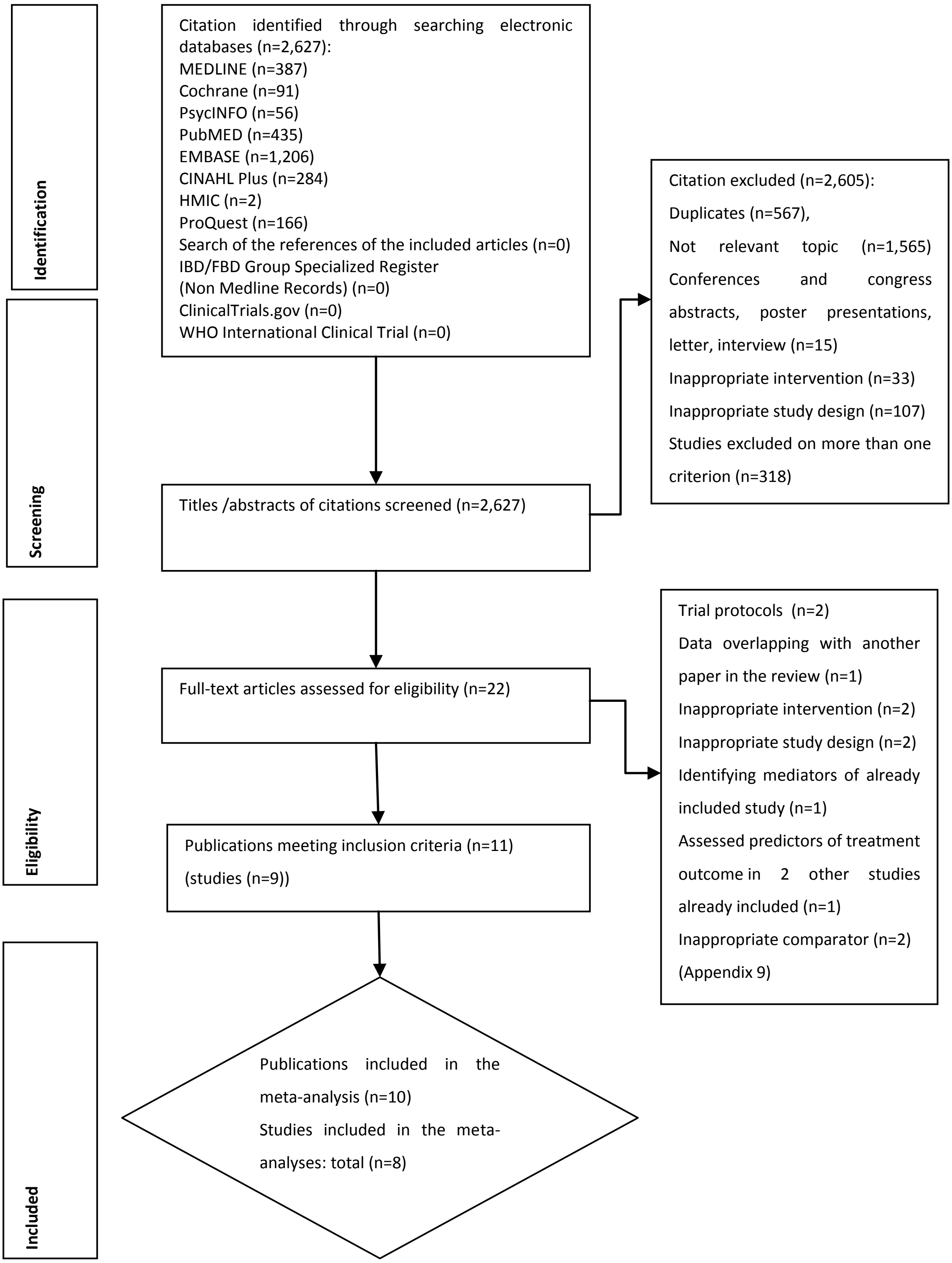


Figure 4 - PRISMA diagram for selection of studies included in the systematic review.

2.3.2 Excluded Studies

The electronic search identified 2,627 studies of which 2,605 were excluded (Figure 4). Most studies (n=1,565) were not relevant to the topic (the intervention of interest was broadly used for patients with cystic fibrosis and cancer). Other reasons for exclusion were: duplicates (n=567), conferences and congress abstracts, poster presentations, letter, interview (n=15), inappropriate intervention (II) (n=33), inappropriate study design (ISD) (n=107), studies excluded on more than one criterion (n=318). Of the twenty-two articles that full-text was accessed, eleven were excluded. The table in Appendix 9 presents these excluded studies and reasons for exclusion.

2.3.3 Included Studies

All nine of the included studies (11 articles) were randomised controlled trials (RCT) and conducted between 2009 and 2017 (Andersson et al., 2011; Bonnert et al., 2017; Ljotsson et al., 2011a; Ljotsson et al., 2011b; McCombie et al., 2016; Mikocka-Walus et al., 2015; Oerlemans et al., 2011; Mikocka-Walus et al., 2016a; Ljotsson et al., 2010; Hunt, Moshier and Milonova, 2009). One of the studies was a feasibility trial (Oerlemans et al., 2011); one was a pilot trial (Mikocka-Walus et al., 2015); and one an exploratory factorial trial (Everitt et al., 2013). The majority of included studies were conducted in Sweden (Bonnert et al., 2017; Ljotsson et al., 2011a; Ljotsson et al., 2010; Ljotsson et al., 2011b; Andersson et al., 2011), one study in Australia (Mikocka-Walus et al., 2015; Mikocka-Walus et al., 2016a) and one study was from each of the following countries: Netherlands (Oerlemans et al., 2011), New Zealand (McCombie et al., 2016), the USA (Hunt et al., 2009) and the UK (Everitt et al., 2013).

Sample sizes ranged from 54 (Hunt et al., 2009) to 199 (McCombie et al., 2016). The total sample size across these studies was 1080; this excludes data from the two studies that were associated papers of two already included studies using the same patient cohort (Andersson et al., 2011; Mikocka-Walus et al., 2016a).

With regards to the type of GI disease, eight papers (including seven studies) examined irritable bowel syndrome (IBS) (Hunt et al., 2009; Andersson et al., 2011; Bonnert et al., 2017; Everitt et al., 2013; Ljotsson et al., 2011a; Ljotsson et al., 2010; Ljotsson et al., 2011b; Oerlemans et al., 2011) and three papers (including two studies) IBD

(McCombie et al., 2016; Mikocka-Walus et al., 2015; Mikocka-Walus et al., 2016a). The follow-up time varied in the studies, the majority of studies had a just post-intervention assessment with the longest follow up being 24 months (Mikocka-Walus et al., 2016a). The characteristics of the extracted studies are presented in Table 1. Because many studies provided several outcomes and some of them were collected at a few different points of follow up, the results of the outcome measures were presented in separate tables (see Table 4 -Table 9).

Table 1 Characteristics of studies

Study ID	Country of origin and Setting	Design	Participants (diagnosis, age, gender and disease activity status)	Sample size	Interventions (type and duration)	Outcomes	Attrition	Duration of follow up	Comparison treatment, co-interventions
(Andersson et al., 2011) (Ljotsson et al., 2010)	Sweden, self-referred IBS patients from the general adult population	RCT	IBS, Rome III criteria; male/female 13/72, Age mean years (SD): total = 34.6 (9.4), Years since diagnosis mean years (SD) total = 6.3 (7.3).	Total (n= 85) IG1 (n=42) CG2 (n=43)	10-week online CBT with therapist support via e-mail	TIC-P; The GI symptom diary; GSRS-IBS; Total pain; IBS-QOL; VSI; MADRS-S; Sheehan disability scales	post-intervention: IG 9.5% (n=4) CG (n=0) 3 months: IG 9.5% (n=4)	10 weeks, 3 months for IG	wait-list with a discussion forum, after 10 weeks switched to the active intervention
(Bonnert, 2017)	Sweden, primary, secondary and tertiary care clinics	RCT	IBS, Rome III criteria; subtype: constipation 30%, diarrhoea 15%, mixed 55%. Age mean years (SD): total =15.54 (1.56); Adolescents (age 13–17 years).	Total (n=101) IG (n=47) CG (n=54)	10 weeks online CBT	GSRS-IBS; Faces; Pain frequency; PedsQL; School absence; VSI; PSS; SCAS; CSI-24; CSQ; IBS- BRQ.	post-intervention IG 6.4% (n=3); CG 5.7% (n=3); 6 months follow-up (n=5) in IG	6 months after the intervention (IG)	wait-list, after the post-intervention assessment at 10 weeks crossed over to the online CBT
(Everitt et al., 2013)	The UK, recruited via GP practices in Southampton	RCT	IBS, Rome III criteria; moderate severity of IBS Age years (16 - 60) Age mean years (SD): total = 44.39 (10.33), females = 78%. The mean length of	Total (n=135) IG (n=90) CG (n=45)	6 weeks online CBT self-management programme (Regul8) or online CBT + telephone support.	IBS SSS score; IBS-QOL; HADS; PEQ; SGA of Relief.	post-intervention IG 25% (n=7) CG 31% (n=8) 12 weeks 9%	12 weeks	standard patient information and mebeverine or methylcellulose or placebo

Study ID	Country of origin and Setting	Design	Participants (diagnosis, age, gender and disease activity status)	Sample size	Interventions (type and duration)	Outcomes	Attrition	Duration of follow up	Comparison treatment, co-interventions
			symptoms of 10.8 years (SD = 8.7).		Alongside all participants received mebeverine or methylcellulose or placebo.				
(Hunt et al., 2009)	The USA recruited via various IBS relevant websites	RCT	IBS, self-selected cohort, (44 female, 10 male). Age mean years(SD): total = 38.52 (10.91)	Total (n=54) IG (n=28) CG (n=26)	5 weeks online CBT	GSRS-IBS; ASI; IBS–QOL; CPSQ.	6 weeks post-intervention: IG 53%, (n=15) CG 31% (n=8) 3 months: IG 64 % (n=18) CG 92% (n=24)	6 weeks IG and CG; 3 months for the IG	wait-list, after post-intervention assessment at 6 weeks crossed over to online CBT.
(Ljotsson et al., 2011a)	Sweden, sample from a gastroenterological clinic, referral or self-referral	RCT	IBS, Rome III criteria, 74% females. Age mean years (SD): total = 34.9 (11.3); subtype 21% constipation, 30% diarrhoea, 49% mixed).	Total (n=61) IG (n =30) CG (n = 31)	10 weeks online CBT	GSRS-IBS; VSI	post-intervention IG 23% (n=7) CG 12.9% (n=4)	10 weeks	waiting list, after post intervention assessment at 10 weeks crossed over to online CBT.
(Ljotsson et al., 2011b)	Sweden, internet-recruited	RCT	IBS, Rome III-criteria, telephone interview	Total (n=195)	10 weeks online CBT, and online	GSRS-IBS; IBS-QOL;	post-intervention	6 months	ISM (relaxation,

Study ID	Country of origin and Setting	Design	Participants (diagnosis, age, gender and disease activity status)	Sample size	Interventions (type and duration)	Outcomes	Attrition	Duration of follow up	Comparison treatment, co-interventions
			with a psychologist skilled with IBS and reviewed by a gastroenterologist. Age mean years (SD): total = 38.9 (11.1), years with IBS (SD) 14.9 (11.2). 79% female.	IG (n=98) CG (n=97)	closed discussion forum, where the participants discuss the treatment.	VSI; PSS; HADS anxiety and depression;	IG 1%; CG 3% 6-months IG 11%, CG 15%		dietary advice, problem-solving, sleep hygiene).
(McCombie, 2016)	New Zealand, hospital gastroenterology outpatient clinic, Nelson Crohn's and Colitis Support group, private clinics, database from previous observational studies, unrelated to this RCT	RCT	IBD clinically established. Age mean years (SD): total = 38.86 (12.36) IBD CG group Crohn's disease 62 (72.1), Ulcerative colitis 20 (23.3%), IBD-unspecified 4 (4.7%).	Total (n=199) IG (n=113) CG (n=86)	8 weeks online CBT	IBDQ; HRQOL (SF); HADS anxiety and depression; SCCAI (UC and IBD-U); HBI (CD); Brief COPE; PSS-10; SFQ; EPQ.	12 weeks, IG 42.5% CG 9.3%. 6 months IG 53.1% CG 17.2%	6 months	Treatment as usual (TAU)
(Mikocka-Walus et al., 2015) (Mikocka-Walus et	Australia, Gastroenterology Clinics	RCT	IBD clinically established. Age mean years (SD): total = 49.11 (16.47); male= 54%, Years since diagnosis mean (SD):	Total (n=174) IG (n=90: F2F=22, online =68)	10 weeks CBT +CBT arm had two subgroups: F2F CBT and online CBT	HRQOL (SF) IBDQ HADS anxiety and depression; Brief COPE; RSRRS; STAI; CDAI; SCCAI	6 months: IG 43.3% (n=39); CG 22.6% (n=19) 12 months:	6 months, 12 months, 24 months	Standard care (SC)

Study ID	Country of origin and Setting	Design	Participants (diagnosis, age, gender and disease activity status)	Sample size	Interventions (type and duration)	Outcomes	Attrition	Duration of follow up	Comparison treatment, co-interventions
al., 2016a)			IG = 11.8 (10.4) CG = 11.7 (11.8) Years with IBD symptoms mean (SD): IG 16.1 (12.1); CG=14.3 (11.7)	CG (n=84).		(UC and IBD-U).	IG 53.3% (n=48); CG 23.8% (n=20) 24months: IG 66.6% (n=60) CG 46% (n=39)		
(Oerlemans, 2011)	Netherlands, GPs and through advertisements by the Dutch IBS patient association.	RCT	IBS, Rome III criteria Age mean years (SD): total = 38.31(13.89) Female 85 %	Total (n=76) IG (n=37) CG (n=39)	4 weeks online CBT	IBS-QoL; Abdominal pain; PCS; CSFBD	post-intervention IG 2.7% (n=1) CG 5.1% (n=2) 3 months IG 29% CG 7.7%	4 weeks 3 months	Standard care (SC)

Note: 1- (IG) intervention group, 2 - (CG) control group; CBT - cognitive behaviour therapy; F2F - face to face; GSRS-IBS - Gastrointestinal Symptom Rating Scale; (IBS SSS score) - Irritable Bowel Symptom Severity Scale; SCCAI (UC and IBD-U) - Simple Clinical Colitis Activity Index (ulcerative colitis); CDAI - Crohn's Disease Activity Index; (HBI) (CD) - Harvey-Bradshaw Index; HADS - Hospital Anxiety and Depression Scale; VSI - Visceral sensitivity index; (MADRS-S) - The Montgomery Åsberg Depression Rating Scale-- Self report; STAI - the State-Trait Anxiety Inventory; SCAS - Spence Childhood Anxiety Scale; ASI = Anxiety Sensitivity Index; PSS-10 - perceived stress questionnaire; RSRRS - Revised Social Readjustment Rating Scale; IBS–QOL - IBS Quality of Life Impairment; PedsQL - Paediatric Quality of Life Inventory; IBDQ - Inflammatory Bowel Disease Questionnaire; HRQOL (SF) - health-related quality of life short form; TIC-P - Trimbos and Institute of Medical Technology Assessment Cost Questionnaire for Psychiatry; CSI-24 - Children's Somatisation Inventory- parents version; CSQ - Client Satisfaction Questionnaire; PEQ - Patient Enablement Questionnaire; IBS - BRQ - behavioural responses questionnaire; SGA of Relief - Subjects Global Assessment of Relief; CPSQ - The Consequences of Physical Sensations Questionnaire; SFQ - Social Functioning Questionnaire, EPQ - Eysenck Personality Questionnaire (Brief Version) for measuring neuroticism; PCS - Pain Catastrophising Scale; CSFBD - The Cognitive Scale for Functional Bowel Disorders.

2.3.3.1 Interventions

The psychological intervention explored in all included studies was online CBT; hence, the planned analysis of the effect of each individual psychological intervention on the physical and mental outcomes was not feasible. The duration of the intervention varied, the majority of participants received a ten-week internet-delivered CBT course (Andersson et al., 2011; Ljotsson et al., 2010; Ljotsson et al., 2011b; Mikocka-Walus et al., 2015; Bonnert et al., 2017; Ljotsson et al., 2011a), though some received eight-week (McCombie et al., 2016), six-week (Everitt et al., 2013), five-week (Hunt et al., 2009) and four-week (Oerlemans et al., 2011) online therapy. Along with CBT the participants in the intervention groups received limited therapist support via e-mail or text messages (Andersson et al., 2011; Ljotsson et al., 2010; Hunt et al., 2009; Ljotsson et al., 2011a; Bonnert et al., 2017; Oerlemans et al., 2011; Ljotsson et al., 2011b; Everitt et al., 2013), and the participants in two other studies could contact a psychologist if they needed (McCombie et al., 2016; Mikocka-Walus et al., 2015; Mikocka-Walus et al., 2016a). Additionally, during the online CBT treatment, participants of some studies had access to a group online treatment discussion forum (Ljotsson et al., 2011a; Ljotsson et al., 2010). For one study (Mikocka-Walus et al., 2015) the patients in the intervention arm could choose the mode of delivery of CBT, face-to-face (n=22) or online (n=68). For this systematic review, since 75% of patients selected online delivery, we did not disaggregate the results by mode of delivery and included all those allocated to receive CBT as the intervention group.

The participants in the control group in most studies were on a wait-list (Bonnert et al., 2017; Andersson et al., 2011; Ljotsson et al., 2010; Ljotsson et al., 2011a; Hunt et al., 2009). The participants in the other studies received usual standard care (Mikocka-Walus et al., 2015; McCombie et al., 2016; Oerlemans et al., 2011; Mikocka-Walus et al., 2016a). In the study by Everitt et al., (2013) participants were randomised to the following 9 groups: groups: 1) website only CBT + Mebeverine, 2) website only CBT + Methylcellulose, 3) website only CBT + placebo, 4) website CBT + support + Mebeverine, 5) website CBT + support + Methylcellulose, 6) website CBT + support + placebo, 7) no website + Mebeverine, 8) no website + Methylcellulose, 9) no website + placebo. Therefore, for this systematic review, the control group of this study was all those participants who did not receive online CBT. In the study by Ljotsson et al., (2011b), the participants in the control group received internet-delivered stress management (ISM) intervention.

2.3.3.2 Included studies outcomes measures

The summaries of the outcome measures reported in the included studies are presented in Table 2.

Table 2 The outcome measures of the included studies

Outcomes	(Andersson et al., 2011), (Ljotsson et al., 2010)	(Bonnert, 2017)	(Everitt et al., 2013)	(Hunt et al., 2009)	(Ljotsson et al., 2011a)	(Ljotsson et al., 2011b)	(McCombie, 2016)	(Mikocka-Walus et al., 2015), (Mikocka-Walus et al., 2016a)	(Oerlemans, 2011)
GSRS-IBS	x	x		x	x	x			
IBS SSS score			x						
SCCAI (UC and IBD-U)							x	x	
CDAI								X	
HBI (CD)							X		
The GI symptom diary	x								
HADS anxiety/depression			x			x	x	x	
MADRS-S	x								
STAI								x	
SCAS		x							
PSS-10		x				x	x		
RSRRS								x	
the Brief COPE							x	x	
IBS-QOL	x		x	x	x	x			x
PedsQL		x							
IBDQ							x		
HRQOL (SF)							x	x	
TIC-P, Cost assessment	x				x				
School absence		x							
VSI	x	x			x	x			
ASI				x					
Pain frequency		x							
Abdominal pain									x
Total pain	x								
Faces Pain Scale-Revised		x							
Sheehan Disability Scales	x				x				
CSI-24		x							
CSQ		x							
IBS - BRQ		x							
PEQ			x						
SGA of Relief			x						
CPSQ				x					
SFQ							x		
PCS									x
CSFBD									x
EPQ							x		

Note: GSRS-IBS - Gastrointestinal Symptom Rating Scale; (IBS SSS score) - Irritable Bowel Symptom Severity Scale ; SCCAI (UC and IBD-U) - Simple Clinical Colitis Activity Index (ulcerative colitis); CDAI - Crohn’s Disease Activity Index; (HBI) (CD) - Harvey-Bradshaw

Index; HADS - Hospital Anxiety and Depression Scale; VSI - Visceral sensitivity index; (MADRS-S) - The Montgomery Åsberg Depression Rating Scale-- Self report; STAI - the State-Trait Anxiety Inventory; SCAS - Spence Childhood Anxiety Scale; ASI = Anxiety Sensitivity Index; PSS-10 - perceived stress questionnaire; RSRRS - Revised Social Readjustment Rating Scale; IBS–QOL - IBS Quality of Life Impairment; PedsQL - Paediatric Quality of Life Inventory; IBDQ - Inflammatory Bowel Disease Questionnaire; HRQOL (SF) - health-related quality of life short form; TIC-P - Trimbos and Institute of Medical Technology Assessment Cost Questionnaire for Psychiatry; CSI-24 - Children's Somatisation Inventory- parents version; CSQ - Client Satisfaction Questionnaire; PEQ - Patient Enablement Questionnaire; IBS - BRQ - behavioural responses questionnaire; SGA of Relief - Subjects Global Assessment of Relief; CPSQ - The Consequences of Physical Sensations Questionnaire; SFQ - Social Functioning Questionnaire; PCS - Pain Catastrophizing Scale; CSFBD - The Cognitive Scale for Functional Bowel Disorders; EPQ - Eysenck Personality Questionnaire-Brief Version for measuring neuroticism.

2.3.3.2.1 Studies reporting the IBD disease activity and the IBS severity of symptoms

Only one study reported a remission rate for IBD (Mikocka-Walus et al., 2015). All studies, except for one (Oerlemans et al., 2011), reported disease activity or severity of symptoms and used six different scales: Gastrointestinal Symptom Rating Scale-IBS (GSRS-IBS) (Andersson et al., 2011; Bonnert et al., 2017; Hunt et al., 2009; Ljotsson et al., 2011a; Ljotsson et al., 2010; Ljotsson et al., 2011b), Irritable Bowel Symptom Severity Scale (IBS SSS score) (Everitt et al., 2013), the GI symptom diary (Ljotsson et al., 2010), Simple Clinical Colitis Activity Index (SCCAI) (UC and IBD-U) (McCombie et al., 2016; Mikocka-Walus et al., 2015; Mikocka-Walus et al., 2016a), Crohn's Disease Activity Index (CDAI) (Mikocka-Walus et al., 2015; Mikocka-Walus et al., 2016a) and Harvey-Bradshaw Index (HBI) (CD) (McCombie et al., 2016). Therefore, in this systematic review, we analysed the mean score for IBD disease activity, but not the IBD remission rates as was anticipated initially.

2.3.3.2.2 Studies reporting anxiety and depression

Seven papers reported on the level of anxiety and/or depression and used various outcome measures (Bonnert et al., 2017; Ljotsson et al., 2010; Ljotsson et al., 2011b; Everitt et al., 2013; McCombie et al., 2016; Mikocka-Walus et al., 2015; Mikocka-Walus et al., 2016a). Two of these articles (the same cohort) used two different scales to assess the level of anxiety: the State-Trait Anxiety Inventory (STAI) and the Hospital Anxiety and Depression Scale (HADS) (Mikocka-Walus et al., 2015; Mikocka-Walus et al., 2016a). Five papers used the HADS score for depression and anxiety (Everitt et al., 2013; Ljotsson et al., 2011b; McCombie et al., 2016; Mikocka-Walus et al., 2015; Mikocka-Walus et al., 2016a). One study used the Montgomery–Asberg Depression Rating Scale (MADRS)-S (Ljotsson et al., 2010). One additional scale was used to assess the level of anxiety: the SCAS (Spence Childhood Anxiety Scale) (Bonnert et al., 2017).

2.3.3.2.3 Studies reporting on stress

Four studies reported the level of stress (Bonnert et al., 2017; Ljotsson et al., 2011b; McCombie et al., 2016; Mikocka-Walus et al., 2015; Mikocka-Walus et al., 2016a). Three of these studies assessed the level of stress using the Perceived Stress Scale (PSS) (Bonnert et al., 2017; Ljotsson et al., 2011b; McCombie et al., 2016) and one the Social Readjustment Rating Scale (RSRRS) (Mikocka-Walus et al., 2015; Mikocka-Walus et al., 2016a).

2.3.3.2.4 Studies reporting the levels of coping

Two studies explored levels of coping, and both used the Brief Coping Operations Preference Enquiry scale (Mikocka-Walus et al., 2015; McCombie et al., 2016; Mikocka-Walus et al., 2016a).

2.3.3.2.5 Studies reporting the levels of HRQoL

Eleven of the included articles reported on HRQoL. Only one paper did not report on HRQoL (Andersson et al., 2011), but this outcome was reported in a separate article included in the current review (Ljotsson et al., 2010). The majority of studies used the IBS Quality of Life Questionnaire (IBS-QOL) (Everitt et al., 2013; Hunt et al., 2009; Ljotsson et al., 2011a; Ljotsson et al., 2010; Ljotsson et al., 2011b; Oerlemans et al., 2011). Other studies used PedsQL (Pediatric Quality of Life Inventory) (Bonnert et al., 2017), IBD-specific HRQOL (IBDQ), and Generic HRQOL (SF-12 and SF-36) (McCombie et al., 2016; Mikocka-Walus et al., 2015; Mikocka-Walus et al., 2016a).

2.3.3.2.6 Studies reporting related outcomes

Nine articles reported related outcomes, with three examining pain (Bonnert et al., 2017; Oerlemans et al., 2011; Ljotsson et al., 2010). Two studies looked into the cost-effectiveness (Andersson et al., 2011; Ljotsson et al., 2011a) of online therapy and both used the same scale, The Trimbos and Institute of Medical Technology Assessment Cost Questionnaire for Psychiatry (TIC-P). Two studies assessed disability using the Sheehan disability scale (Ljotsson et al., 2011a; Ljotsson et al., 2010).

Three studies by the same author used the VSI (Visceral sensitivity index), a measure of gastrointestinal symptom-specific anxiety (Ljotsson et al., 2011a; Ljotsson et al., 2011b; Ljotsson et al., 2010). One study used the Anxiety Sensitivity Index (ASI) for measuring fear of anxiety-related symptoms (Hunt et al., 2009). One study used three additional scales: Children’s Somatisation Inventory - parent's version (CSI-24) to assess other somatic symptoms, Client Satisfaction Questionnaire (CSQ) to assess satisfaction with treatment and Behavioural Responses Questionnaire IBS - BRQ to measure IBS-specific pattern of avoidance behaviour (Bonnert et al., 2017). Bonnert et al., (2017) also reported school absence and medication use. Another study measured participants’ enablement as an indicator of GP consultation quality using the Patient Enablement Questionnaire (PEQ) and their rate of relief from IBS symptoms using the Subjects Global Assessment of Relief (SGA of Relief) (Everitt et al., 2013). One study measured the tendency to catastrophise the social and functional implications of different physical sensations and symptoms using the Consequences of Physical Sensations Questionnaire (CPSQ) (Hunt et al., 2009). Two further related outcomes were measured in another study, social functioning using the Social Functioning Questionnaire (SFQ) and neuroticism using the brief version of the Eysenck Personality Questionnaire (McCombie et al., 2016). Finally, another study used the Pain Catastrophizing Scale (PCS) scale to measure the degree of pain catastrophising thoughts and the Cognitive Scale for Functional Bowel Disorders (CSFBD) to measure GI symptom-related dysfunctional cognitions (Oerlemans et al., 2011).

2.3.3.3 Characteristics of included participants

The majority of the included studies were in adults. Only one study (n=101) examined an adolescent (age 13–17 years) population (Bonnert et al., 2017) (hence were not included in the meta-analyses), and another study included participants from the age of 16 years and upwards (Everitt et al., 2013). In the studies with adult populations, the mean age varied from 34.6 (9.4) to 49.11 (16.47). In the majority of studies, there were more females than males, except for the study by Mikocka-Walus et al., (2015), where the male population was slightly bigger at 54%. Also, this study had the highest average age of participants (mean age of 46.5 (SD=15.7) years in the intervention group and 51.9 (SD=16.9) years in the control group). The lowest mean age (in the studies with adult populations) was in the two articles representing one cohort (in the intervention group 36.4 (SD=10.1) years and 32.8 (SD=8.6) years in the control group) and the participants in this study had the shortest mean duration of symptoms of 6.3 years (Andersson et al., 2011; Ljotsson et al., 2010). The population in three other studies had the longest average duration of symptoms over 14 years (Mikocka-Walus et al., 2015; Ljotsson et al., 2011b; Mikocka-Walus et al., 2016a). In the study with the adolescent population, the parent-reported mean duration of symptoms was 5.12 (SD=4.11) years (Bonnert et al., 2014). Three studies did not report on the length of symptoms or years since diagnosis (Hunt et al., 2009; McCombie et al., 2016; Oerlemans et al., 2011).

2.3.3.4 The severity of anxiety and/or depression

Of the six studies reporting severity of anxiety and depression as an outcome measure, patients in two studies (n=373) had low anxiety, and depression scores means at baseline (Mikocka-Walus et al., 2015; McCombie et al., 2016; Mikocka-Walus et al., 2016a), in three studies patients (n=330 adults; n=101 adolescents) had mild anxiety scores (Everitt et al., 2013; Ljotsson et al., 2011b; Bonnert et al., 2017) and in one study patients (n=85) had mild scores for depression MADRS-S Mean (SD) = 12.19 (7.8) (Ljotsson et al., 2010).

Four studies by design excluded participants with severe depressive symptoms (Ljotsson et al., 2010; Mikocka-Walus et al., 2015; Mikocka-Walus et al., 2016a; McCombie et al., 2016; Ljotsson et al., 2011b), one with severe psychosocial or psychiatric distress (Bonnert et al., 2017) and two due to psychological disorders but did not specify which disorders (Oerlemans et al., 2011; Ljotsson et al., 2011a). The final study did not provide the patients' baseline level of anxiety or depression or describe these characteristics in the exclusion/inclusion criteria (Hunt et al., 2009).

2.3.4 Risk of bias assessment

Different sources of bias in the included studies are presented in Table 3 and Figure 5.

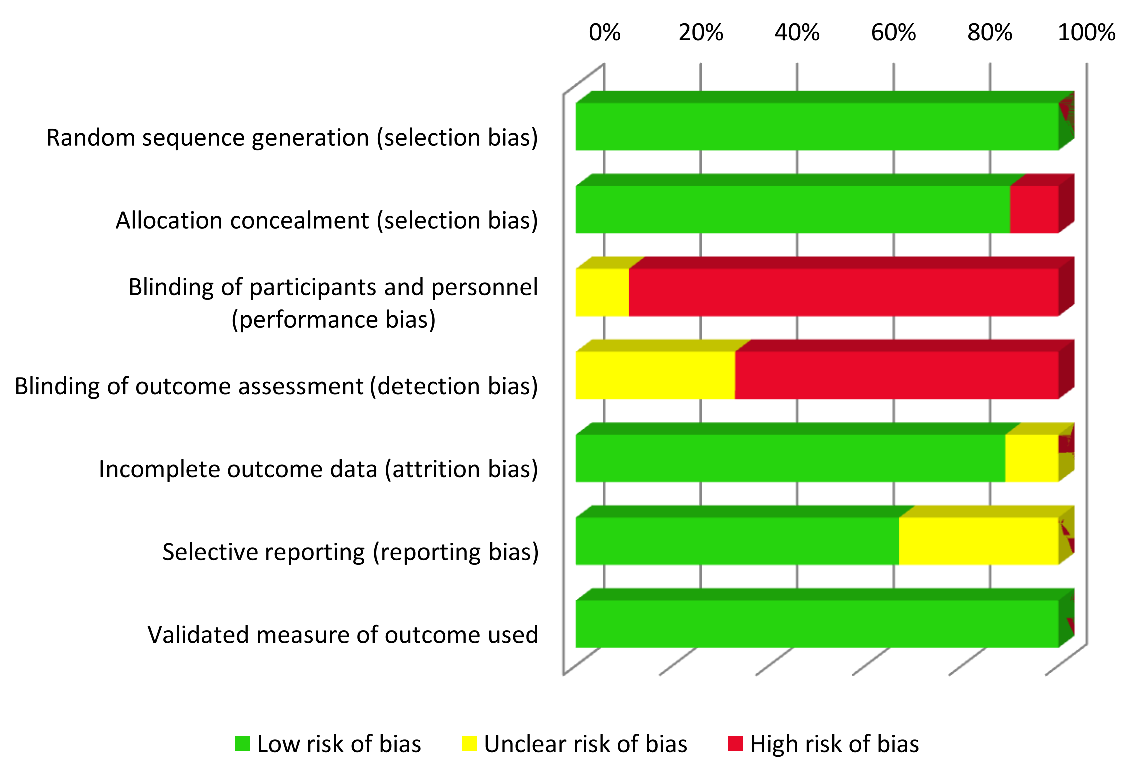


Figure 5 Risk of bias graph: methodological items presented as a percentage across all included studies.

Table 3 Risk of bias assessment. Methodological quality: review author's judgment about each methodological quality item for each included study.

Study ID	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)[a]	Blinding of outcome assessment (detection bias)[a]	Incomplete outcome data (attrition bias) [b]	A validated measure of outcome used	Selective reporting (reporting bias)
(Andersson et al., 2011)	+	+	-	-[9]	+	+	+
(Ljotsson et al., 2010)							

Study ID	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)[a]	Blinding of outcome assessment (detection bias)[a]	Incomplete outcome data (attrition bias) [b]	A validated measure of outcome used	Selective reporting (reporting bias)
(Bonnert, 2017)	+	+	-	-	+[11]	+	+
(Everitt et al., 2013)	+	+	-[6]	-[7]	+	+	? [13]
(Hunt et al., 2009)	+	+[1]	-	-[8]	+	+	? [12]
(Ljotsson et al., 2011a)	+	+[5]	-	-[9]	+	+	+
(Ljotsson et al., 2011b)	+	+	-[3]	-[10]	+	+	+
(McCombie, 2016)	+	-[2]	-	?	+	+	? [12]
(Mikocka-Walus et al., 2015; Mikocka-Walus et al., 2016a)	+	+	-[4]	?	+	+	+
(Oerlemans, 2011)	+	+	?	?	?	+	+

Support for judgment:

1 "participants were randomly assigned to a condition based on order of enrolment" Comment: probably done.

2 "Allocation concealment was not used, but participants were present when they were randomized; therefore, they could see how they were allocated."

3 "The participants were informed that they would be randomized to one of two different psychological treatments, but they were not aware of the differences between the treatments". Comment: partial concealment for patients. "... therapists in the study were not blinded and were likely to be biased toward the ICBT protocol". Comment. Not blinding of personnel.

4 "patients (in the control group) were told that we were examining how psychological health influenced IBD behaviour and was unaware of the +CBT arm of the study". Comment: Partial concealment, for the control group.

5 "Since all outcomes that were waiting list controlled were self-assessed, there was no concealment of allocation". Comment: Done. The author describes the procedure of allocation. Probably, the author confused blinding of allocated interventions with concealment of allocation.
6 "To ensure double-blinding, all participants took three over-encapsulated identical tablets ". Comment: partial blinding for tablets intake and single-blinding for the website (participants were not able to be blind to website access).
7 Outcome data was "patient self-completed away from the study team, thus avoiding any influence of the study team on the responses". Comment: Patients were not blind.
8 Independently "Two of the authors, who remained blind to symptom severity and treatment condition, served as raters". Comment: Partial for the personal, but patients' self-reported outcomes.
9 "self-report measurements", "all outcomes that were waiting list controlled were self-assessed" Comment: not done.
10 "All measures were administered online" Comment: does not mention how.
11 Restricted maximum likelihood mixed models used that included all randomised participants and took any missing data into account.
12 Outcomes reported for completers only
13 There was a slight discrepancy in the number of participants in the CONSORT diagram and the text, and the number of participants per arm for some of the outcomes was unclear
a - Blinding the experimental group is often impossible in psychotherapy trials. In addition, the waiting list controls in the majority of studies were transferred to active intervention after post-intervention assessment.
b - Missing data have been imputed.

2.3.4.1 Selection bias

The majority of studies met the Cochrane Risk of Bias Tool for randomised controlled trials criteria for low risk of selection bias (Table 3). All of them used a random method of sequence generation describing the procedure and methods of allocation concealment. One study was at a higher risk of bias, namely, it indicated that allocation concealment was not used (McCombie et al., 2016). In one study the author described the procedure of allocation but saying that it was not done (Ljotsson et al., 2011a). It appears that the author confused blinding of allocated interventions with concealment of allocation (Higgins and Green, 2011).

2.3.4.2 Blinding

All studies were considered to have a high risk of performance and detection bias. It has to be taken into account that blinding the experimental group is often difficult in psychotherapy trials. The patients and the personnel are subject to bias due to the knowledge of the intervention status, but this does not imply low quality (Higgins and Green, 2011). Some authors attempted to partially blind the participants (Mikocka-Walus et al., 2015; Ljotsson et al., 2011b) or the researchers who rated the scales to the symptom severity (Hunt et al., 2009) (Table 3). In fact, in trials where the outcome measure involves subjectivity, blinding the assessor of the outcome can be more essential than blinding the implementation of the intervention (Day and Altman, 2000). Those clinicians and participants who are not blinded are more likely to have predetermined attitudes during the assessments of the effectiveness of the intervention compared to those who are blinded (Karanicolas, Farrokhyar and Bhandari, 2010; Hróbjartsson et al., 2012; Hrobjartsson et al., 2014). The level of discrepancies between the self-reports scales and clinician ratings varies greatly (Dunlop et al., 2010; Domken, Scott and Kelly, 1994; Enns, Larsen and Cox, 2000; Corruble et al., 1999). Generally, clinician-rated scales have greater validity and are preferred over the self-reports (Rush et al., 2005; Schatzberg and Nemeroff, 2009; Prusoff, Klerman and Paykel, 1972). However, to comprehensively assess certain outcomes, for instance, the severity of depression, both clinician-rated and self-report measures should be incorporated (Cuijpers et al., 2010; Uher et al., 2012).

2.3.4.3 Incomplete outcome data

The attrition rates varied amongst the studies and the points of follow-up. The study with the largest sample size (n=199) had the highest dropout rate of 53.1% in the intervention group at six months, but only 17.2% in control (McCombie et al., 2016). The smallest study (n=54) had the highest dropout rate of 92% from the enrol numbers in the control group at three months, but only 64% in the intervention (Hunt et al., 2009). Despite the high attrition rates in some studies, missing data in all studies, except for one (Oerlemans, 2011), have been managed using intent-to-treat analysis where missing data were imputed using the last observation carried forward method (Everitt et al., 2013; Ljotsson et al., 2010; Hunt et al., 2009), full information maximum likelihood estimation under the assumption of data missing at random in a linear mixed-effects model (Ljotsson et al., 2011a; Ljotsson et al., 2011b), multivariate analyses using linear mixed-effects models (Mikocka-Walus et al., 2015; Mikocka-Walus et al., 2016a; McCombie et al., 2016), and restricted maximum likelihood mixed models (Bonnert et al., 2017). Only one study did not use the intention-to-treat analysis, and it is unclear how missing data was dealt with (Oerlemans, 2011).

2.3.4.4 Selective reporting

2.3.4.4.1 Publication/small study bias

Publication bias was not explored for each type of outcome due to the low number of studies included in each meta-analysis.

2.3.4.4.2 Outcome reporting bias

Outcome reporting bias was defined as the discrepancy between the listed outcomes in the methods section and the reported outcomes in the results. Also, where the protocols of the studies were available, the intended outcomes in the methods of the protocol were compared with the reported outcomes of the actual trials to assess reporting bias. All studies met the Cochrane Risk of Bias Tool for randomised controlled trials criteria for low risk of outcome reporting bias (Table 3).

2.3.4.4.3 Other types of reporting bias

One study had an unclear risk of reporting bias (Everitt et al., 2013). There was a slight discrepancy in the number of participants in the CONSORT diagram and the text, and the number of participants per arm for some of the outcomes was unclear. We contacted the author, who however, no longer had access to the trial data. Two studies by Hunt et al., (2009) and McCombie et al., (2016) reported the results for the completers of the intervention programme only, hence the reporting bias is unclear. We could not obtain the score for the whole intervention group from the authors.

2.3.5 Data synthesis and meta-analysis

2.3.5.1 Data synthesis and meta-analysis of the IBD disease activity and IBS severity of symptoms

The IBS severity of symptoms were reported in six studies (Table 4), involving a total of 631 people (Andersson et al., 2011; Ljotsson et al., 2010; Ljotsson et al., 2011a; Ljotsson et al., 2011b; Bonnert et al., 2017; Hunt et al., 2009; Everitt et al., 2013) and two studies reported the disease activity for IBD (n=373) (McCombie et al., 2016; Mikocka-Walus et al., 2016a; Mikocka-Walus et al., 2015). Two papers reported on the same cohort but used different units to report the outcome hence were not included in the total number and data only from one of them were combined in the meta-analysis (Andersson et al., 2011; Ljotsson et al., 2010). One study assessed an adolescent population (n=101) (Bonnert et al., 2017). All these studies have reported the outcome of the post-intervention assessment. After that, patients were not followed-up or were crossed-over into the treatment. Only one study had three months follow-up (Everitt et al., 2013) and one six months (Ljotsson et al., 2011b). The results from all, except one (Everitt et al., 2013), of the studies reporting the level of severity of IBS symptoms demonstrated that online CBT improved gastrointestinal symptoms in the adolescent and adult populations with IBS at the point of post-intervention assessment. There was no difference in the IBD disease activity reported in one study (Mikocka-Walus et al., 2015; Mikocka-Walus et al., 2016a) and an improvement in the IBD disease activity in the online CBT group only for the completers of the online programme, compared to the control group in the other study (McCombie et al., 2016). The meta-analysis was performed for IBS severity and IBD remission rate separately (Figure 6, Figure 7, Figure 8).

Table 4 Results of studies reporting the IBD disease activity and the severity of symptoms for IBS.

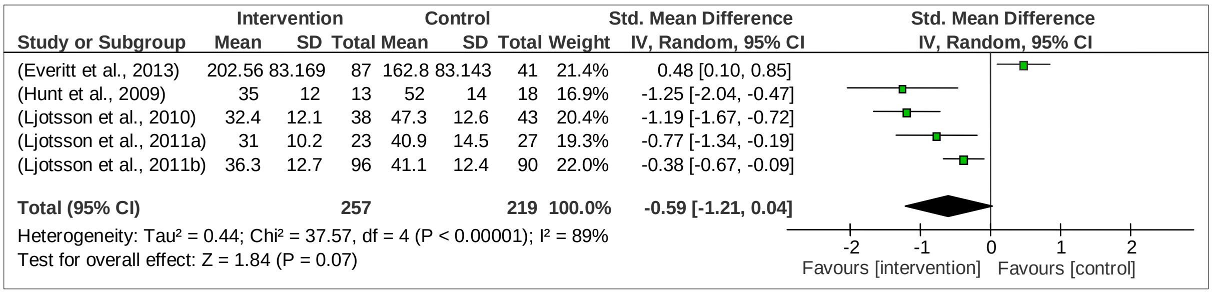
Study ID	Outcome measure	Results for the outcome measure			
		Treatment participants (n)	Treatment	Control participants (n)	Control
(Andersson et al., 2011) (Ljotsson et al., 2010)			fraction of recovered participants		the fraction of recovered participants
	post-intervention (10 weeks)	38	15/42 = 0.36	43	1/43 = 0.02
	follow up 3 months	38	14/42 = 0.33	43*	-
	12 months	37	18/42 = 0.43	-	-
	GSRS-IBS		Mean (SD)		Mean (SD)
	pre-intervention	42	48.5(8.8)	43	49.6(11.8)
	post-intervention (10 weeks)	38	32.4(12.1)	43	47.3(12.6)
	follow up 3 months	38	34.1(12.8)	43*	-
(Ljotsson et al., 2011a)	GSRS-IBS		Mean (SD)		Mean (SD)
	pre-intervention	30	44.6 (11.1)	31	39.8 (12.0)
	post-intervention (10 weeks)	23	31.0 (10.2)	27	40.9 (14.5)
	12-month follow-up	19	29.9 (12.6)	-*	-
(Ljotsson et al., 2011b)	GSRS-IBS		Mean (SD)		Mean (SD)
	pre-intervention	98	47.5 (10.5)	97	47.3 (9.4)
	post-intervention (10 weeks)	96	36.3 (12.7)	90	41.1 (12.4)
	6-Month follow-up	87	33.4 (13.4)	82	39.3 (13.3)
(Bonnert, 2017)[a]	GSRS-IBS		Mean (SE)		Mean (SE)
	pre-intervention	47	43.19 (1.95)	54	42.40 (1.82)
	post-intervention (10 weeks)	47	32.05 (2.20)	54	37.67 (2.05)
	follow up 6 months	47	30.87 (2.0)	-*	-
Everitt et al., 2013)	IBS SSS score, total mean (n = 123)				Mean (95% CI)
	*post-intervention (*6 weeks) significance p = 0.037	43 44	*website* 197.0 (172.4 – 221.7) *website + support* 208.0 (188.1- 233.0)	41	162.8 (137.4-188.3)
	calculated total mean (SD) *at* 6 weeks	87	202.56 (83.169)	41	162.8 (83.143)
	12 weeks significance p = 0.243	42 42	*website* 207.9 (187.6 – 228.1) *website + support* 193.4 (173.0- 213.8)	40	218.2 (197.4-238.9)
	calculated total mean (SD) *at 12* weeks	84	200.65 (67.196)	40	218.2 (66.956)
(Hunt et al., 2009)	GSRS		Mean (SD)		Mean (SD)
	pre-intervention	28	57 (13)	26	61 (14)
	post-intervention (5weeks)	13[b]	35 (12)	18	52 (14)
	3-month follow-up	10[b]	39 (13)	-	-

Study ID	Outcome measure	Results for the outcome measure			
		Treatment participants (n)	Treatment	Control participants (n)	Control
(McCombie, 2016)	SCCAI (UC and IBD-U)		Mean (SD)		Mean (SD)
	baseline	113	2.3 (2.4)	86	2.2 (2.3)
	change Score at 12weeks	29[b]	-1.73 (4.82)	78	-0.05 (1.90)
	change Score at 6 months	29[b]	-1.82 (2.75)	66	-0.44 (1.54)
	HBI (CD)		Mean (SD)		Mean (SD)
	baseline	113	3.6 (4.000	86	4.5 (4.5)
	Change Score at 12weeks	29 [b]	-0.69 (3.04)	78	-0.68 (3.50)
	Change Score at 6 months	29[b]	-0.42 (3.96)	66	-1.60 (4.70)
(Mikocka-Walus et al., 2015; Mikocka-Walus et al., 2016a)	SCCAI (UC and IBD-U)		Mean (SD)		Mean (SD)
	baseline	90	3.4 (1.4)	84	3.2 (1.3)
	6 months	51	3.5 (1.8)	65	3.7 (1.6)
	12 months	42	2.9 (1.6)	64	3.5 (2.5)
	24 months	31	4.7 (1.7)	45	4.9 (2.1)
	CDAI		Mean (SD)		Mean (SD)
	baseline	90	110.8 (72.5)	84	87.4 (104.8)
	6 months	51	91.3 (90.3)	65	83.2 (92.2)
	12 months	42	84.1 (95.3)	64	88.4 (105.9)
	24 months	31	60.4 (91.2)	45	53.1 (70.6)

Note: GSRS-IBS - Gastrointestinal Symptom Rating Scale; (IBS SSS score) - Irritable Bowel Symptom Severity Scale; SCCAI (UC and IBD-U) - Simple Clinical Colitis Activity Index (ulcerative colitis); CDAI - Crohn's Disease Activity Index; (HBI) (CD) - Harvey-Bradshaw Index. * - after assessment, they were offered the active treatment phase; a- outcome measures with estimated means, SE (analysed intention to treat); a - the number of completers, such as data provided for completers only.

2.3.5.1.1 A meta-analysis of data on the severity of symptoms for IBS

The random-effects model (Figure 6) was used to perform the meta-analysis at post-intervention assessment due to the studies substantial statistical (Tau² = 0.44; Chi² = 37.59, df = 4 (P < 0.00001); I² = 89%) and clinical heterogeneity. Patients varied in age, disease duration, treatment alongside intervention or control conditions.



Study or Subgroup	Intervention Mean	Intervention SD	Intervention Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI
(Everitt et al., 2013)	202.56	83.169	87	162.8	83.143	41	21.4%	0.48 [0.10, 0.85]
(Hunt et al., 2009)	35	12	13	52	14	18	16.9%	-1.25 [-2.04, -0.47]
(Ljotsson et al., 2010)	32.4	12.1	38	47.3	12.6	43	20.4%	-1.19 [-1.67, -0.72]
(Ljotsson et al., 2011a)	31	10.2	23	40.9	14.5	27	19.3%	-0.77 [-1.34, -0.19]
(Ljotsson et al., 2011b)	36.3	12.7	96	41.1	12.4	90	22.0%	-0.38 [-0.67, -0.09]
Total (95% CI)			**257**			**219**	**100.0%**	**-0.59 [-1.21, 0.04]**

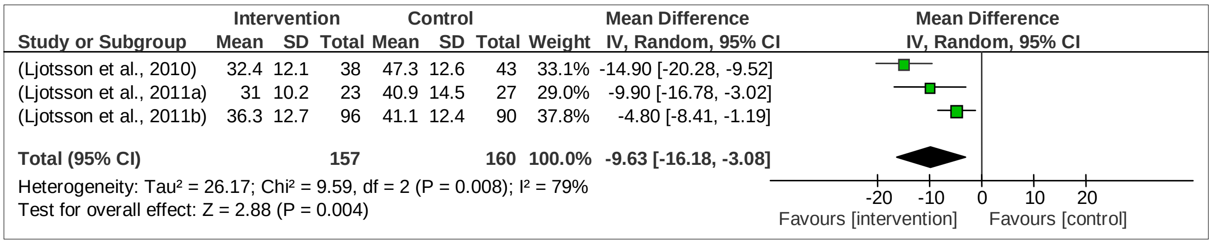
Heterogeneity: Tau² = 0.44; Chi² = 37.57, df = 4 (P < 0.00001); I² = 89%
Test for overall effect: Z = 1.84 (P = 0.07)

Figure 6 Meta-analysis of studies reporting IBS symptoms severity at post-intervention assessment 1.

The standardised mean difference varied from 0.48 (0.10, 0.85) to -1.25 (-2.04, -0.47) in the studies. Four out of five studies show statistical significance in favour of the intervention (Hunt et al., 2009; Ljotsson et al., 2010; Ljotsson et al., 2011a; Ljotsson et al., 2011b). Only one study showed a significant statistical evidence in favour of the control condition (Everitt et al., 2013) although this difference disappeared by three months of follow-up (Table 4).

The pooled standardised mean difference shows a positive effect of online CBT compared to control, but this difference was not statistically significant (-0.59 (-1.21, 0.04), p=0.07).

Despite the fact that the study by Everitt et al., (2013) (n=135) carried the second biggest weight in the meta-analysis, there was a slight discrepancy between the number of patients in the CONSORT diagram and the text of this study. A study by Hunt et al. (2009) also reported only data for completers only, thus also introduces bias in the analysis. Therefore, the meta-analysis was repeated this time excluding the two studies (Figure 7).



	Intervention			Control				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
(Ljotsson et al., 2010)	32.4	12.1	38	47.3	12.6	43	33.1%	-14.90 [-20.28, -9.52]
(Ljotsson et al., 2011a)	31	10.2	23	40.9	14.5	27	29.0%	-9.90 [-16.78, -3.02]
(Ljotsson et al., 2011b)	36.3	12.7	96	41.1	12.4	90	37.8%	-4.80 [-8.41, -1.19]
Total (95% CI)			**157**			**160**	**100.0%**	**-9.63 [-16.18, -3.08]**

Heterogeneity: Tau² = 26.17; Chi² = 9.59, df = 2 (P = 0.008); I² = 79%
Test for overall effect: Z = 2.88 (P = 0.004)

Figure 7 Meta-analysis on the level of IBS symptom severity at post-intervention assessment 2.

All three studies favour the intervention concerning the post-intervention effect on symptom severity (Ljotsson et al., 2010; Ljotsson et al., 2011a; Ljotsson et al., 2011b). The pooled mean difference was -9.63 (-16.18, -3.08) in favour of the intervention and this difference was statistically significant (p=0.004).

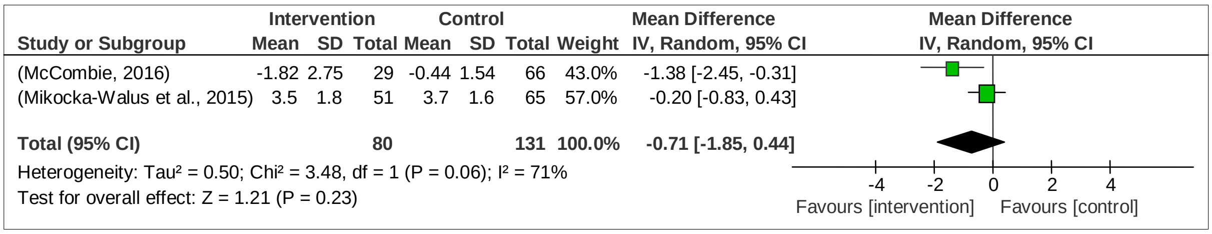
2.3.5.1.2 A meta-analysis of data on the IBD disease activity

A meta-analysis of data on the disease activity in UC

There were a total of 373 people in the studies which reported IBD disease activity (Mikocka-Walus, 2015; Mikocka-Walus et al., 2016a; McCombie et al., 2016). One study reported this outcome at three and six months (McCombie et al., 2016) and another study at six, twelve and 24 months (Mikocka-Walus et al., 2015; Mikocka-Walus et al., 2016a). The meta-analysis was conducted using the 6 months follow-up data.

The random-effects model was used to perform the meta-analysis (Figure 8) at post-intervention assessment due to the studies substantial statistical (Tau² = 0.50; Chi² = 3.48, df = 1 (P = 0.06); I² = 71%) and clinical heterogeneity. Patients varied in age and length since the onset of symptoms.

Both studies included in the meta-analysis used the SCCAI (UC and IBD-U) to assess the IBD disease activity. A study by McCombie et al., (2016) used the change score from baseline for completers of the CBT intervention, rather than a raw score. Hence the mean difference was used as a measure of effect.



	Intervention			Control				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
(McCombie, 2016)	-1.82	2.75	29	-0.44	1.54	66	43.0%	-1.38 [-2.45, -0.31]
(Mikocka-Walus et al., 2015)	3.5	1.8	51	3.7	1.6	65	57.0%	-0.20 [-0.83, 0.43]
Total (95% CI)			**80**			**131**	**100.0%**	**-0.71 [-1.85, 0.44]**

Heterogeneity: Tau² = 0.50; Chi² = 3.48, df = 1 (P = 0.06); I² = 71%

Test for overall effect: Z = 1.21 (P = 0.23)

Figure 8 Meta-analysis on IBD remission rates at 6 months of follow-up.

One study showed a significant change in disease activity in favour of the intervention (McCombie et al., 2016), while another (Mikocka-Walus et al., 2015) showed no significant difference with the confidence intervals crossing 0.

The disease activity as measured on the SCCAI (UC and IBD-U) for the patients who received online CBT intervention was higher than for patients in the control group but was not statistically significant (MD: -0.71, 95% CI: -1.85 to 0.44, p=0.23).

This meta-analysis combined one study that had a high attrition rate and provided data for completers only (McCombie et al., 2016), hence the results could have been different if the intention-to-treat (ITT) analysis was reported.

Meta-analysis of data on the disease activity in CD

Only two studies reported disease activity for the CD group alone. McCombie et al., (2016) reported the change from baseline score on the HBI (CD) scale, while another study reported a final outcome score and used the CDAI to assess the disease activity

(Mikocka-Walus et al., 2015), making the meta-analysis using the common effect measure impossible to perform.

2.3.5.2 Data synthesis and meta-analysis of the mean levels of anxiety and depression

Not all studies that reported on the level of anxiety reported also the level of depression. The total population of individuals in the studies that reported the mean level of anxiety was 804, of which 101 were adolescents, and sample in the studies that reported the mean level of depression was 788 (Mikocka-Walus et al., 2015; Mikocka-Walus et al., 2016a; McCombie et al., 2016; Everitt et al., 2013; Ljotsson et al., 2010; Ljotsson et al., 2011b; Bonnert et al., 2017). There was no statistically significant difference on anxiety or depression between online CBT and control groups reported in the individual studies (Table 5).

Table 5 Results of studies reporting the rates of anxiety and depression and/or mean levels of anxiety and depression

Study ID	outcome measure	results for the outcome measure			
		Treatment participants (n)	Treatment	Control participants (n)	Control
(Bonnert, 2017)a	SCAS		Mean (SE)		Mean (SE)
	pre-intervention	47	28.45 (2.28)	54	22.87 (2.12)
	post-intervention	47	25.23 (2.38)	54	22.62 (2.22)
	6-Month follow-up	47	21.05 (2.65)	-	-
Everitt et al., 2013)	HADS anxiety (n=114)		Mean (95% CI)		Mean (95% CI)
	6 weeks	43	website 8.9 (7.9-9.8)	41	8.3 (7.3-9.2)
	significance p = 0.109	44	website + support 9.7 (8.8-10.6)		
	total calculated mean (SD) at 6 weeks	87	9.3 (3.12)	41	8.3 (3.1)
	HADS anxiety (n=114)		Mean (95% CI)		Mean (95% CI)
	12 weeks	42	website 8.8 (8.0- 9.7)	40	8.0 (7.1 -8.8)
	significance p = 0.123	42	website + support 9.2 (8.3 -10.0)		
	total calculated mean (SD) at 12 weeks	84	9 (2.866)	40	8 (2.743)
	HADS depression (n=114)		n (%)		n (%)
	6 weeks Normal (0–7)	87	website 35 (89.7) website + support 28 (71.8)	41	31 (79.5)
	6 weeks Mild (8–10)	87	website 2 (5.1) website + support 8 (20.5)	41	8 (20.5)
	6 weeks Moderate or Severe (11–21)	87	website 2 (5.1) website + support 3 (7.7)	41	0 (0)
	12 weeks Normal (0–7)	84	website 32 (84.2) website + support 31 (79.5)	40	30 (81.1)
	12 weeks Mild (8–10)	84	website 6 (15.8) website + support 4 (10.3)	40	4 (10.8)
	12 weeks Moderate or Severe (11–21)	84	website 0 (0) website + support 4 (10.3)	40	3 (8.1)

Study ID	outcome measure	results for the outcome measure			
		Treatment participants (n)	Treatment	Control participants (n)	Control
(Ljotsson et al., 2010)	MADRS-S		Mean (SD)		Mean (SD)
	pre intervention	42	11.9 (8.1)	43	12.5 (7.6)
	post intervention	38	6.9 (8.1)	43	10.5 (8.6)
(Ljotsson et al., 2011b)	HADS anxiety		Mean (SD)		Mean (SD)
	pre-intervention	98	8.8 (4.2)	97	8.7 (3.8)
	post-intervention	97	7.2 (4.6)	94	7.3 (3.9)
	6-month follow-up	87	7.2 (4.2)	82	7.8 (4.4)
	HADS depression		Mean (SD)		Mean (SD)
	pre-intervention	98	5.4 (3.5)	97	5.5 (3.3)
	post intervention	97	4.4 (4.3)	94	4.4 (4.0)
	6-month follow-up	87	4.4 (4.1)	82	4.7 (3.9)
(McCombie, 2016)	HADS anxiety		Mean (SD)		Mean (SD)
	baseline	113	7.0 (4.1)	86	6.9 (4.1)
	Change Score at 12weeks	62	-1.07 (2.51)	78	-1.08 (2.60)
	Change Score at 6 months	53	-1.63 (3.37)	66	-0.66 (2.96)
	HADS depression		Mean (SD)		Mean (SD)
	baseline	113	4.6 (3.5)	86	4.9 (4.4)
	Change Score at 12weeks	29b	-1.33 (2.24)	78	-0.86 (2.74)
	Change Score at 6 months	29b	-0.48 (2.68)	66	-0.51 (3.12)
(Mikocka-Walus et al., 2015; Mikocka-Walus et al., 2016a)	HADS anxiety		Mean (SD)		Mean (SD)
	baseline	90	7.1 (3.9)	84	6.2 (4.3)
	6 months	51	5.9 (3.4)	65	5.9(4.6)
	12 months	42	6.5 (4.2)	64	6.1 (4.6)
	24 months	31	5.3 (4.1)	45	5.5 (4.7)
	HADS depression		Mean (SD)		Mean (SD)
	baseline	90	4.3 (3.4)	84	4.4(4.1)
	6 months	51	3.5 (2.9)	65	4.4 (4.1)
	12 months	42	4.1 (3.3)	64	4.5 (4.8)
	24 months	31	3.2 (3.7)	45	3.9 (3.7)
	STAI State Anxiety		Mean (SD)		Mean (SD)
	baseline	90	37.5 (13.1)	84	35.9 (13.7)
	6 months	51	34.5 (10.9)	65	35.9 (12.8)
	12 months	42	35.9 (13.1)	64	35.3 (13.4)
	24 months	31	32.2 (11.3)	45	37.7 (14.7)
	STAI Trait Anxiety		Mean (SD)		Mean (SD)
	baseline	90	39.3 (11.9)	84	37.4 (11.7)
	6 months	51	36.1 (11.1)	65	37.5 (11.8)
	12 months	42	39.5 (12.5)	64	36.9 (13.1)
	24 months	31	33.6 (10.4)	45	38 (14.1)

Note: HADS - Hospital Anxiety and Depression Scale; (MADRS-S) - The Montgomery Åsberg Depression Rating Scale-- Self report; STAI - the State-Trait Anxiety Inventory; SCAS - Spence Childhood Anxiety Scale; a- outcome measures with estimated means, SE (analysed intention to treat); b - the number of completers, such as data provided for completers only.

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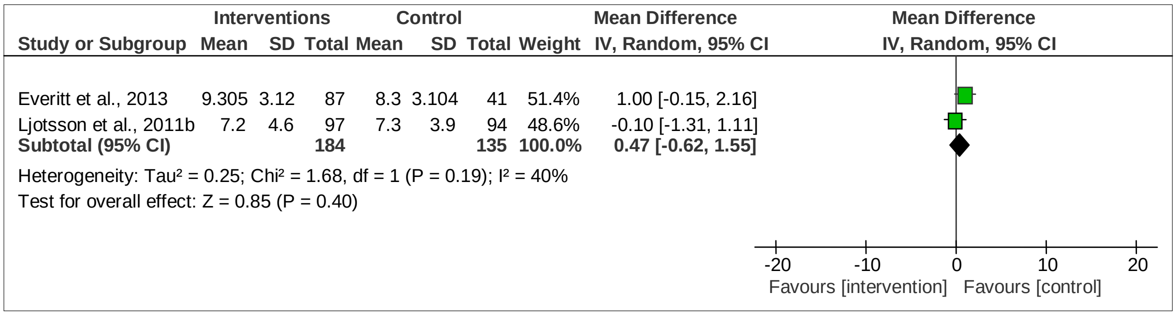
2.3.5.2.1 A meta-analysis of data reporting the mean levels of anxiety and depression

A meta-analysis of data reporting the mean levels of anxiety

Two studies reported anxiety at post-intervention (Everitt et al., 2013; Ljotsson et al., 2011b), two studies at 3 months follow-up (Everitt et al., 2013; McCombie et al., 2016), three studies at 6 months follow-up (Mikocka-Walus et al., 2015; Ljotsson et al., 2011b; McCombie et al., 2016) and only one author reported anxiety at 12 and 24 months follow-up (Mikocka-Walus et al., 2016a). All of these studies used the HADS anxiety scale to measure anxiety and only one study presented data as a change score on this scale (McCombie et al., 2016). Therefore, a mean difference was used as a measure of effect in the meta-analyses where the change score was combined.

A meta-analysis of data reporting the mean levels of anxiety at post-intervention assessment



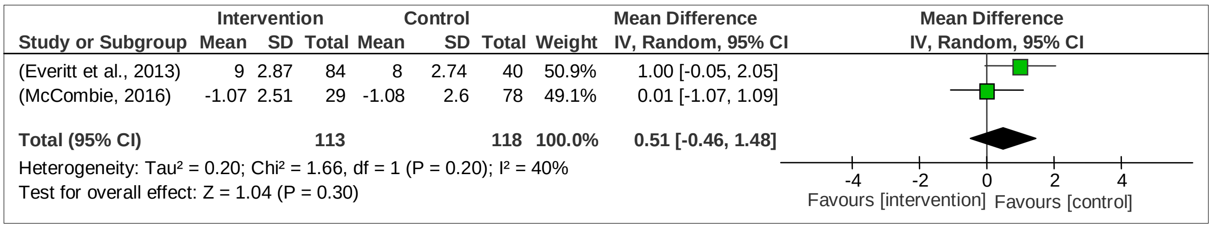
Study or Subgroup	Interventions Mean	Interventions SD	Interventions Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Random, 95% CI
Everitt et al., 2013	9.305	3.12	87	8.3	3.104	41	51.4%	1.00 [-0.15, 2.16]
Ljotsson et al., 2011b	7.2	4.6	97	7.3	3.9	94	48.6%	-0.10 [-1.31, 1.11]
Subtotal (95% CI)			**184**			**135**	**100.0%**	**0.47 [-0.62, 1.55]**

Heterogeneity: Tau² = 0.25; Chi² = 1.68, df = 1 (P = 0.19); I² = 40%
Test for overall effect: Z = 0.85 (P = 0.40)

Figure 9 Meta-analysis assessing the level of anxiety at post-intervention assessment.

As shown in Figure 9, there was moderate levels of heterogeneity (Tau² = 0.25; Chi² = 1.68, df = 1 (P = 0.19); I² = 40%). The pooled mean difference was 0.47 (95% CI: -0.62, 1.55). The level of anxiety at post-intervention was slightly lower in the control group compared to those individuals who received online CBT but was not statistically significant (p=0.40).

A meta-analysis of data reporting the mean levels of anxiety at 3 months of follow-up



Study or Subgroup	Intervention Mean	Intervention SD	Intervention Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Random, 95% CI
(Everitt et al., 2013)	9	2.87	84	8	2.74	40	50.9%	1.00 [-0.05, 2.05]
(McCombie, 2016)	-1.07	2.51	29	-1.08	2.6	78	49.1%	0.01 [-1.07, 1.09]
Total (95% CI)			**113**			**118**	**100.0%**	**0.51 [-0.46, 1.48]**

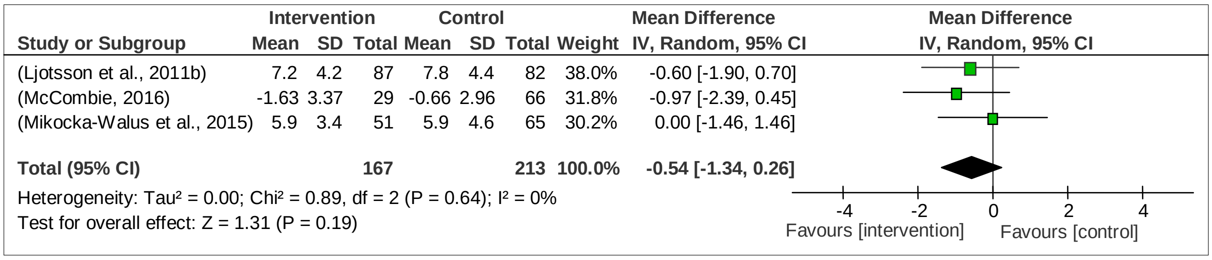
Heterogeneity: Tau² = 0.20; Chi² = 1.66, df = 1 (P = 0.20); I² = 40%
Test for overall effect: Z = 1.04 (P = 0.30)

Figure 10 Meta-analysis assessing the level of anxiety at 3 months of follow-up.

A similar result was found for the level of anxiety at three months of follow-up (Figure 10). There was a moderate level of heterogeneity (Tau² = 0.20; Chi² = 1.66, df = 1 (P = 0.20); I² = 40%). The pooled mean difference for the level of anxiety in the online CBT group versus control was 0.51 (95% CI: -0.46, 1.48). This suggests that the level of anxiety was slightly lower in the controls compared to the intervention group, but the difference was not significant (p=0.30).

A meta-analysis of data reporting the mean levels of anxiety at 6 months of follow-up

Despite the fact that there was little evidence for heterogeneity found across these three studies (Tau² = 0.00; Chi² = 0.89, df = 2 (P = 0.64); I² = 0%; all CIs overlapped), a random effect model was used due to clinical heterogeneity (the sample included IBD and IBS patients, with a different disease duration, a different medication regime alongside the intervention, and a different standard care in the control condition).



	Intervention			Control				Mean Difference
Study or Subgroup	**Mean**	**SD**	**Total**	**Mean**	**SD**	**Total**	**Weight**	**IV, Random, 95% CI**
(Ljotsson et al., 2011b)	7.2	4.2	87	7.8	4.4	82	38.0%	-0.60 [-1.90, 0.70]
(McCombie, 2016)	-1.63	3.37	29	-0.66	2.96	66	31.8%	-0.97 [-2.39, 0.45]
(Mikocka-Walus et al., 2015)	5.9	3.4	51	5.9	4.6	65	30.2%	0.00 [-1.46, 1.46]
Total (95% CI)			**167**			**213**	**100.0%**	**-0.54 [-1.34, 0.26]**

Heterogeneity: Tau² = 0.00; Chi² = 0.89, df = 2 (P = 0.64); I² = 0%

Test for overall effect: Z = 1.31 (P = 0.19)

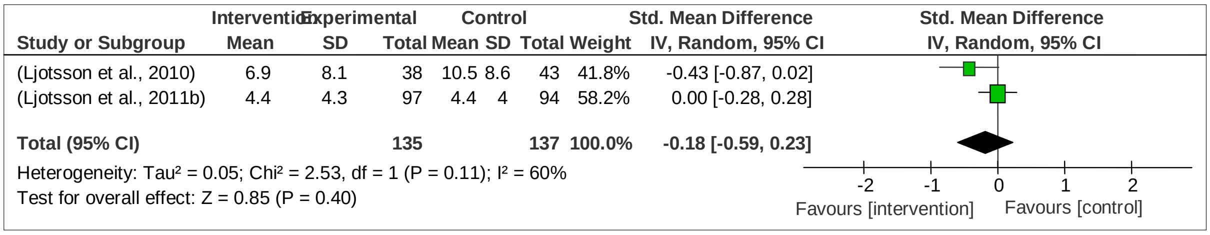
Figure 11 Meta-analysis assessing the level of anxiety at 6 months of follow-up.

At 6 months follow-up, the result changed in favour of the CBT intervention group, although this difference was not statistically significant (p=0.19), a pooled mean difference was -0.54 (95% CI: -1.34, 0.26) (Figure 11).

A meta-analysis of data reporting the mean levels of depression

The level of depression was reported at post-intervention assessment in two studies (Ljotsson et al., 2010; Ljotsson et al., 2011b), at three months follow-up in one (McCombie et al., 2016), and at six months follow-up in two studies (Mikocka-Walus et al., 2015; Mikocka-Walus et al., 2016a; Ljotsson et al., 2011b) and only one author presented data at 12 and 24 months follow-up (Mikocka-Walus et al., 2015; Mikocka-Walus et al., 2016a). All studies, except one (Ljotsson et al., 2010), which used MADRS-S, used the HADS to assess the level of depression. One study presented data as a change score on this scale (McCombie et al., 2016). Therefore, a mean difference was used as a measure of effect in the first meta-analysis where the change score was combined and the same outcome measures were used (Figure 13) and standardised mean difference in the second meta-analysis where two different scales were used combining a raw data (Figure 12). A random-effects model was used in meta-analyses assessing the level of depression.

A meta-analysis of data reporting the mean levels of depression at post-intervention assessment



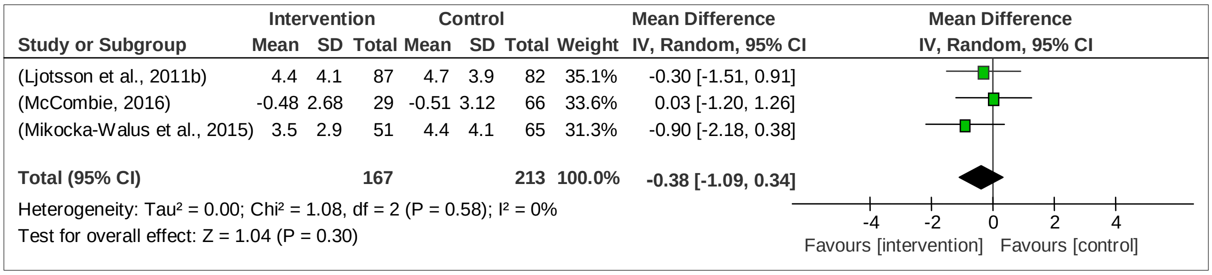
	InterventioExperimental			Control				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
(Ljotsson et al., 2010)	6.9	8.1	38	10.5	8.6	43	41.8%	-0.43 [-0.87, 0.02]
(Ljotsson et al., 2011b)	4.4	4.3	97	4.4	4	94	58.2%	0.00 [-0.28, 0.28]
Total (95% CI)			**135**			**137**	**100.0%**	**-0.18 [-0.59, 0.23]**

Heterogeneity: Tau² = 0.05; Chi² = 2.53, df = 1 (P = 0.11); I² = 60%
Test for overall effect: Z = 0.85 (P = 0.40)

Figure 12 Meta-analysis assessing the level of depression at post-intervention assessment.

The level of heterogeneity was high (Tau² = 0.05; Chi² = 2.53, df = 1 (P = 0.11); I² = 60%). The pooled mean difference for the level of depression at post-intervention was -0.18 (95% CI: -0.59, 0.23). This suggests that the level of depression was slightly lower in the controls compared to the intervention group but the difference was not significant (p=0.40) (Figure 12).

A meta-analysis of data reporting the mean levels of depression at 6 months of follow-up



	Intervention			Control				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
(Ljotsson et al., 2011b)	4.4	4.1	87	4.7	3.9	82	35.1%	-0.30 [-1.51, 0.91]
(McCombie, 2016)	-0.48	2.68	29	-0.51	3.12	66	33.6%	0.03 [-1.20, 1.26]
(Mikocka-Walus et al., 2015)	3.5	2.9	51	4.4	4.1	65	31.3%	-0.90 [-2.18, 0.38]
Total (95% CI)			**167**			**213**	**100.0%**	**-0.38 [-1.09, 0.34]**

Heterogeneity: Tau² = 0.00; Chi² = 1.08, df = 2 (P = 0.58); I² = 0%
Test for overall effect: Z = 1.04 (P = 0.30)

Figure 13 Meta-analysis of data assessing the level of depression at 6 months of follow-up.

There was little evidence of heterogeneity among the studies (Tau² = 0.00; Chi² = 1.08, df = 2 (P = 0.58); I² = 0%). The pooled estimate comparing online CBT against the control group was -0.38 (95% CI: -1.09, 0.34), indicating that there was little or no evidence of a difference in the mean level of depression at 6 months of follow-up between the two groups (p=0.30) (Figure 13).

2.3.5.3 Data synthesis and meta-analysis on the level of coping

There was no statistically significant difference reported between groups on the total level of coping in two studies (sample n=373) that examined this outcome (Table 6)

(Mikocka-Walus et al., 2015; Mikocka-Walus et al., 2016a; McCombie et al., 2016). Though, in one of the studies, the results varied for different components of the score at six months follow-up. For example, substance use decreased but venting increased more for completers in the intervention group compared to the control group, while religion decreased more in the last group (McCombie et al., 2016).

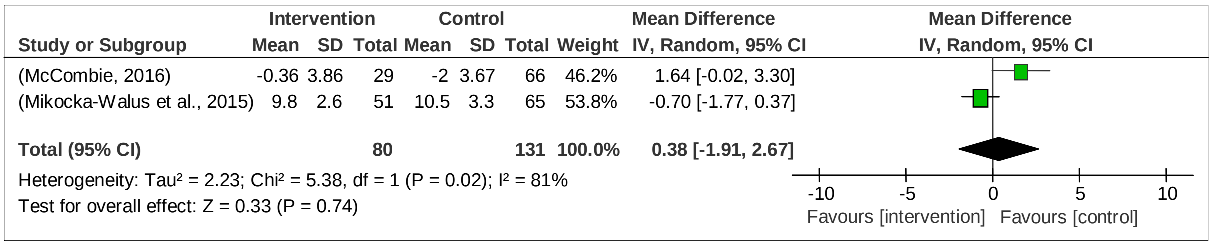
Table 6 Results of studies reporting the level of coping

Study ID	outcome measure	results for the outcome measure			
		Treatment participants (n)	Treatment	Control participants (n)	Control
(McCombie, 2016)	Problem-focus coping; total		Mean (SD)		Mean (SD)
	baseline	113	12.7 (4.7)	86	13.4 (4.9)
	Change Score at 12weeks	29[a]	-0.64 (4.83)	78	-1.01 (4.31)
	Change Score at 6 months	29	-2.52 (3.31)	66	-2.07 (4.14)
	Emotional-focus coping; total		Mean (SD)		Mean (SD)
	baseline	113	20.6 (5.8)	86	21.3 (5.7)
	Change Score at 12weeks	29[a]	-0.05 (5.58)	78	-1.49 (4.31)
	Change Score at 6 months	29[a]	-1.32 (4.32)	66	-3.60 (4.54)
	Maladaptive coping		Mean (SD)		Mean (SD)
	baseline	113	18.2 (5.0)	86	19.0 (6.0)
	Change Score at 12weeks	29	-1.17 (2.96)	78	-1.99 (4.14)
	Change Score at 6 months	29	-0.36 (3.86)	66	-2.00 (3.67)
(Mikocka-Walus et al., 2015; Mikocka-Walus et al., 2016a)	Adaptive coping		Mean (SD)		Mean (SD)
	baseline	90	42.7 (12.8)	84	39.5 (11.3)
	6 months	51	42.1 (13.6)	65	37.1 (11.2)
	12 months	42	40.5 (12.9)	64	37.5 (11.7)
	24 months	31	43.5 (17.5)	45	41.1 (24.1)
	Maladaptive coping		Mean (SD)		Mean (SD)
	baseline	90	10.9 (3.6)	84	10.7 (3.7)
	6 months	51	9.8 (2.6)	65	10.5 (3.3)
	12 months	42	10.6 (3.7)	64	10.5 (3.6)
	24 months	31	11.6 (10.3)	45	12.2 (9.9)
	TTM Stage				
	Pre-contemplation		Mean (SD)		Mean (SD)
	baseline	90	4.5 (1.6)	84	4.4 (1.6)
	6 months	51	4.3 (1.9)	65	4.2 (1.9)
	12 months	42	4.2 (1.9)	64	4.7 (1.9)
	24 months	31	4.6 (2.2)	45	4.9 (2.9)
	Contemplation *		Mean (SD)		Mean (SD)
	baseline	90	6.7 (2.1)	84	6.3 (2.1)
	6 months	51	6.6 (1.9)	65	6.2 (2.1)
	12 months	42	6.6 (1.6)	64	6.4 (1.9)
	24 months	31	6.5 (2.1)	45	6.1 (2.7)
	Preparation		Mean (SD)		Mean (SD)
	baseline	90	6.3 (2.3)	84	5.7 (2.3)
	6 months	51	6.5 (2.4)	65	6.1 (2.2)
	12 months	42	6.4 (2.3)	64	6.1 (2.1)
	24 months	31	6.8 (2.1)	45	6.7 (3.1)
	Action		Mean (SD)		Mean (SD)
	baseline	90	5.8 (2.2)	84	5.5 (2.1)
	6 months	51	6.3 (2.3)	65	5.8 (2.3)
	12 months	42	6.1 (2.3)	64	5.9 (2.3)
	24 months	31	6.4 (2.1)	45	6.3 (3.3)
	Maintenance		Mean (SD)		Mean (SD)
	baseline	90	7.1(1.9)	84	7.2 (1.3)
	6 months	51	7.7 (1.7)	65	7.1 (1.9)
	12 months	42	7.3 (1.8)	64	7.3 (1.9)
	24 months	31	7.5 (1.6)	45	7.6 (2.4)

Note: * Range: 2–10 (higher scores mean greater agreement); a - the number of completers, such as data provided for completers only.

2.3.5.3.1 A meta-analysis of data on the levels of coping

Of two studies reporting the level of coping, one reported total maladaptive and total adaptive scores (Mikocka-Walus et al., 2015), whereas another study reported the results for total maladaptive coping, but adaptive coping was presented as two components of this score: problem-focus and emotional-focus coping (McCombie et al., 2016). One study reported this outcome at three and six months of follow-up (McCombie et al., 2016) and other at six, 12 and 24 months of follow-up. Therefore, only maladaptive coping scores from both studies at six months were combined (Figure 14).



	Intervention			Control				Mean Difference
Study or Subgroup	**Mean**	**SD**	**Total**	**Mean**	**SD**	**Total**	**Weight**	**IV, Random, 95% CI**
(McCombie, 2016)	-0.36	3.86	29	-2	3.67	66	46.2%	1.64 [-0.02, 3.30]
(Mikocka-Walus et al., 2015)	9.8	2.6	51	10.5	3.3	65	53.8%	-0.70 [-1.77, 0.37]
Total (95% CI)			**80**			**131**	**100.0%**	**0.38 [-1.91, 2.67]**

Heterogeneity: Tau² = 2.23; Chi² = 5.38, df = 1 (P = 0.02); I² = 81%
Test for overall effect: Z = 0.33 (P = 0.74)

Figure 14 Meta-analysis of maladaptive coping at 6 months of follow up.

There were significant levels of heterogeneity (Tau² = 2.23; Chi² = 5,38, df = 1 (P = 0.02); I² = 81%). Data from the study by McCombie et al., (2016) shows that the maladaptive score was worse in the control group, but this was based on the change from the baseline score only for completers and hence could be biased.

The pooled estimate comparing online CBT against the control group was 0.38 (95% CI: -1.91, 2.67), indicating that there was little or no evidence of a difference in total maladaptive coping between the two groups (p=0.74) (Figure 14).

2.3.5.4 Data synthesis and meta-analysis of the levels of stress

There was no significant difference in the level of stress between control and intervention groups reported in four studies (n=669, of which adolescent n=101) examining this outcome (Table 7) (Bonnert et al., 2017; Ljotsson et al., 2011b; McCombie et al., 2016; Mikocka-Walus et al., 2015; Mikocka-Walus et al., 2016a).

Table 7 Results of studies reporting the levels of stress

Study ID	outcome measure	results for the outcome measure			
		Treatment participants (n)	Treatment	Control participants (n)	Control
(Bonnert, 2017)[a]	PSS-10 pre-intervention post-intervention 6-Month follow-up	 47 47 47	Mean (SE) 16.23 (1.00) 13.68 (1.21) 12.91 (1.22)	 54 54 -*	Mean (SE) 16.11 (0.94) 13.14 (1.13) -
(Ljotsson et al., 2011b)	PSS-10 pre-intervention post-intervention 6-month follow-up	 98 95 87	Mean (SD) 17.3(7.6) 15.0(8.4) 15.5(8.8)	 97 93 82	Mean (SD) 17.2(6.5) 14.8(8.6) 16.0(7.8)
(McCombie, 2016)	PSS-10 *baseline* *Change Score at 12weeks* *Change Score at 6 months*	 113 29[b] 29[b]	Mean (SD) 16.6 (7.4) -1.81 (6.21) 1.51 (7.89)	 86 78 66	Mean (SD) 17.6 (7.1) -1.49 (5.61) 1.05 (7.12)
(Mikocka-Walus et al., 2015; Mikocka-Walus et al., 2016a)	RSRRS* *baseline* *6 months* *12 months* *24 months*	 90 51 42 31	Mean (SD) 638.3 (665.9) 474.2 (653.7) 301.3 (347.5) 338.7 (308.1)	 84 65 64 45	Mean (SD) 453.6 (490.5) 350.7 (403.4) 338.5 (364.2) 442.9 (551.1)

Note: PSS-10 - perceived stress questionnaire; RSRRS - Revised Social Readjustment Rating Scale; ** >300 high stress 150–299 moderate stress <150 low stress*; a- outcome measures with estimated means, SE (analysed intention to treat); b - the number of completers, such as data provided for completers only.

2.3.5.4.1 A meta-analysis of data reporting the levels of stress

Three studies assessed the level of stress, one at post-intervention (Ljotsson et al., 2011b), one at three months (McCombie et al., 2016), three at six months (McCombie et al., 2016; Mikocka-Walus et al., 2015; Mikocka-Walus et al., 2016a; Ljotsson et al., 2011b) and one at 12 and 24 months of follow-up (Mikocka-Walus et al., 2015; Mikocka-Walus et al., 2016a). Three studies reporting outcomes at 6 months could not be combined using the common effect measure due to the use of a different scale and a change score (McCombie et al., 2016). Therefore, two meta-analyses were performed, one where a different scale was used and raw data were available (Figure 15), and one where the same scale was used, but a mixture of a raw and change score data was used (Figure 16).

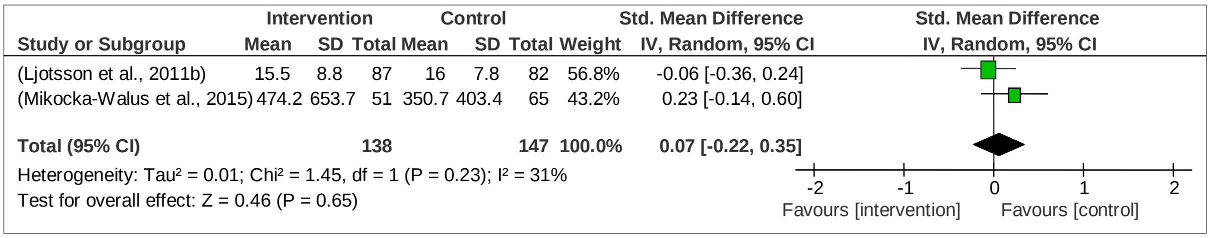


Figure 15 Meta-analysis of data reporting the level of stress at 6 months of follow-up 1.

There was a moderate levels of statistical heterogeneity in the data on the level of stress (Tau² = 0.01; Chi² = 1.45, df = 1 (P = 0.23); I² = 31%) and the pooled standardised mean difference was 0.07 (95% CI: -0.22, 0.35, p=0.65).

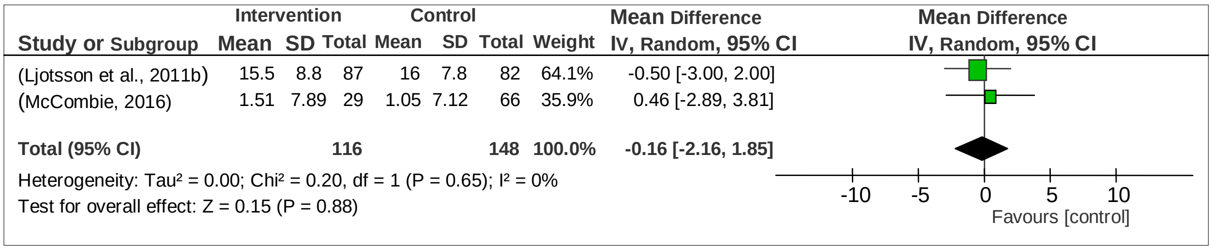


Figure 16 Meta-analysis on the level of stress at 6 months of follow-up 2.

There was little evidence of heterogeneity in the data on the level of stress (Tau^2 = 0.00; Chi^2 = 0.20, df = 1 (P = 0.65); I^2 = 0%). The pooled mean difference was -0.16 (95% CI: -2.16, 1.85, p=0.88).

Both meta-analyses showed little or no evidence of a difference between the intervention and control groups in the level of stress.

2.3.5.5 Data synthesis and meta-analysis of the levels of HRQoL

Of seven studies (n=619) that assessed HRQoL in IBS (Bonnert et al., 2017; Everitt et al., 2013; Hunt et al., 2009; Ljotsson et al., 2011a; Ljotsson et al., 2011b; Ljotsson et al., 2010; Oerlemans et al., 2011) (Table 8), one study examined adolescent population (n=101) (Bonnert et al., 2017) and showed significant improvement in this outcome at post-intervention assessment. Amongst studies in adult populations, one study showed no difference in HRQoL at post-intervention assessment or 3 months follow-up (Everitt et al., 2013). Three studies reported a significant improvement in HRQoL in favour of online CBT at post-intervention assessment (Ljotsson et al., 2011b; Ljotsson et al., 2010; Ljotsson et al., 2011a). One study stated significant improvement in IBS-QOL at post-intervention assessment but reported only an F statistic and p-value of <0.05 or the mean (SD) for completes only (Hunt et al., 2009).

Two studies (n=373) that reported HRQoL in IBD showed no significant improvement on this outcome at any of the points of follow-up (McCombie et al., 2016; Mikocka-Walus et al., 2015; Mikocka-Walus et al., 2016a). One study that measured this outcome using two scales did not find a significant difference between the intervention and control group on either of the scales (IBDQ and SF-12) at 12 weeks and 6 months follow up (Table 8) (McCombie et al., 2016). Other study showed that CBT improved HRQoL for patients with high scores on mental health subscales in a subgroup analysis at six months follow-up, but the longer-term effects were difficult to assess given the high attrition rate (Mikocka-Walus et al., 2015; Mikocka-Walus et al., 2016a).

Table 8 Results of studies reporting the levels of HRQoL

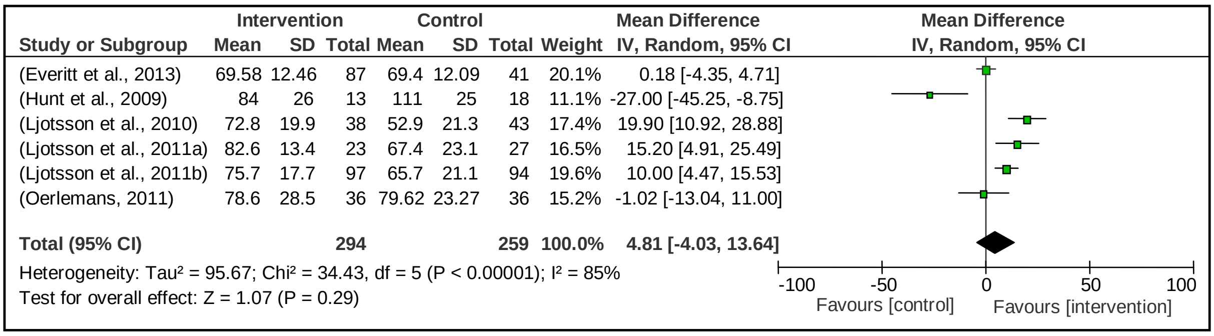
Study ID	outcome measure	results for the outcome measure			
		Treatment participants (n)	Treatment	Control participants (n)	Control
(Bonnert, 2017)[a]	PedsQL		Mean (SE)		Mean (SE)
	pre-intervention	47	71.28 (2.06)	54	74.90 (1.93)
	post-intervention	44	76.92 (2.11)	51	74.89 (1.99)
	6-Month follow-up	42	81.63 (2.17)	-*	-
(Everitt et al., 2013)	IBS-QOL total mean (95% CI) (n= 123)	43	*website* 71.6 (67.9-75.2)	41	69.4 (65.7-73.1)
	6 weeks	44	website + support 67.6 (63.9-71.3)		
	calculated total mean (SD)	87	69.577(12.46)	41	69.4 (12.088)
	significance p = 0.315	42	*website* 71.6 (67.2 - 76.1)	40	64.3 (59.8 – 68.9)
	12 weeks	42	website + support 69.5 (65.0 - 74.0)		
	significance p = 0.068				
	calculated total mean (SD)	84	70.55 (14.745)	40	64.3 (14.682)
(Hunt et al., 2009)	IBS-QOL		Mean (SD)		Mean (SD)
	pre-intervention	24[b]	122 (27)	25	123 (26)
	post-intervention	13[b]	84 (26)	18	111 (25)
	3-month follow-up	10	85 (23)	-*	-
(Ljotsson et al., 2011a)	IBS-QOL		Mean (SD)		Mean (SD)
	pre-intervention	30	67.4 (20.9)	31	76.1 (18.8)
	post-intervention	23	82.6 (13.4)	27	67.4 (23.1)
	12-month follow-up	20	87.6 (11.8)	-	-
(Ljotsson et al., 2011b)	IBS-QOL		Mean (SD)		Mean (SD)
	pre-intervention	98	57.1 (19.1)	97	55.5 (18.9)
	post-intervention	97	75.7 (17.7)	94	65.7 (21.1)
	6-month follow up	87	74.9 (20.8)	82	68.7 (19.0)
(Ljotsson et al., 2010)	IBS-QOL		Mean (SD)		Mean (SD)
	pre-intervention	42	52.2 (19.9)	43	53.8 (18.9)
	post-intervention	38	72.8 (19.9)	43	52.9 (21.3)
	follow up 3 months	38	74.6 (20.7)	-	-
(McCombie, 2016)	IBDQ		Mean (SD)		Mean (SD)
	baseline	113	163.6 (32.3)	86	160.5 (35.7)
	Change Score at 12weeks	29[b]	15.39 (22.97)	78	6.63 (25.21)
	Change Score at 6 months	29[b]	12.64 (26.93)	66	11.74 (29.52)
	HRQOL (SF-12 mental)		Mean (SD)		Mean (SD)
	baseline	113	45.2 (10.1)	86	44.4 (12.00)
	Change Score at 12weeks	29[b]	5.61 (9.32)	78	2.57 (8.40)
	Change Score at 6 month	29[b]	2.62 (12.72)	66	0.91 (9.77)
	HRQOL (SF-12 physical)		Mean (SD)		Mean (SD)
	baseline	113	47.4 (8.9)	86	43.5 (9.9)
	Change Score at 12weeks	29[b]	3.22 (9.19)	78	2.52 (7.50)
	Change Score at 6 months	29[b]	3.58 (9.30)	66	3.73 (8.87)
(Mikocka-Walus et al., 2015; Mikocka-Walus et al., 2016a)	HRQOL (SF) mental QoL		Mean (SD)		Mean (SD)
	baseline	90	44.8 (11.4)	84	48.1 (11.5)
	6 months	51	48.3 (9.2)	65	48.1 (11.9)
	12 months	42	45.5 (11.1)	64	48.3 (11.5)
	24 months	31	49.8 (8.8)	45	48.8 (10.9)
	HRQOL (SF) physical QoL		Mean (SD)		Mean (SD)
	baseline	90	46.7 (9.3)	84	47 (10.3)
	6 months	51	46.7 (10.3)	65	47.2 (9.8)
	12 months	42	48.3 (10.3)	64	48.3 (10.1)
	24 months	31	48.8 (10.9)	45	48.8 (8.5)
(Oerlemans, 2011)	IBS-QOL		Mean (95% CI)		Mean (95% CI)
	4 weeks	36	78.60 (69.29-87.91)	36	79.62 (72.02-87.22)
	3-months	26	78.46 (69.08-87.85)	35	80.21 (72.01-88.41)
			Mean (SD)		Mean (SD)
	calculated SD at 4 weeks	36	78.60 (28.5)	36	79.62 (23.265)
	calculated SD at 3 months	26	78.46 (24.42)	35	80.21 (24.75)

Note: IBS–QOL - IBS Quality of Life Impairment; PedsQL - Paediatric Quality of Life Inventory; IBDQ - Inflammatory Bowel Disease Questionnaire; HRQOL (SF) - health-related quality of life short form; a - outcome measures with estimated means, SE (analysed intention to treat); b - the number of completers, such as data provided for completers only.

2.3.5.5.1 A meta-analysis of data on the levels of HRQoL

A meta-analysis of data on the levels of HRQoL at post-intervention assessment

Six studies reported quality of life at post-intervention assessment and used the same scale (IBS-QOL) hence were combined in the meta-analysis (Figure 17). The result from two intervention groups: online CBT and online CBT plus support were combined (Table 8) in the study by Everitt et al. (2013).



	Intervention			Control				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
(Everitt et al., 2013)	69.58	12.46	87	69.4	12.09	41	20.1%	0.18 [-4.35, 4.71]
(Hunt et al., 2009)	84	26	13	111	25	18	11.1%	-27.00 [-45.25, -8.75]
(Ljotsson et al., 2010)	72.8	19.9	38	52.9	21.3	43	17.4%	19.90 [10.92, 28.88]
(Ljotsson et al., 2011a)	82.6	13.4	23	67.4	23.1	27	16.5%	15.20 [4.91, 25.49]
(Ljotsson et al., 2011b)	75.7	17.7	97	65.7	21.1	94	19.6%	10.00 [4.47, 15.53]
(Oerlemans, 2011)	78.6	28.5	36	79.62	23.27	36	15.2%	-1.02 [-13.04, 11.00]
Total (95% CI)			**294**			**259**	**100.0%**	**4.81 [-4.03, 13.64]**

Heterogeneity: Tau² = 95.67; Chi² = 34.43, df = 5 (P < 0.00001); I² = 85%

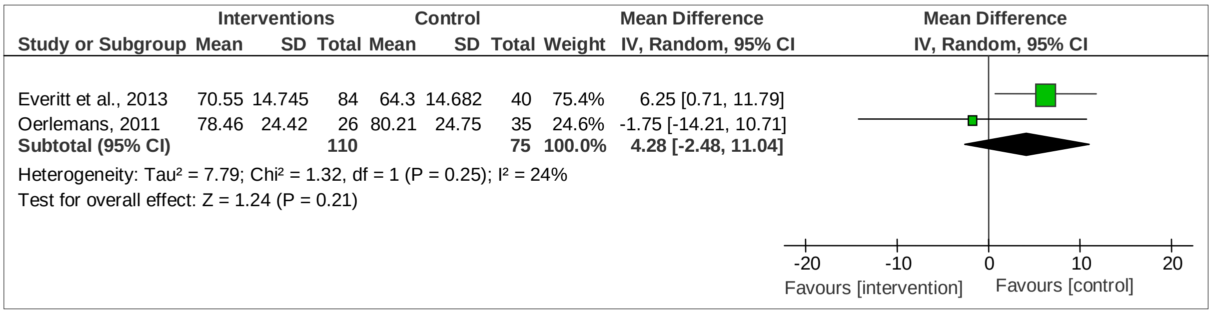
Test for overall effect: Z = 1.07 (P = 0.29)

Figure 17 Meta-analysis on the level of IBS-QOL at post-intervention assessment.

There was significant levels of heterogeneity (Tau² = 95.67; Chi² = 34.43, df = 5 (P < 0.00001); I² = 85%). The results demonstrate an effect in favour of the intervention group but this differences was not-statistically significant (p=0.29). The pooled mean difference was 4.81 (95% CI: -4.03, 13.64).

A meta-analysis of data on the levels of HRQoL at 3 months of follow-up

Three studies reported HRQoL at 3 months of follow-up (Everitt et al., 2013; Oerlemans et al., 2011; McCombie et al., 2016). One of them uses change from the baseline score and different measure of outcome (McCombie et al., 2016) making possible to combine in the meta-analysis using a common measure of effect only two studies (Figure 18).



	Interventions			Control				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
Everitt et al., 2013	70.55	14.745	84	64.3	14.682	40	75.4%	6.25 [0.71, 11.79]
Oerlemans, 2011	78.46	24.42	26	80.21	24.75	35	24.6%	-1.75 [-14.21, 10.71]
Subtotal (95% CI)			**110**			**75**	**100.0%**	**4.28 [-2.48, 11.04]**

Heterogeneity: Tau² = 7.79; Chi² = 1.32, df = 1 (P = 0.25); I² = 24%

Test for overall effect: Z = 1.24 (P = 0.21)

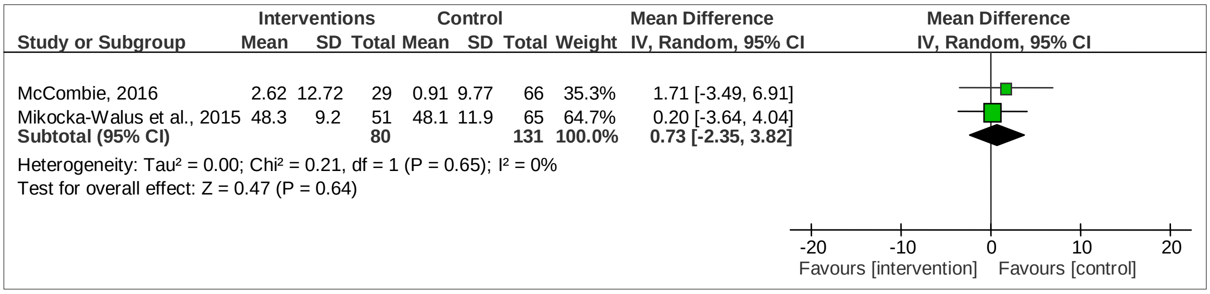
Figure 18 Meta-analysis on the level of IBS-QOL at 3 months of follow-up.

There was low level of heterogeneity between the studies on IBS-QOL at three months of follow-up (Tau² = 7.79; Chi² = 1.32, df = 1 (P = 0.25); I² = 24%). A study by Everitt et al., (2013) carried bigger weight and had narrow CI, hence reflects the fact that the study has better accuracy than the other studies and it demonstrated the quality of life was better in the intervention group. However, this study had a discrepancy between the number of participants in the flowchart and the text.

The result of the meta-analysis showed that there was little or no evidence of a difference in QoL between CBT and control group (4.28, 95% CI: -2.48, 11.04, p=0.21).

A meta-analysis of data on the levels of HRQoL at 6 months of follow-up

Two studies reported QoL at 6 months follow-up could not be combined, such as they used different scales (IBS-QOL and IBDQ) and provided a raw and change from the baseline score (McCombie et al., 2016; Ljotsson et al., 2011b) and two studies reported HRQoL using two subscales (SF-12 mental) and (SF-12 physical) at 6 months follow-up, hence two meta-analyses were performed to investigate online CBT effect on physical and mental HRQoL (Figure 19, Figure 20).



	Interventions			Control				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
McCombie, 2016	2.62	12.72	29	0.91	9.77	66	35.3%	1.71 [-3.49, 6.91]
Mikocka-Walus et al., 2015	48.3	9.2	51	48.1	11.9	65	64.7%	0.20 [-3.64, 4.04]
Subtotal (95% CI)			**80**			**131**	**100.0%**	**0.73 [-2.35, 3.82]**

Heterogeneity: Tau² = 0.00; Chi² = 0.21, df = 1 (P = 0.65); I² = 0%
Test for overall effect: Z = 0.47 (P = 0.64)

Figure 19 Meta-analysis on HRQoL (mental) at 6 months of follow-up.

There was little evidence of heterogeneity in the data on mental component of HRQoL (Tau² = 0.00; Chi² = 0.21, df = 1 (P = 0.65); I² = 0%).

The meta-analysis showed little or no evidence of a difference between the intervention and control groups in the mean mental component score for HRQoL (0.73, 95% CI:-2.35, 3.82, p=0.64) (Figure 19).

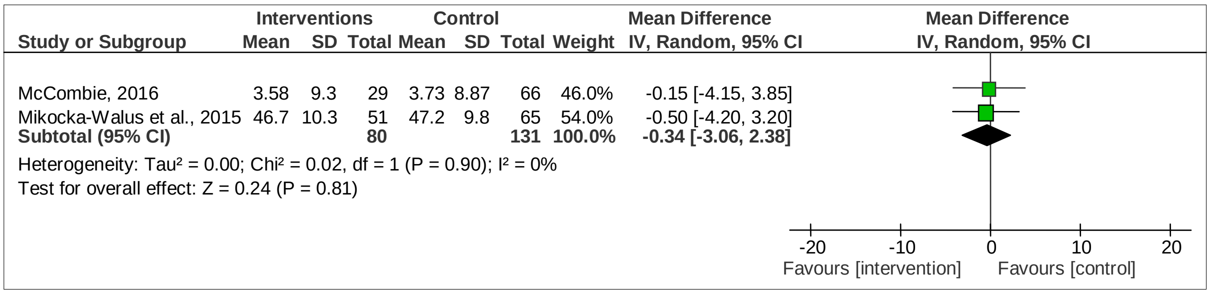


Figure 20 Meta-analysis on HRQoL (physical) at 6 months of follow-up.

There was little evidence of heterogeneity on data for HRQoL (physical) (Tau² = 0.00; Chi² = 0.02, df = 1 (P = 0.90); I² = 0%). The meta-analysis showed little or no evidence of a difference between the intervention and control groups in the physical component score of HRQoL (-0.34, 95% CI: -3.06, 2.28, p=0.81) (Figure 20).

2.3.5.6 Data synthesis and meta-analysis of the studies reporting the related outcomes

Eight studies reported related outcomes (Table 9).

Table 9 Results of studies reporting the related outcomes

Study ID	outcome measure	results for the outcome measure			
		Treatment participants (n)	Treatment	Control participants (n)	Control
(Andersson et al., 2011), (Ljotsson et al., 2010)	Total (incl. intervention) costs post-intervention follow up 3 month 12 month	 38 38 37	Annual per capita cost $ (SE) 16,988 (3068) 15,736 (2645) 17,382 (3038)	 43 43(CBT) 39	Annual per capita cost $ (SE) 16,872 (2720) - -
	Work cutback post-intervention Follow up 3 month 12 month	 38 38 37	$ (SE) 1,097 (292) 1,262 (323) 1,362 (402)	 43 43(CBT) 39	$ (SE) 2,945 (734) - -
	Workloss post-intervention follow up 3 month 12 month	 38 38 37	$ (SE) 10,086 (2567) 9,561 (2511) 12,314 (2951)	 43 43(CBT) 39	$ (SE) 9,674 (2505) - -
	Indirect non-medical costs post-intervention follow up 3 month 12 month	 38 38 37	$ (SE) 11,227 (2544) 11,324 (2478) 13,677 (2906)	 43 43(CBT) 39	$ (SE) 12,619 (2482) - -
	Direct non-medical costs post-intervention follow up 3 month 12 month	 38 38 37	$ (SE) 958 (449) 735 (330) 371 (131)	 43 43(CBT) 39	$ (SE) 571 (305) - -
	Direct medical costs post-intervention follow up 3 month 12 month	 38 38 37	$ (SE) 3,222 (756) 2,096 (445) 1,754 (450)	 43 43(CBT) 39	$ (SE) 3,547 (790) - -
	VSI pre-intervention post-intervention follow up 3 months	 42 38 38	Mean (SD) 44.7 (15.6) 30.2 (17.8) 27.1 (18.1)	 43 43 -*	Mean (SD) 43.3 (17.5) 41.9 (18.7) -
	Sheehan Disability Scales pre-intervention post-intervention	 42 38	Mean (SD) 12.7 (7.4) 7.5 (7.4)	 43 43	Mean (SD) 11.8 (8.2) 11.4 (9.0)

Study ID	outcome measure	results for the outcome measure				
		Treatment participants (n)	Treatment		Control participants (n)	Control
(Bonnert, 2017)b	School absence a		Mean (SE)			Mean (SE)
	pre-intervention	47	1.55 (0.15)		54	1.43 (0.14)
	post-intervention	47	1.04 (0.16)		54	1.31 (0.15)
	follow-up 6 months	47	0.82 (0.15)		-*	-
	VSI a		Mean (SE)			Mean (SE)
	pre-intervention	47	32.28 (2.53)		54	28.30 (2.36)
	post-intervention	47	22.72 (2.64)		54	27.49 (2.46)
	follow-up 6 months	47	16.63 (2.52)		-*	-
	Pain frequency a		Mean (SE)			Mean (SE)
	pre-intervention	47	4.25 (0.26)		54	4.04 (0.25)
	post-intervention	47	3.19 (0.31)		54	3.66 (0.29)
	follow-up 6 months	47	2.59 (0.32)		-*	-
	Faces Pain Scale-Revised a		Mean (SE)			Mean (SE)
	pre-intervention	47	5.85 (0.30)		54	5.72 (0.28)
	post-intervention	47	4.53 (0.37)		54	5.53 (0.33)
	follow-up 6 months	47	4.41 (0.41)		-*	-
	CSI-24 (parents rated)		Mean (SE)			Mean (SE)
	pre intervention	47	17.78 (1.26)		54	17.08 (1.17)
	post intervention	47	12.42 (1.20)		54	16.36 (1.11)
	follow-up 6 months	47	13.47 (1.14)		-*	-
	CSQ a	47	83% (n=39) good or excellent treatment; 91% (n=43) good or excellent therapist's support; 81% (n=38) satisfied or very satisfied with the overall intervention.			
	IBS - BRQ a		Mean (SE)			Mean (SE)
	pre-intervention	47	79.80 (3.38)		54	73.55 (3.16)
	post-intervention	47	58.70 (3.92)		54	65.27 (3.64)
	follow-up	47	54.50 (3.27)		-*	-
	Medication use a		Mean (SE)			Mean (SE)
	pre-intervention	47	0.77 (0.15)		54	0.67 (0.14)
	post-intervention	47	0.41 (0.14)		54	0.75 (0.13)
	follow-up	47	0.34 (0.13)		-*	-
Everitt et al., 2013)	PEQ Enablement score	113	n (%) website	n (%) website+support		n (%)
	follow-up 6 weeks					
	0		7 (18.4)	4 (10.5)		21 (56.8)
	1-2		7 (18.4)	5 (13.2)		4 (10.8)
	3-5		13 (34.2)	15 (39.5)		7 (18.9)
	6-12		11 (28.9)	14 (36.8)		5 (13.5)
	12 weeks follow-up					
	0		7 (18.4)	4 (10.5)		21 (56.8)
	1-2		7 (18.4)	5 (13.2)		4 (10.8)
	3-5		13 (34.2)	15 (39.5)		7 (18.9)
	6-12		11 (28.9)	14 (36.8)		5 (13.5)
	SGA of Relief		n (%) website	n (%) website + support		n (%)
	follow-up 12 weeks					
	responders		16 (45.7)	24 (63.2)		12 (32.4)
	non-responders		19 (54.3)	14 (36.8)		25 (67.6)
(Hunt et al., 2009)	ASI Mean (SD)		Mean (SD)			Mean (SD)
	pre-intervention	28b	2.9 (0.91)		26	2.7 (0.99)
	post-intervention	13b	1.9 (0.93)		18	2.5 (0.95)
	follow-up	10b	1.5 (0.59)		-	-
	ASI-Non-GI Mean (SD)		Mean (SD)			Mean (SD)
	pre-intervention	28b	2 (0.83)		26	1.92 (0.90)
	post-intervention	13b	1.4 (0.69)		18	1.96 (0.94)
	follow-up	10b	1.2 (0.41)		-	-
	CPSQ-GI		Mean (SD)			Mean (SD)
	pre intervention	19b	2.1 (0.31)		18	2.1 (0.57)
	post intervention	6b	1.25 (0.39)		9	2.1 (0.56)
	follow-up	10b	1.5 (0.32)		-	-
	CPSQ-Non GI		Mean (SD)			Mean (SD)
	pre intervention	19b	1.5 (0.31)		18	1.4 (0.35)
	post intervention	6b	1.2 (0.16)		9	1.6 (0.40)
	follow-up	10b	1.3 (0.20)		-	-
(Ljotsson et al., 2011a)	VSI Mean (SD)		Mean (SD)			Mean (SD)
	pre-intervention	30	32.5 (18.0)		31	27.5 (16.3)
	post-intervention	23	14.1 (15.1)		27	26.2 (17.9)
	12-month follow-up	20	15.5 (15.9)		-*	-

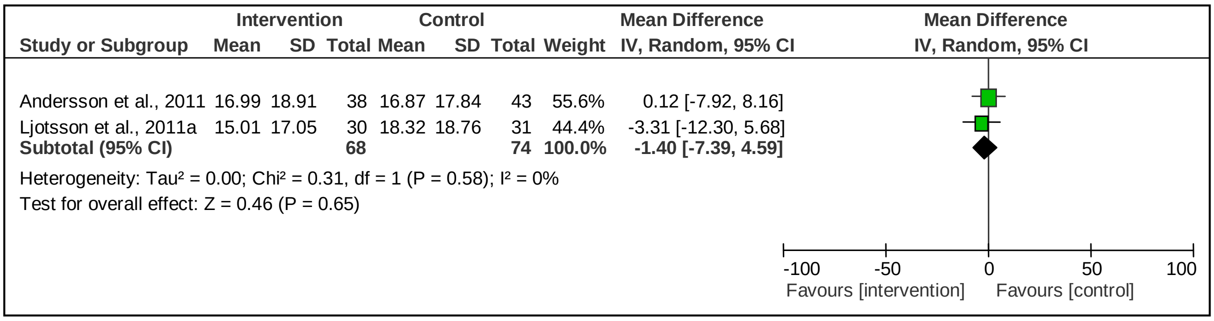
Study ID	outcome measure	results for the outcome measure			
		Treatment participants (n)	Treatment	Control participants (n)	Control
	Total (incl. intervention costs)		Mean (SE)		Mean (SE)
	pre-intervention	30	17808 (3866)	31	15542 (3029)
	post-intervention	30	15014 (3112)	31	18323 (3370)
	12-month follow-up	24	15871 (3343)	-*	-
	Sick-leave		Mean (SE)		Mean (SE)
	pre-intervention	30	3492 (1531)	31	5547 (1439)
	post-intervention	30	3028 (940)	31	6295 (1698)
	12-month follow-up	24	2816 (900)	-*	-
	Unemployment		Mean (SE)		Mean (SE)
	pre-intervention	30	10204 (3435)	31	7054 (2937)
	post-intervention	30	8747 (3248)	31	8465 (3155)
	Follow up	24	8747 (3248)	-	-
	Work cutback		Mean (SE)		Mean (SE)
	pre-treatment	30	376 (138)	31	211 (78)
	post-treatment	30	515 (233)	31	998 (287)
	12-month follow-up	24	426 (167)	-*	-
	Direct medical costs		Mean (SE)		Mean (SE)
	pre-intervention	30	2487 (633)	31	2115 (689)
	post-intervention	30	1148 (301)	31	1453 (417)
	12-month follow-up	24	1868 (566)	-	-
	Direct non-medical costs		Mean (SE)		Mean (SE)
	pre-intervention	30	504 (265)	31	88 (42)
	post intervention	30	150 (105)	31	338 (243)
	12-month follow-up	24	405 (177)	-*	-
	Sheehan Disability Scales		Mean (SD)		Mean (SD)
	pre-treatment	30	11.9 (8.1)	31	8.7 (6.3)
	Post-treatment	23	6.4 (6.7)	27	7.8 (7.6)
	12-month follow-up	20	5.2 (6.6)	-*	-
(Ljotsson et al., 2011b)	VSI		Mean (SD)		Mean (SD)
	pre-intervention	98	43.1 (14.3)	97	42.7 (15.6)
	post intervention	96	24.9 (16.9)	91	30.5 (16.8)
	6-month follow-up	85	23.1 (16.8)	81	29.4 (17.5)
(McCombie, 2016)	SFQ		Mean (SD)		Mean (SD)
	at baseline	113	5.8 (3.6)	86	6.7 (3.7)
	Change Score at 12weeks	29b	-0.18 (2.60)	78	-0.86 (2.23)
	Change Score at 6 months	29b	-0.03 (2.71)	66	-0.76 (2.87)
(Oerlemans, 2011)	Abdominal pain		Mean (95% CI)		Mean (95% CI)
	4 weeks	36	1.46 (1.03-1.90)	36	1.89 (1.44 - 2.33)
	3-months	26	1.75 (1.31-2.19)	35	2.03 (1.55 - 2.50)
	PCS		Mean (95% CI)		Mean (95% CI)
	4 weeks	36	23.57 (18.44–28.70)	36	24.13 (19.03–29.23)
	3-months	26	22.21 (16.83–27.59)	35	23.10 (18.13–28.07)
	CSFBD		Mean (95% CI)		Mean (95% CI)
	4 weeks	36	70.83 (52.16–89.49)	36	75.90 (59.21–92.59)
	3-months	26	68.74 (49.13–88.34)	35	72.08 (54.39–89.77)

Note: a - the outcomes presented are adolescent-rated outcome measures; b- outcome measures with estimated means, SE (analysed intention to treat); TIC-P - Trimbos and Institute of Medical Technology Assessment Cost Questionnaire for Psychiatry; VSI - Visceral sensitivity index; ASI = Anxiety Sensitivity Index. CSI-24 - Children's Somatisation Inventory- parents version; CSQ - Client Satisfaction Questionnaire; PEQ - Patient Enablement Questionnaire; IBS - BRQ - behavioural responses questionnaire; SGA of Relief - Subjects Global Assessment of Relief; CPSQ - The Consequences of Physical Sensations Questionnaire; SFQ - Social Functioning Questionnaire, EPQ - Eysenck Personality Questionnaire (Brief Version) for measuring neuroticism; PCS - Pain Catastrophizing Scale; CSFBD - The Cognitive Scale for Functional Bowel Disorders; *- patients were crossed over to active treatment; b - the number of completers, such as data provided for completers only.

2.3.5.6.1 A meta-analysis of the related outcomes data

2.3.5.6.1.1 A meta-analysis of the cost-effectiveness data

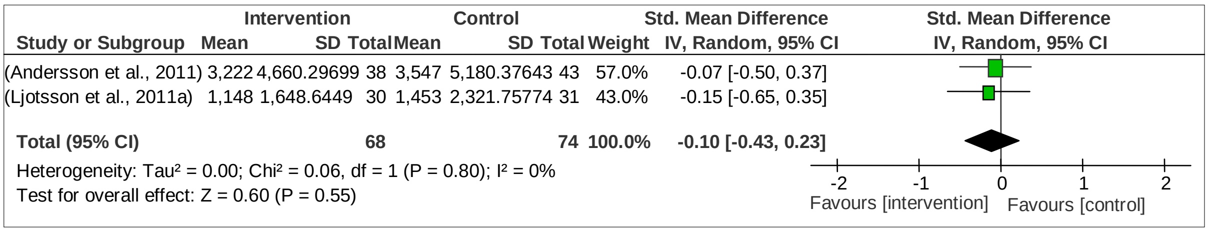
The cost-effectiveness at post-intervention was assessed in two studies (Ljotsson et al., 2011a; Andersson et al., 2011). The random-effect model was used and SMD as a measure of effect in the meta-analysis. Three meta-analyses were performed on the total cost (include the cost of intervention), direct medical cost and direct non-medical cost (Figure 21, Figure 22, Figure 23).



Study or Subgroup	Intervention Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Andersson et al., 2011	16.99	18.91	38	16.87	17.84	43	55.6%	0.12 [-7.92, 8.16]
Ljotsson et al., 2011a	15.01	17.05	30	18.32	18.76	31	44.4%	-3.31 [-12.30, 5.68]
Subtotal (95% CI)			**68**			**74**	**100.0%**	**-1.40 [-7.39, 4.59]**

Heterogeneity: Tau² = 0.00; Chi² = 0.31, df = 1 (P = 0.58); I² = 0%
Test for overall effect: Z = 0.46 (P = 0.65)

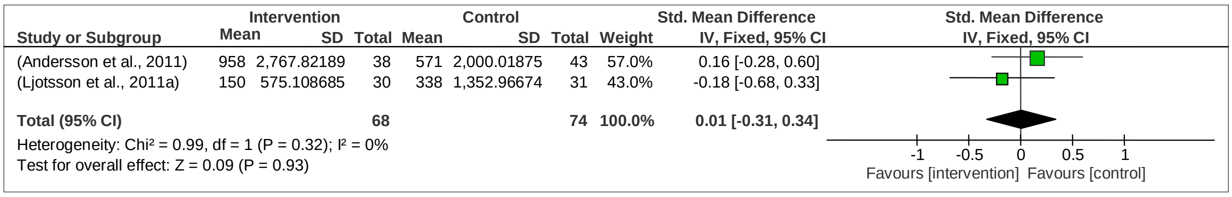
Figure 21 Meta-analysis on the total cost (include intervention) at post-intervention.



Study or Subgroup	Intervention Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
(Andersson et al., 2011)	3,222	4,660.29699	38	3,547	5,180.37643	43	57.0%	-0.07 [-0.50, 0.37]
(Ljotsson et al., 2011a)	1,148	1,648.6449	30	1,453	2,321.75774	31	43.0%	-0.15 [-0.65, 0.35]
Total (95% CI)			**68**			**74**	**100.0%**	**-0.10 [-0.43, 0.23]**

Heterogeneity: Tau² = 0.00; Chi² = 0.06, df = 1 (P = 0.80); I² = 0%
Test for overall effect: Z = 0.60 (P = 0.55)

Figure 22 Meta-analysis on direct medical cost at post-intervention.



Study or Subgroup	Intervention Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
(Andersson et al., 2011)	958	2,767.82189	38	571	2,000.01875	43	57.0%	0.16 [-0.28, 0.60]
(Ljotsson et al., 2011a)	150	575.108685	30	338	1,352.96674	31	43.0%	-0.18 [-0.68, 0.33]
Total (95% CI)			**68**			**74**	**100.0%**	**0.01 [-0.31, 0.34]**

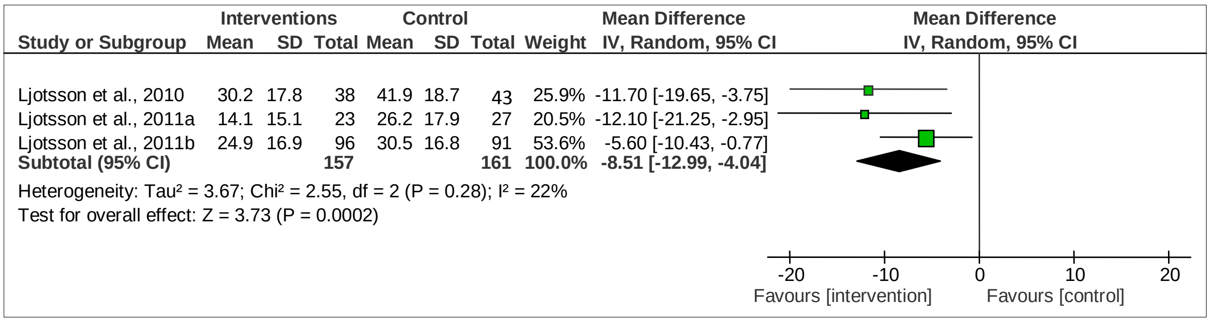
Heterogeneity: Chi² = 0.99, df = 1 (P = 0.32); I² = 0%
Test for overall effect: Z = 0.09 (P = 0.93)

Figure 23 Meta-analysis on direct non-medical cost at post-intervention.

There was little evidence of heterogeneity in all three of the meta-analysis. All three meta-analyses showed little or no evidence of a difference between the intervention and control groups in direct no-medical cost (p=0.93), total cost (include the cost of the intervention) (p=0.66) and direct medical cost (p=0.55).

2.3.5.6.1.2 A meta-analysis of the visceral sensitivity data

Three studies by the same author assessed visceral sensitivity at post-intervention assessment (Ljotsson et al., 2010; Ljotsson et al., 2011a; Ljotsson et al., 2011b) and used the same scale to measure this outcome.



Study or Subgroup	Interventions Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Ljotsson et al., 2010	30.2	17.8	38	41.9	18.7	43	25.9%	-11.70 [-19.65, -3.75]
Ljotsson et al., 2011a	14.1	15.1	23	26.2	17.9	27	20.5%	-12.10 [-21.25, -2.95]
Ljotsson et al., 2011b	24.9	16.9	96	30.5	16.8	91	53.6%	-5.60 [-10.43, -0.77]
Subtotal (95% CI)			**157**			**161**	**100.0%**	**-8.51 [-12.99, -4.04]**

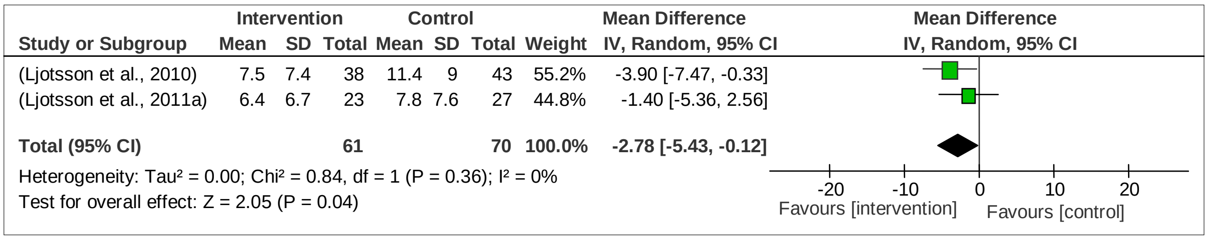
Heterogeneity: Tau² = 3.67; Chi² = 2.55, df = 2 (P = 0.28); I² = 22%
Test for overall effect: Z = 3.73 (P = 0.0002)

Figure 24 Meta-analysis of data reporting VSI at post-intervention assessment.

There was a low level of heterogeneity (Tau² = 3.67; Chi² = 2.55, df = 2 (P = 0.28); I² = 22%). The results demonstrate an effect in favour of the intervention group in VSI and this differences was statistically significant (p=0.0002). The pooled mean difference was -8.51 (95% CI: -12.99, -4.04) (Figure 24).

2.3.5.6.1.3 A meta-analysis of the Sheehan Disability Scales data

Two studies which examined the Sheehan Disability Scales at post-intervention assessment (Ljotsson et al., 2010; Ljotsson et al., 2011a) were included in the meta-analysis (Figure 25).



Study or Subgroup	Intervention Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
(Ljotsson et al., 2010)	7.5	7.4	38	11.4	9	43	55.2%	-3.90 [-7.47, -0.33]
(Ljotsson et al., 2011a)	6.4	6.7	23	7.8	7.6	27	44.8%	-1.40 [-5.36, 2.56]
Total (95% CI)			**61**			**70**	**100.0%**	**-2.78 [-5.43, -0.12]**

Heterogeneity: Tau² = 0.00; Chi² = 0.84, df = 1 (P = 0.36); I² = 0%
Test for overall effect: Z = 2.05 (P = 0.04)

Figure 25 Meta-analysis of data of Sheehan Disability Scales at post-intervention.

The evidence of heterogeneity was low (Tau² = 0.00; Chi² = 0.84, df = 1 (P = 0.36); I² = 0%). Pooled mean difference (-2.78, 95% CI: -5.43, -0.12, p=0.04) showed that there were a statistically significant difference in favour of intervention. This means that people in the online CBT group experienced less symptom induced disability, compared to the control group.

2.3.5.7 The long-term follow-up

Only one author (Mikocka-Walus et al., 2016a) reported follow-up over 12 months, making meta-analysis impossible.

This study shows that CBT did not significantly change disease activity (Table 4), mental health (Table 5), coping (Table 6) or quality of life (Table 8). At 24 months, there was a significant attrition rate (67% in the intervention group and 46 % in the control group were lost to follow-up).

2.4 Discussion

2.4.1 Principal Findings

This is the first systematic review with a meta-analysis which has addressed the usefulness of online psychological interventions for mental and physical outcomes in gastrointestinal diseases. The review firstly demonstrates little evidence that online CBT improves IBS symptoms severity. However, four out of five studies that examined IBS symptoms severity showed statistical significance in favour of online CBT (Hunt et al., 2009; Ljotsson et al., 2010; Ljotsson et al., 2011a; Ljotsson et al., 2011b). One study (Everitt et al., 2013) (n=135), which carried the second biggest weight, showed findings in the opposite direction, making the overall difference not statistically significant. This study had a slight discrepancy between the number of participants in the text of the article and the CONSORT diagram. Another study reported data only for the completers (Hunt et al., 2009). A repeated meta-analysis without these two studies showed a significant improvement in IBS symptom severity at post-intervention. Therefore, future research is needed to clarify this result.

Another systematic review which assessed the effectiveness of online CBT on IBS symptom severity showed no significant beneficial effect (Ford et al., 2014); this was based on two studies which were also included in the current systematic review (Ljotsson et al., 2010; Hunt et al., 2009). The previous review (Ford et al., 2014) showed that CBT, dynamic psychotherapy, hypnotherapy, and multicomponent psychological therapy, delivered F2F or using the telephone, were all more effective compared to control groups. Consequently, the mode of delivery appears to make a difference in the level of effectiveness of the intervention. The development of the new or improved online CBT programs might enhance the effectiveness of the intervention.

Regarding the disease activities in IBD, there was little or no evidence that online CBT affected this outcome, which is consistent with other systematic reviews (Gracie et al., 2017; Timmer et al., 2011). The studies included in the systematic review Chapter 2 recruited the unselected patients with IBD however one of these trials (Mikocka-Walus et al., 2015) also conducted a post-hoc analysis on a subpopulation of patients suggesting that CBT might be beneficial for patients at risk of suboptimal outcomes rather than the unselected IBD patients (Mikocka-Walus et al., 2015). Conducting an individual participant data meta-analysis could clarify if the interventions work across these subgroups in other studies but was not feasible in this review due to the lack of access to the raw data. Future studies should target these subgroups of patients to explore whether this result holds.

Further, this review demonstrated that there was little or no evidence that online CBT is effective in improving the levels of anxiety and depression, stress, maladaptive coping, HRQoL, in patients with IBD and IBS. Also, there was little or no evidence of the cost-effectiveness of online CBT intervention. These results are contradictory with a recent systematic review by Gracie et al., (2017) which showed that depression scores and quality of life in IBD patients might slightly be improved in the short-term after psychological therapy intervention, particularly CBT and identify the efficacy gap between online and F2F psychotherapy modalities. This suggests that human contact might be necessary for psychotherapy to improve the outcomes. Combining online and F2F approaches have been found to increase the effectiveness and cost-effectiveness of psychological interventions and to reduce the attrition rates (Newman et al., 2011; Erbe et al., 2017). Therefore, the researchers should consider a combination of F2F and online intervention during the design of future trials.

Of relevance, two previous systematic reviews on the effect of online interventions in gastroenterology (Knowles and Mikocka-Walus, 2014; Jackson et al., 2016) showed that online disease management improves a variety of disease outcomes such as medication adherence, disease activity, number of acute visits and healthcare costs, among others. However, the findings from the current review show little or no evidence of the effectiveness of online psychotherapy on physical or mental health outcomes or cost-effectiveness. This may suggest that disease management could be more suited to online delivery than psychotherapy though more good quality studies are needed.

Furthermore, findings from present review provide some preliminary evidence that online CBT may be an effective intervention for gastrointestinal symptom-specific anxiety as measured on the VSI scale and symptom induced disability as measured on the Sheehan Disability Scales. Both these findings came from the studies conducted by the same author (Ljotsson et al., 2010; Ljotsson et al., 2011a; Ljotsson et al., 2011b), hence the generalisability of the result could be questionable and the future studies should confirm this observation (Higgins et al., 2003).

2.4.2 Limitations of the studies included in the review and recommendations for future studies

There are several important issues identified in the previous studies which should be addressed by future research to improve the quality of evidence base around the efficacy of online psychotherapy in gastroenterological conditions. First, the review was mainly based on the comparisons at post-intervention, and long-term impact of online CBT is not known, with only one author reporting outcomes after 12 months of follow-up (Mikocka-Walus et al., 2016a). CBT aims to teach patients to be their own therapists to apply ideas and understanding of the principal of CBT after the intervention ends (Beck and Beck, 2011). To modify very firm dysfunctional beliefs and patterns of behaviour and maintain stabilisation, some patients might require over a year of therapy (Beck and Beck, 2011). A recent trial showed long-term clinical and cost-effectiveness of CBT in addition to usual care that includes antidepressants for certain group of people with depression who were unresponsive to drug therapy (Wiles et al., 2016). Long-term follow-up is necessary to understand the impact of online psychotherapy in GI disorders in the longer term.

Further, participants in the control groups in most of the included studies were on a wait-list (Bonnert et al., 2017; Andersson et al., 2011; Ljotsson et al., 2010; Ljotsson et al., 2011a; Hunt et al., 2009) and were crossed over to treatment after the assessment, when the intervention group completed the treatment (Hunt et al., 2009; Ljotsson et al., 2011a; Ljotsson et al., 2010; Bonnert et al., 2017; Andersson et al., 2011) or participants received multiple interventions (Everitt et al., 2013). These factors could affect the outcomes in the control groups due to the expectation of recovery. To limit this effect, standard care in the control groups should be chosen in future studies.

Most studies were inconsistent with the reporting outcomes. One study had a discrepancy between the numbers of participants in the CONSORT diagram and the numbers provided in the text, and it was unclear what was the number of participants per arm for several reported outcomes (Everitt et al., 2013). We contacted the authors, but they could not access the trial data and clarify the numbers. One study used change scores rather than follow-up scores (McCombie et al., 2016). Two studies reported outcomes for completers of the online intervention programme only (McCombie et al., 2016; Hunt et al., 2009). Future studies should present the outcomes in the format facilitating meta-analysis (n, means, SD or mean difference with associated 95% confidence intervals).

Sample sizes varied in the studies from 54 (Hunt et al., 2009) to 199 (McCombie et al., 2016), with high dropout rates. The largest study had the highest attrition rate (McCombie et al., 2016). To address this issue, the researchers should focus on the reduction of attrition. The reduction of attrition could be achieved by introducing a follow-up booster session of online CBT. CBT with a booster session has been found to be more effective and more sustainable for mood and anxiety disorders than CBT interventions without a booster session (Gearing et al., 2013). Initiating partial contact with the psychologist can build the working alliance and hence encourage patients to comply with the online CBT programme. There is evidence that the working alliance between the therapist and the patients receiving online CBT for depression can be as good as in F2F psychotherapy (Preschl, Maercker and Wagner, 2011). Also, the dropout rate for patients with depression is significantly higher in CBT than in other psychotherapies (Cuijpers et al., 2008). Consistently, future trials of online psychotherapies other than CBT in gastroenterology populations are warranted.

Although all studies overall met the Cochrane Risk of Bias Tool for randomised controlled trials criteria for moderate risk of bias, one of them did not use allocation concealment and was thus considered to be at high risk of bias (McCombie et al., 2016). An inadequately concealed allocation could be subject to exaggerated estimates of intervention effect (Higgins and Green, 2011). Future studies should use allocation concealment during randomisation.

All studies were considered to have a high risk of performance and detection bias. It is often impossible to blind patients and the personnel in psychotherapy trials. Nevertheless, the knowledge of the intervention does not necessarily result in a low-quality study (Higgins and Green, 2011). Some authors attempted to partially blind the participants (Mikocka-Walus et al., 2015; Ljotsson et al., 2011b) or the researchers who rated the scales to the symptom severity (Hunt et al., 2009) (Table 3). Future studies should use blinding of outcome assessors (the assessors could be masked to therapy), which is possible but rarely used in RCTs of psychological interventions (Grant et al., 2013).

2.4.3 Strengths and Limitations of the present review

Strengths of this systematic review and meta-analysis lie in the use of rigorous methodology and following the protocol registered on PROSPERO. A comprehensive search strategy with a broad definition of the terms, a wide range of databases including the “grey” literature, with no language restriction was performed, and a formal critical appraisal tool was used. The screening of the titles and assessment of eligibility for inclusion was performed independently by two reviewers. A second reviewer checked the quality and risk of bias assessment.

This review unavoidably has some limitations. There was significant heterogeneity between included studies in most of the meta-analyses, but the sources of this heterogeneity were not explored due to a small number of studies included. Furthermore, it was not possible to assess evidence of publication bias or to conduct subgroup analyses due to a small number of studies included in the meta-analysis.

Further, four out of all included studies were conducted in one country, Sweden (Bonnert et al., 2017; Ljotsson et al., 2011a; Ljotsson et al., 2010; Ljotsson et al., 2011b; Andersson et al., 2011) and three of them combined in the same meta-analysis (Ljotsson et al., 2010; Ljotsson et al., 2011b; Ljotsson, 2011), hence the generalisability of these results is unclear.

Several studies recruited patients by self-referral (Ljotsson et al., 2011a; Andersson et al., 2011; Ljotsson et al., 2010; Ljotsson et al., 2011b; Hunt et al., 2009). Therefore, the results from these studies must be interpreted with caution, as the consequence of this recruitment method could be that the sample of participants was more willing to participate in this kind of intervention and were more responsive to it.

Another limitation was the choice of the points of follow-up, at which the results of the outcomes could be combined in the meta-analysis. It has been decided that the data would be combined at post-intervention assessment, at three, six, 12 months follow-up, as these were the most common assessment points in the included studies. However, the duration of the intervention varied greatly among the studies with the longest being a ten-week internet-delivered CBT course (Andersson et al., 2011; Ljotsson et al., 2010; Ljotsson et al., 2011b; Mikocka-Walus et al., 2015; Bonnert et al., 2017; Ljotsson et al., 2011a) and the shortest a four-week (Oerlemans et al., 2011) therapy.

To minimise language bias, we did not exclude studies published in languages other than English initially, with attempts to have them translated. However, during the screening process of titles and abstracts, none of the articles published in other languages was selected for the full-text assessment for eligibility. Retrieval bias in favour of studies published in English cannot be discounted due to the nature of the databases used and given that the search strategy was developed in English.

2.4.4 Conclusions

This review was conducted to examine the effect of online psychological interventions on physical and mental outcomes in GI diseases. Nine studies met inclusion criteria, and eight were included in the meta-analyses.

Despite the limitations of the primary studies, findings of the present systematic review suggest insufficient evidence of an association between online CBT and disease severity/activity, level of anxiety and depression, stress, maladaptive coping, HRQoL, and cost-effectiveness in patients with IBD and IBS. However, online psychotherapy was shown to improve gastrointestinal symptom-specific anxiety and lessen symptom induced disability significantly. These results may suggest that human contact might be necessary for CBT interventions to work.

We were able to assess in the meta-analysis only a short-term CBT effect. Therefore, future studies should examine the long-term effectiveness of online therapies including interventions other than CBT. Also, the future meta-analysis would benefit from the use uniform instruments for measuring outcomes in primary studies, reporting of data in a format suitable for meta-analysis, employing larger sample sizes and using strategies to reduce high attrition levels and differential attrition. Future studies should focus on targeting the populations which are likely to benefit from psychological interventions, such as patients with a high baseline IBD activity, recently diagnosed, who are young and patients with comorbid psychological distress. A broader range of psychological interventions with booster sessions should be considered when planning future trials.

3 Chapter 3: Patients' and health professionals' views about the lived experience of people with IBD and comorbid anxiety and/or depression: a qualitative exploratory study.

This chapter focuses on the identification and development of the appropriate theory phase of the intervention, which involves the conduct of the qualitative study. It reports the IBD patients' with comorbid anxiety and/or depression lived experience to identify challenges and gaps in the management of the disease in this population. This chapter is methodologically linked to Chapter 4 which reports the views on the online psychological intervention from the same groups of participants.

3.1.1 Background

The chronic nature of IBD means that its symptoms will affect patients during most of their lives and, as a result, may jeopardise their QOL and mental health (WHO, 2003).

The risk of developing depression and anxiety in patients with IBD is significantly higher than in the healthy population; and psychological factors contribute to worsening of the somatic symptoms of IBD (Mikocka-Walus et al., 2016b). It is also suggested that generalised anxiety disorders or depression could moderately increase the risk of surgery in patients with Crohn's disease (Ananthakrishnan et al., 2013). The largest study to date (n=2000) by Mikocka-Walus et al., (2016c), with a 9-year follow-up, noted a significant relationship between anxiety/depression and disease activity over time in IBD (Mikocka-Walus et al., 2016c), thus indicating the need for psychological care in this population.

In recent years, several qualitative studies have examined IBD patients’ lived experiences (Matini and Ogden, 2015; McMullan et al., 2017; Luo et al., 2018). These studies focused on the investigation of the patients' adaptation and resilience. A recent qualitative systematic review explored patients' experiences of living with IBD and found that "fatigue, incontinence and uncertainty about future, body image, and lack of information from healthcare professionals" formed the theme "living in isolation and exclusion" (Fourie et al., 2018). This study also highlighted that the patients felt that health professionals did not believe them, non specialists health professionals had limited IBD knowledge and did not provide the information about the disease, which led to the lost of trust in health professionals and fear of unpredictable outcomes (Fourie et al., 2018).

One recent qualitative study examined the experience of people with IBD and anxiety and low mood (Jordan et al., 2018). However, this study only focused on the patients' perspective. Hence, there is currently no data on both patients' and health professionals' views about the lived experience of IBD patients with comorbid anxiety and/or depression and if they are the same or different to those with IBD alone. Therefore, the present qualitative exploratory study looked to address this gap. The study of both patients’ and health providers’ perspectives is important as the delivery of adequate patient-centred care could best be achieved by understanding the views of both groups. The findings from the current study could help to identify any challenges and/or gaps in the management of IBD comorbid with mental illness.

This study aims to explore and develop a detailed understanding of health professionals' and patients' perceptions, believes and assumptions regarding the lived experiences of patients with IBD and comorbid anxiety and/or depression and management of the disease.

The study had the following question:
What are the views of patients and health professionals on lived experience and management of IBD with comorbid anxiety and/or depression?

3.1.2 Methods

3.1.2.1 Design

An exploratory qualitative design was used in the current study (Al-Busaidi, 2008). This design was chosen to explore the thoughts and feelings that might affect behaviour in those with IBD and comorbid anxiety and/or depression . The intention was to gather the feedback from the patients and health professionals, to explore their beliefs, analyse and understand phenomena in the natural settings and through the description to determine its meaning and develop concepts of what is IBD patients with comorbid anxiety and/or depression lived experience is. The perspective of both patients and health professionals was necessary as health professionals provide care for these patients and have their own views of the different interventions available and are a source of information for patients on these interventions.

Qualitative research is increasingly important within a health context (Al-Busaidi, 2008) as it gives insight into what factors could affect the implementation of new interventions and why and how patients and health professionals make decisions and respond (Sidhu, Jones and Stevenson, 2017). "Qualitative research fits well within the interpretative approach to knowledge, in which the main goal is to search for meaning and understanding..." (Greenhalgh, 2007, p. 66). Therefore, a general interpretive approach was adopted in the current study.

Within the Medical Research Council (MRC) framework, as discussed in Chapter 1, this primary qualitative research fits within the identifying/developing appropriate theory stage of the framework (Craig et al., 2013).

3.1.2.2 Participants

3.1.2.2.1 Patients

Inclusion Criteria: IBD patients over 18 years old who have comorbid anxiety and/or depression (subthreshold, mild or moderate), who access gastroenterology services in the hospitals of one of the regions in England included in the study.

Exclusion Criteria: Individuals with learning or communication difficulties; those with severe anxiety and/or depression in whom it is thought that the interview may cause emotional distress; considered by their nurse or doctor not to be suitable to participate in the interview; do not adequately understand written or verbal information in English.

3.1.2.2.2 Health professionals

Inclusion Criteria: health professionals who work within the gastroenterology service team and have experience of working with IBD patients for at least two years. This length of experience was chosen so the health professional would be familiar with the patients' lived experience, the challenges in managing IBD alongside anxiety and/or depression and the associated relevant health care provision for these patients.

Exclusion Criteria: health professionals with fewer than two years of experience of working with IBD patients.

3.1.2.2.3 The strategy used for sampling

Purposeful maximum variation sampling was used in this study (Patton, 1990). The strength of this sampling strategy is that "any common patterns that emerge from great variation are of particular interest and value in capturing the core experiences and central, shared aspects or impacts of a program" (Patton, 1990, p. 172). The diverse characteristics of the sample were chosen to maximise variation and were applied across participant variables: age, gender, disease duration and severity; and across health professionals' length of working experience. In the current study, "a maximum variation sampling strategy would not be attempting to generalise findings to all people or all groups but would be looking for information that elucidates programmatic variation and significant common patterns within that variation" (Patton, 1990, p. 172). However, in practice, overarching purposeful sampling approaches are used to meet various interests, requirements and flexibility (Marshall, 1996; Patton, 1990). Within this study, there was also an overarching purposeful sampling used as elements of a convenience sampling strategy alongside purposeful maximum variation sampling were used. Potential participants of various age, gender, disease activity and duration, with comorbid subthreshold, mild or moderate depression and/or anxiety were purposely selected from the database of three gastroenterology services in hospitals one region of England to ensure the richness of perspectives and to minimise the danger of altering the study to a single view. A similar purposive sampling strategy was implied to select various ages, lengths of experience and specialities of health professionals at these sites. The participants were purposely sampled across three different sites to make sure that the geographical variation among selected sites was represented in the study.

The representation of gender variation in the sample was important as male and female patients have a different perception of QOL, IBD concerns specific to gender and the overall experience of IBD (Pittet et al., 2017).

The maximum variation of the health professionals’ sample in the full range of characteristics such as gender, age, length of working experience, a wide range of health professionals' staff working with IBD patients (doctors, IBD nurses, research nurses, psychologist, and dietitian) was achieved. However, there were some limitations in the selection process of the patient participants as some were not willing to participate in the study. Therefore, there was also an element of a convenience sampling strategy used to obtain the patient numbers and simultaneously trying to ensure that the overall desired variation was achieved.

Precise sample sizes for qualitative studies are usually impossible to specify prior to the study (Gentles et al., 2016). It was attempted to gain in-depth data which "from a small number of people can be very valuable, especially if the cases are information-rich. Less depth from a larger number of people can be especially helpful in exploring a phenomenon and trying to document diversity or understand variation" (Patton, 1990, p. 184). Collecting and analysing data from a small sample would obtain: "(1) high-quality, detailed descriptions of each case, which are useful for documenting uniqueness, and (2) important shared patterns that cut across cases and derive their significance from having emerged out of heterogeneity" (Patton, 1990, p. 172). Therefore, it was intended that the sample size for both groups would be determined by monitoring data saturation during the project. Data were collected until the point where data saturation was reached (that is, until no new themes, or the detail for existing themes was detected) and "where additional data collection contributes little or nothing new to the study" (Gentles et al., 2015, p. 1781). Although the sample size was guided by principles of data saturation, a pragmatic approach also was taken based on similar qualitative research within the field (Mikocka-Walus, 2013). A priori, it was expected that a minimum of 10 health professionals and a minimum of 10 patients would be recruited into the study.

3.1.2.2.4 Patient and Public Involvement (PPI)

A Patient and Public Involvement (PPI) representative was also interviewed in line with current best practice (National Institute for Health Research, 2014). PPI can greatly enhance the quality and appropriateness of the research and was considered important within this study (Brett et al., 2014). The PPI representative was a person from the IBD patient panel at one of the participating hospitals. The PPI person was familiarised with the purpose of the study and the patient materials. The study procedures were discussed with the PPI person prior to the actual focus group to ensure that the burden placed on participants is justifiable and well explained. A practice interview was conducted with the PPI representative before undertaking the focus group, using the same topic guide intended to be used for the focus group. The PPI person was invited and took part in the focus group with other patients. The data gathered from the original interview with the PPI person was included in the analysis, and during the focus group, the PPI person contributed less to allow other participants to talk and share their views. PPI continued throughout this project by gaining feedback on the study conduct and input into the reporting and dissemination strategies.

3.1.2.3 Method of Recruitment

Both patients and health professionals were recruited across three different sites in one region of England, thus providing different perspectives and variation from these regions.

3.1.2.3.1 Patients and the PPI person

PPI person was contacted and recruited directly with the help and assistance of the mentors involved in the project.

Eligible patients were identified by asking participating sites to identify IBD patients with comorbid depression and/or anxiety. Following this selection, the prospective participants were initially sent information letters from their treating doctor or nurse. During a hospital visit, the nurse or doctor discussed the research project with them. At the same time, some patients were initially approached during the IBD clinic and the information pack (the information sheet about the project, the research participant rights, the expression of interest form, the consent form, General Data Protection Regulation: Transparency Information, glossary, key demographics, illness characteristics form and contact details for more information) were distributed in person. The participants were given the opportunity to discuss the study with their family or friends. The patients who agreed to participate signed the consent form, which was sent to the primary researcher who then contacted them to agree on the time and date for the focus group or interview. A stamped addressed envelope was provided with the consent form for ease. The health professionals from the gastroenterology service team were not aware which patients had agreed to participate in the research. However, in some cases when patients expressed an interest in the study and were willing to conduct the interview "on the spot", then the health professional would be aware and directed the patient to the interview room with the primary researcher.

3.1.2.3.2 Health professionals

Participating sites provided a list of eligible health professionals for those who had contact details (email or postal address) available. Consequently, the health professionals were contacted and recruited directly with the help and assistance of the mentors involved in the project. The prospective participants were initially approached by the collaborators at the hospital. The collaborators discussed the research project with the health professionals, and the information packs (the information sheet about the project, the research participant rights, the expression of interest form, the consent form, General Data Protection Regulation: Transparency Information and glossary) were distributed to them. The health professionals who agreed to participate signed the consent form, which was sent to the primary researcher who then contacted them to agree on the time and date for the interview. A stamped addressed envelope was provided with the consent form for ease. Some health professionals signed and scanned the consent forms and emailed them.

3.1.2.4 Procedure for data collection

Individual semi-structured interviews with open-ended questions were used for the health professional data collection so that the participants could "best voice their experiences unconstrained by any perspectives of the researcher or past research findings" (Creswell, 2015, p. 216). In addition, the interview with health professionals was preferred to the focus group from a practical point of view (i.e., busy schedule, availability at different times, possible power issues between nurses and doctors).

Probing, prompting and summarising was used to help the flow of the interview (Holloway and Wheeler, 2010). A semi-structured one-to-one interview format with health professionals and a focus group format or interviews with IBD patients were performed in English at a mutually convenient time in a private room at the hospital facilities or via the phone with health professionals.

A focus group format was chosen to explore the patients' perception of the online psychological intervention programme. The focus group method is increasingly becoming accepted in health research, as it allows the exploration of complex behaviours and motivations and to collect the data quickly and cost-effectively (Holloway and Wheeler, 2010; Reed and Payton, 1997; Jayasekara, 2012). A focus group was preferred for the participant data collection method to stimulate memory and thoughts, facilitate and motivate discussion, leading to enhanced impulsive responses of participants and to explore the group's dynamic (Jayasekara, 2012; Holloway and Wheeler, 2010). The participants' opinions emerging during the discussions in focus groups can bring the immediate evidence of similarities and differences in the experiences, compared to interviews were the comparability can be seen only in post hoc analysis (Morgan, 1997). During a focus group, participants are acting in response not only to the researchers' questions, but also to the other participants and the group dynamics, despite having similar experiences, opinions, and thoughts (Hesse-Biber and Leavy, 2011). Therefore, focus group interviews can be considered as moderated by group effects discussions (Taylor and Francis, 2013). Usually, the researcher would play the moderator role to influence the focus group dynamic and to stimulate the conversation flow and would in advance plan the topic guide for the discussion, which would be presented during the focus group (Hesse-Biber and Leavy, 2011). However, in the field of health sciences, focus groups tend to be less controlled and structured (Taylor and Francis, 2013). Therefore, in the current study, the primary researcher let the conversation in the focus group to flow. Simultaneously, to fulfil the research purpose the researcher took a moderator role and guided the conversation by asking the participants more specific questions and using prompts to encourage participants' involvement in the discussion. The procedure for conducting the focus groups followed 'Guidelines for Conducting a Focus Group' (Duke University, 2005). There is disagreement about the perfect number of participants in a focus group; however, it has been suggested that the group sizes should be between 4 and 12 persons (Holloway and Wheeler, 2010; Morse, 1994). Initially, the group of five people was chosen, for the participants to feel more comfortable and to provide further opportunity for them to talk (Morse, 1994), with patients forming 2-3 focus groups to be run at three gastroenterology services in hospitals. However, there were difficulties in patient recruitment with only one focus group of three people recruited. To increase the recruitment, the research team offered an option of an individual interview to further participants. The relevant changes were made to the original patient recruitment pack (information sheet, the patient's consent form and invitation letter). The same topic guide was used for the interview as the focus group. These interviews were audiotaped, transcribed verbatim by the primary researcher and then, according to the Data Protection Act 1998, stored securely on the University of York servers. Data was collected until the point where information saturation was reached, that is until no new themes or the detail for existing themes could be detected (Creswell, 2015) and this determined the final sample size for participants (Kerr, Nixon and Wild, 2010). After the interviews with 12 health professionals and 13 patients, the data reached saturation.

3.1.2.5 Dissemination of findings

All the participants were informed about the study results via email, as per their preference. A wider stakeholder network of organisations with interest in IBD, which includes the public, clinicians working in and outside the NHS, and charitable and commercial organisations involved in IBD and mental health were informed about the study result via newsletters.

3.1.2.6 Study quality

While arguably it is impossible for the settings to be totally unfamiliar or well known and "the researcher's insider-outsider status varies over the lifetime of a project" (Bourgeault, Dingwall and de Vries, 2010, p. 356), the researcher entered the settings as a "stranger" attempting to view the experience from the viewpoint of the participant to add validity to the qualitative research (Morse, 1994). The researcher gathered information using a triangulation strategy by encouraging patients to tell their story, using open questioning techniques, facilitating patients responses, picking up verbal and nonverbal cues, clarifying patients augmentation or ambiguous statements (Silverman, Kurtz and Draper, 2013; Miles and Gilbert, 2005; Patton, 2002), as well as writing the descriptive and reflective field notes (Creswell, 2015). A richer and balanced description of the phenomenon can be generated as a result of the use of this strategy (Miles and Gilbert, 2005). The interviewer was a woman, a PhD student, who trained in medicine, public health and cognitive behaviour therapy (CBT). The participants had not met her prior to the start of the study, but they were aware that she was conducting the research as part of her PhD project. The primary researcher attempted to disregard her professional experience, affiliations in the research field, and methodological assumptions to reach the true understanding of the participants' perception (Bailey, 2008; Bourgeault et al., 2010; Ahern, 1999). It is inevitable that these influences could occur during the data collection, decision making on what important "findings" are, on the coding process and on how data should be analysed, but this was reflected through linking field notes and memos to the lines in the transcribed text (Bailey, 2008; Bourgeault et al., 2010; Ahern, 1999).

The participants were invited to review the transcripts and comment on them, and the research team members cross-examined the process of the research to assure the trustworthiness of the study (Creswell, 2015). However, none of the participants expressed an interest in this. One health professional was asked to review the transcript of her interview, as there were technical difficulties with the recording of the interview, to make sure the presented information was accurate. The intention of the research was not to generalise the results but to ensure their transferability, which will be reached through a detailed description of the participants' perceptions (Creswell, 2015).

3.1.2.7 Materials

3.1.2.7.1 Topic guides

After consultation with experts and literature review, an interview guide was developed to help focus the interview and still allow some flexibility (Miles and Gilbert, 2005). For the interview and focus group topic guides see Appendix 11-12. This guide contained a list of open-ended questions, but if the participants deviated from the research topic or hesitated to speak, the researcher used short, helpful phrases and prompts to assist the steady flow of the interview (Taylor and Francis, 2013). The PPI person was able to offer input into the topic guide for the focus group to ensure it was understandable and addressed issues and outcomes of relevance.

3.1.2.7.2 Patients

It was anticipated that the focus group of the IBD patients would last up to 90 minutes and the in-person interviews would last between 25 and 45 minutes. The interview schedule was piloted with the PPI person and one health professional before the study commenced. The glossaries of terms to assist patients were distributed before the interview. The IBD patients who expressed an interest in taking part in future research-related activities were invited to participate in the development of the intervention and the future feasibility trial.

3.1.2.7.3 Health professionals

A similar approach was applied to interviews with health professionals. It was anticipated that the in-person or phone interviews would last between 25 and 45 minutes. All health professionals opted to undertake the interview over the telephone.

3.1.2.8 Data Analysis

Thematic analysis was used to analyse the interviews and focus group transcripts, to help move from broad qualitative data towards discovering patterns (Braun and Clarke, 2006). The method enables "systematically identifying, organising and offering insight into patterns of meaning (themes) across a data set" (Braun et al., 2019, p. 57). The method was chosen due to its flexible approach and accessibility and was driven by theoretical assumptions and the research questions (Braun and Clarke, 2006). According to Braun and Clarke (2006), the thematic analysis should be carried out in six steps, which were followed in this study analysis:

1. Familiarising yourself with your data
2. Generating initial codes
3. Searching for themes
4. Reviewing themes
5. Defining and naming themes
6. Producing the report

The field notes were read and revised, audio records were replayed, and preliminary reflection was written. The data were coded to help summarise its interpretation. The final primary codes were created by grouping the secondary and tertiary codes forming several levels of code within the primary codes (see codebook Appendix 21, and concept maps Appendix 13, Appendix 14). All relevant codes were consolidated to form the themes. These themes were reassessed to see how they interrelated to each other and the whole data set. At this stage, the themes were split, combined with other themes or removed. Final themes were named, and an analytical description of the data written (Clarke and Braun, 2013). The analysis of the data was undertaken in two parts. At first, the health professionals' and patients' data were coded separately. The themes from both participant groups were closely aligned hence it was decided to combine them collectively with the differences and similarities discussed.

After the data were coded, the themes emerged on the patient experience of living with IBD and anxiety and/or depression, according to the patients and health professionals. This data identified the perceived gaps in the management of the disease. NVivo was used to assist with the data analysis. The transcripts and analysis were checked and validated by other members of the supervisory team.

3.1.2.9 Ethical Considerations

The ethical approval for this study was obtained from the NHS Health Research Authority and the Department of Health Sciences Research Ethics Committee. All participants received written informed consent before they participated in the study. This research was conducted according to the requirements of the Declaration of Helsinki (World Medical Association, 2013).

3.1.3 Results

The data saturation was reached and determine the final sample size of 13 patients and 12 health professionals in this study. The focus group of three IBD patients lasted approximately 90 minutes. The in-person interviews with patients lasted between 25 and 45 minutes. The interviews with the health professionals lasted between 20 and 45 minutes.

3.1.3.1 Demographics

3.1.3.1.1 Patients demographics

Patients' ages ranged from 20 to 70 years old, with a median age of 45 years (Table 10). Of the 13 patients included, nine had Crohn's disease and four had ulcerative colitis. Patients had different lengths since they were first diagnosed with some 1 to 2 years ago and others over 10 years ago, thus demonstrating the diversity in experience across the sample (Table 10). There was a relatively even split of genders in the sample with seven (54%) males and six (46%) females and all, except one, were Caucasian. Six participants were employed, two were unemployed, two were retired due to illness with an addition two who retired and there was one student (Table 10). A different number of patients were recruited from three different sites (six, five and two patients from the first, second and third site consequently) (Table 10).

Table 10 Key demographic and illness characteristic of patient participants

	Diagnose		
	Crohn's disease	Ulcerative colitis	Total sample
n	9	4	13
Disease length (years)			
≤ 1	-	-	-
1-2	-	1	1
3-5	-	-	-
5-10	4	3	7
10 +	5	-	5
Median age (years)	45	54.5	45
Minimum age of participants (years)	20	39	20
Maximum age of participants (years)	70	70	70
Sex, n (%)			
Men	4 (44%)	3 (75%)	7 (54%)
Women	5 (56%)	1 (25%)	6 (46%)
Ethnicity			
White	9	3	12
Asian	-	1	1
Employment			
Employed	4	2	6
Unemployed	1	1	2
Retired due to the illness	2	-	2
Retired	1	1	2
Student	1	-	1
Hospital site			
1	2	4	6
2	5	-	5
3	2	-	2

3.1.3.1.2 Health professionals' demographics

Eight health professionals were female and four male. The age ranged from 32 to 54 years old. The health professionals were consultant gastroenterologists, nurses, dietitians, or psychologists (Table 11). A different number of health professionals were recruited from three different sites (eight, three and one from the first, second and third site consequently) (Table 11).

Table 11 Key demographic characteristics of health professional participants

Total number	12
Consultant Gastroenterologist	5
IBD nurse	4
Dietitian	1
Psychologist	1
nurse other	1
Age (years)	
25–34	3
35–44	3
45–54	6
55≤	-
Minimum age of participants	32
Maximum age of participants	54
Sex, n (%)	
Men	4 (33%)
Women	8 (67%)
Hospital sites	
1	8
2	3
3	1

3.1.3.2 The experience of living with IBD and comorbid anxiety and/or depression

The analysis identified that health professionals' and patients' responses to the experience of people living with IBD and comorbid anxiety and/or depression were distributed across three main themes: 1) bidirectional relationship between IBD and mental health, 2) the need for health care integration and 3) lack of awareness about the disease. The codebook in Appendix 21 provides the description of the reported codes and the frequency of their occurrence in both groups’ transcripts of the interviews. The concept maps 1 and 2 (see Appendix 13, Appendix 14) provide an overview of the codes and themes and their interrelationship.

Regarding the experience of living with IBD and anxiety and/or depression, there were high levels of agreement between health professionals and patients observed. Three overarching themes were identified and demonstrated the complexity of this chronic long-term condition. The "bidirectional link between IBD and anxiety/or depression" theme indicated the importance of managing both the IBD and mental health simultaneously. Moreover, it indicated the importance of screening IBD patients for psychological health in line with the recent longitudinal follow-up study (Gracie et al., 2018). The "lack of awareness about the disease" theme and "bidirectional link between IBD and anxiety/or depression" signified the need for the "health care integration", the third identified theme, as a care model for these patients to overcome the challenges faced.

3.1.3.2.1 Bidirectional relationship between IBD and mental health

There was an agreement between patients' and health professionals' views regarding the bidirectional link between IBD and mental health. The concept maps highlight several levels of the codes that formed this theme (Appendix 13); three primary codes were described here: IBD impacts on QOL, IBD impacts on mental health, and mental health impacts on IBD.

All patients and health professionals agreed that IBD affected QOL. Mainly, IBD affected individuals' social and family life. Furthermore, participants thought that embarrassment with symptoms, being housebound, and having pain and fatigue that are difficult to manage also impacted on QOL. The patients recognised IBD's influence on all aspects of their lives and the people around them, and thus influenced their QOL:

> *"I think, it impacts hugely on the quality of life. […] because it places so many restrictions on you and on your family." (Patient 7, 67 years old, female).*

They also found that IBD symptoms were embarrassing and as a result, IBD influences their QOL and mental health:

> *"I think […] nobody really knows how bad it is and because it's […] going to the toilet, and it's hard to talk about sometimes to people, like, at work, [...] you often find you go to the toilet, and they've not got solid walls, and it's embarrassing, and you know, it's things like that, that I had to deal with. You know, that's what I find the hardest." (Patient 5, 56 years old, female).*

Both of these female patients had CD, and it has been suggested that female CD patients have a perception of the HRQoL worse than men (Saibeni et al., 2005). However, within this sample, males with CD also related similar impacts of IBD on QOL:

> *"...when you have a flare […] it impacts your life because it is very restricting in both, work, family time, leisure time, it impacts every aspect in your life." (Patient 13, 32 years old, male).*

Concurrently, some patients admitted that during remission they were able to live a reasonably normal life:

> *"75% of the time I'm fine, but when I do have flare-ups and the problems, then it's very hard to get through the day."(Patient 11, 32 years old, male).*

Patients recognised that the diagnosis of IBD itself influenced their life. The reaction to the diagnosis differed among patients: denial accepted the diagnosis, hoped for a cure, traumatised by the news or became angry. One of the patients emphasised the importance of accepting the diagnosis:

> *"It's not going to go away, better it stays part of me, but I don't want to define me." (Patient 1, 50 years old, male).*

Some patients thought that the IBD symptoms made them "housebound", which not only reduced their QOL and affected their mental health, but also, importantly reduced their ability to manage their disease. The patients were frightened to leave the house and were unable to attend their medical appointments. One patient said:

> *"I don't leave the house for ages. [...] you so stressed to the point when [...] you don't want to leave in case you need to go, to the toilet. [...] it's horrible." (Patient 9, 20 years old, female).*

This indicated the need for flexibility in the management of the disease including remote management of the disease to reduce the need for the patients to attend clinic appointments, reduce the burden on patients and still allow the appropriate care and disease management of patients.

Like patients, health professionals believed that IBD influenced patients' QOL as well as their mental health:

> *"IBD is a chronic condition, so affects a person's QOL and mental health; people can become anxious or depressed." (Female, 43 years old).*
>
> *“I think it's about body image, the risk of stoma, medication, diarrhoea, urgency, potentially incontinent [...] people get very anxious. And if somebody has had an accident in front of, you know, colleagues at work, or the children in school, if you are a child or teenager that has a major impact on their mental health and can make people very depressed". (Male, 41 years old).*

However, the health professionals believed that the impact depended on the emotional resilience of the individual:

> *"I think, for some patients if IBD is managed well, it doesn't have a huge impact on patients. However, some patients with relatively moderate IBD symptoms, but they feel anxious and depressed." (Female, 43 years old).*

Both health professionals and patients believed that IBD influenced mental health. More specifically, IBD patients tended to become "anxious", "depressed", "stressed", have a sense of "being out of control" and had "fear and worry". One of the patients initially denied the presence of anxiety, then admitted to having it, but felt the IBD medication was the cause of it:

> *"Yeah, like I say, I've never had anxiety regarding my IBD, but because of the drug that I am on for the IBD, [...] the symptoms are from this drug. This is what is giving me my anxiety. It is nothing to do with my actual IBD symptoms. It's to do with the fact that the drug inside me […] is giving me a side effect." (Patient 11, 32 years old, male).*

Some of the health professionals also thought that the medication for IBD could influence mental wellbeing:

> *"The other issue is we give a lot of steroids which can have a marked effect on people's mental health, causing, um..., exacerbating a mild depression, mania and other problems as well, psychosis [...]. So we can make people pretty unwell."(Male, 41 years old).*

Interestingly, some patients recognised themselves as being lucky about the support they received or in comparison to others, despite feeling unwell and having flares:

> *"I was lucky; I had good support." (Patient 7, 67 years old, female).*
>
> *"I am lucky because I can play the game with my clients. [...] I work from home a lot so that I can manage it (Patient 3, 49 years old, male).*

Patients acknowledged different reasons for "being lucky", some, because of the support they had from the people around them, but some, because they compared themselves to others with a more severe course of the disease. The last statement above, reflected through the whole account, shows how important the experience of the others with IBD is to them. Thus, IBD patients with comorbid anxiety and/or depression are possibly seeking understanding and draw upon the experience of others with the same conditions. They also talked about loneliness, which could be explained by the lack of awareness about the disease that came through in the other themes. Both health professionals and the patients agreed that anxiety and depression influenced IBD. One of the health professionals said that mental health could affect the severity of the disease directly:

> *"So psychological impact can affect directly the severity of the disease." (Male, 54 years old).*

Patients often said that mental health, depression, in particular, led to the lack of motivation in treatment engagement for their IBD, and thus, created another factor that challenged the management of IBD in these patients. One person in the focus group said:

> *"[...] when my depression was getting worse it's hasn't been for a long while, but when it's been very bad, you think what's the point of it all?" (Patient 2, 39 years old, male).*

The other patients in this focus group agreed with this statement:

> *"I'm just living with your phrase of what the point [...]. I cannot talk about a capital D, depression [...], but when I've been low, the motivation to try to make you better yeah, disappears." (Patient 1, 50 years old, male).*
>
> *"[...] I would think what I'm going to get up for, and [...] take the medication." (Patient 3, 49 years old, male).*

These comments suggest the need for health professionals to select the appropriate treatment (pharmacological or psychological) for this group of patients and to find ways to support them to engage with the treatment and this must be considered at the start of the treatment.

Nevertheless, the majority of the health professionals and patients clearly and forcefully articulated the bidirectional link between IBD and anxiety and depression. The majority of patients said that one of the challenges in the management of the disease was mental health and its bidirectional relationship with IBD:

> *"I think they are closely related, I think, one provokes the other. I think one can; I don't say that always does, but it's possible that the physical condition makes it more likely that you will also be mentally and emotionally, I think a little bit depressed." (Patient 6, 68 years old, female).*
>
> *"[...] that is a vicious circle." (Patient, 39 years old, male).*

However, two patients said that this connection was only one way. One admitted that mental health made it difficult to manage IBD:

> *"[...] my depression was worsening my Crohn's, not that my Crohn's [...] contributed to the depression." (Patient 7, 67 years old, female).*

Other said that IBD flare-ups were leading to a problem with mental health:

> *"It's the flare brings on anxiety and the low mood, not the other way round. I don't get another way round. [...] the trigger is IBD for the low mood." (Patient 13, 32 years old, male).*

However, this patient admitted that after attending face to face psychological interventions they saw the improvement in how they felt, thus suggesting the bidirectional link.

Regardless of speciality or hospital site, the health professionals, similar to the patients' views, identified the bidirectional relationship between IBD and mental health:

> *"Because of the nature of the symptoms that it presents with and those symptoms then fuel further anxiety and low mood, which feed into the body and physical symptoms which create a vicious cycle between the physical symptoms and the emotional symptoms. So, I think, sometimes it's a bit of a chicken and an egg, to which one came first, but I think, either regardless which one came first it's a bidirectional relationship between the two.." (Female, 30 years old).*

This link was not only seen as affecting a patient's ability to engage with clinicians and support services but also changing the adherence to medications and interventions, hospital readmissions and the ability to manage the disease:

> *"You can have some very healthy patients who tolerate high degrees of disability from their disease and are not heavy resource users, and the disease sorted out, and they're still able to fulfil their life goals, against those who are more anxious […], and have a greater degree of impact, but less resilient and who has a smaller degree of symptoms actually causing their disease to have a great impact on their life. So, I think, there are both direct effects on the severity and also an indirect effect on the ability to deal with the same degree of disability." (Male, 54 years old).*

Additionally, it was recognised that IBD symptoms could be over or underestimated in people with comorbid anxiety and/or depression, hence leading to inadequate treatment:

> *"So, when somebody has anxiety and cannot control it, they would downplay their symptoms in order to avoid having an investigation from a gastroenterologist, such a colonoscopy. Similarly, but, you know, in a different way, if the patient is depressed and anxious and you're using a pain score. So, if they are depressed and anxious and score more or highly on, "I feel ill", or "I have pain", they will score higher on that. Therefore, they have the potential to be overtreated [...] and then also lack of compliance with the treatment." (Male, 54 years old).*

Therefore, the treatment of mental health in this population appears to improve the management of the IBD itself.

3.1.3.3 The lack of awareness about the disease

"The lack of awareness about the disease" was reported as one of the challenges in managing IBD alongside anxiety and/or depression by many patients. The primary codes included in this theme were: "patients unaware of the psychological problem", "lack of awareness about mental health issue among health professionals", "look well outside and be rotten inside".

Patients reported a lack of awareness among health professionals about mental health issues in patients with IBD:

> *"[...] consultants perhaps need to be more aware that they not just dealing with a medical side of it, not just dealing with the surgical side, but there are mental health issues." (Patient 7, 67 years old, female).*

Despite health professionals admitting they did not actively assess patients for anxiety and/or depression, they were aware of the bidirectional link between anxiety and/or depression, as reported earlier, and in some cases patients would be referred for psychological help. Possibly, scarce resources and short appointment times with the gastroenterology team were culpable for this rather than lack of awareness about the mental health issues among health professionals.

Both health professionals and patients thought that sometimes IBD patients were not aware of the anxiety and depression or did not admit that it was present. Patients thought:

> *"At first, you don't know you're suffering from depression. [...]. I thought it was me failing to cope with the illness." (Patient 7, 67 years old female).*
>
> *"[...] they're not really been truthful to themselves or don't want possibly admit certain elements of their persona or psychological health. That's not right." (Patient 3, 49 years old, male).*

Health professionals also confirmed:

> *"A lot of them don't realise that they have it..." (Female, 53 years old).*

This connected to the other theme "need for the health care integration", where health professionals admitted that they were not actively asking patients about their mental health and were not trained to assess mental health and only relied on their personal judgment.

Patients also highlighted a lack of awareness among the public, but health professionals did not raise this issue. One female patient with Crohn's disease said:

> *"You look well on the outside, but you're absolutely feeling rotten on the inside [...]. I've lost quite lots of weight, and [...] I was so tired, but everybody thought I looked very well [...] you don't want to wear a budge [...] they don't see it as an illness, because you can't see it. If I had a pot on my arm, I'd be ok, because people can see that [...] you don't often get the consideration." (Patient 5, 56 years old, female).*
>
> *"I think the quality of life is affected because people don't understand it. Because it's invisible. Therefore, people look at you and believe that you are fit and well and unfortunately you are not. You are not able to do some of the things that other people could do. So, peoples' expectation of you high and you can't deliver, because you can't deliver. [...]Because you cannot, it's not just about you, it's how other people perceive you. I often, if I had a really bad flare, I don't use the disabled toilets, unless I believe that I do not have choice but to do so, because I wouldn't. I think facilities need to be used how they should not just not take for granted. If I use the disabled toilet, the comments that I get or the looks that I get, or how people perceive me actually adds to my mental*

> *anxiety because people don't understand that I look well but I am not" (Patient 12, Female, 59 years old).*

3.1.3.3.1 The need for health care integration

Health care integration was a combination of a few primary codes: "Cinderella services", "team of people should care for IBD with comorbid anxiety and depression", "holistic care", "both health professionals and patients should manage IBD with anxiety and/or depression", "research is good".

The agreement between health professionals and patients view was observed regarding "Cinderella services", which included a lack of resources, the waiting list to access a psychologist, and limited psychological support. Many patients raised these problems. One patient said:

> *"[...] mental wellbeing [...] they don't take it seriously. And all of the funds are being taken away from those things that you cannot see, those invisible illnesses that are not at the greatest risk. [...]. But the reality is, if you threw resources earlier [...] you would be able to divert those people on much earlier stage. [...] the nurse has 10 minutes appointment [...] for someone who has a chronic illness is ridicules. [...]. We expect to go to charities to find information now because there is not enough support in service. [..]. If I went to my GP and said I am now no longer able to cope, can I have counselling? There would be nine months waiting list, by which point, I would probably slit my wrists." (Patient 12, 59 years old, female).*

Like patients, all health professionals commented on the shortage of psychologists, who should be part of the team in caring for people with IBD and comorbid anxiety and/or depression. The waiting list to see a psychologist impacted negatively on the patients’ experience and satisfaction with health care. It was suggested by health professionals that such "Cinderella services" prevented the IBD team from being able to treat patients appropriately:

> *"We have very limited psychological support at the hospital that we have to save for our in inverted commas for the worst patients if you like, which means that we don't overly promote it because we haven't got the resources to fulfil patients', you know, expectations and needs." (Female, 52 years old*).

Additionally, health professionals believed that there was a major failure for IBD patients to appropriately link with mental health care services. The overstretched resources where an issue for all health professionals; however, it was evident that some hospitals had better psychological facilities for patients than others. Despite having moderate waiting lists, some hospitals, had a specific gastro-psychology team to support these patients, while others, did not have a psychologist in the department or have links with the psychological services/departments. The health professionals pointed out the differences in availability of psychological support for patients at different locations:

> *"We are very fortunate in [hospital location] that we have psychological facilities for patients, lots and lots of hospitals, the majority of the hospitals around the UK don't have that. So when I go to meetings and listen to other IBD colleagues, I always feel that we are lucky to have the services that we have. […] Knowing what you can have and knowing what you are not delivering to patients, it's difficult sometimes, but then I feel for those people who have nothing at all." (Female, 52 years old).*

This might reflect the concept of the NHS postcode lottery, leading to differences in access, quality and availability of NHS treatment/services throughout the country. This also corresponded with the patients' opinion of an inability to get psychological support and long waiting lists to see a psychologist (in some cases being over 15-18 months), with the longer waiting list in areas where health professionals indicated poor integration with psychological services/departments.

Health professionals and patients agreed that the team of health professionals need to care for people with IBD and comorbid anxiety and/or depression. All health professionals indicated this:

> *"I think to look after IBD patients; you need a complete team, you need your gastroenterologist, [...] you need the nurses to support them and the patients. I think you need GPs to be involved; you need the psychological support, um, available through whatever format that comes in, whether it be face to face whether it becomes over the Internet, whether it's via GP. I think we need all of it there, to work together, so everybody is working together to support patients,*

> *and enable them to access the services where they actually want." (Female, age not indicated).*

More specifically, both patients and health professionals regarded the need for different skills from different specialities to provide holistic care. One health professional acknowledged that holistic care relies on the IBD nurse:

> *"So, we probably have more time to spend on counselling, supporting patients than a gastroenterologist would and actually, you know, the training you get, the nurse gets, is very different to that of a gastroenterologist. So, you know holistic care is perhaps more a focus for a nurse, but certainly, you know everybody needs to have their expertise, you know, the gastroenterologist, the nurses specialist, the dietician, the pharmacist, psychologists, you know, we have different roles, haven't we." (Female 53 years old).*

However, some disagreement was observed in the discussion of holistic and integrated care. While health professionals felt that they provided holistic care for the patients, patients felt that, despite having supportive IBD nurses and gastroenterologists, they did not receive holistic care as part of their IBD management. Yet, the patients and health professionals acknowledged that the reason for this was poor funding and overstretched resources for the "invisible illness". Additionally, the health professionals and the patients highlighted the deficiencies in health care integration.

Many patients acknowledged that they received fragmented care:

> *"[...] a holistic approach to things [...] rather than everything in isolation"(Patient 2, 39 years old, male).*

Despite praising the IBD nurses for being supportive and a few patients, with a few being offered psychological help, the patients felt that there was no continuity of care or holistic care:

> *"[...] a problem for IBD patient is fragmentation of treatment. [...]. I had to go to 3 different hospitals. [...]. I have lots of different medications. [...]. I have been in the situation sometimes when they prescribe medication [...] then another consultant would tell me that it's not good and prescribe me something else." (Patient 12, 59 years old, female).*

The same person said that not managing IBD patients' wellbeing was not cost-effective:

> *"[...] not managing the mental wellbeing [...] is a false economy, total false economy. Because the reality is if we put prevention measures in place [...] and we put the support mechanisms in place, we would save ourselves so much money down the line in terms of NHS expense." (Patient 12, 59 years old, female).*

There were mixed responses about support from general practitioners (GPs), some believed that they do not get support from GPs for their IBD:

> *"[...] he knows that I know more about IBD than he does because he is the generalist." (Patient 3, 49 years old, male).*

On the other hand, some patients said that they accessed psychological support from their GPs:

> *"I spoke to my GP, and that was the first time any medic knew about it. And she was a huge support." (Patient 7, 67 years old, female).*

Some patients reported that they did not feel supported or trusted health professionals:

> *"[...] having 30 years of illness that was never diagnosed and made me feel so bad. It means it affects my trust (Patient 12, 59 years old, female).*
>
> *"They are not as helpful as they should be. They just refer you off to somewhere else, and there is a waiting list of 28 weeks." (Patient 9, 20 years old, female).*

At the same time, this patient wanted to be supported by health professionals regarding their anxiety and depression. This suggested that the patient was disillusioned about the lack of support rather than being about trust.

One of the patients expressed fear of being judged if they were open about psychological issues to the gastroenterology specialist and said that there was a gender difference in the care they received, admitting that they found female doctors were more sympathetic:

> *"I doubt I could open so much to the male doctor [...] I can talk a lot easier to a female. [...]. I found them a lot more understanding to your views, [...] male [...] they are thinking you are weak men; you are not really." (Patient 8, 70 years old, male).*

Integrating health care could address these issues with routine screening for anxiety/depression and, where necessary, the provision of appropriate treatments.

Most patients were not receiving any form of psychological support and were relying on family members and friends for support:

> *"It's really been family and friends [...]. My husband; he gets a lot." (Patient 5, 56 years old, female).*

However, patients would like to protect their family from their disease burden:

> *"[...] it actually feels very lonely, and I feel the only person who can help is me. Because even close family members, you can describe it they cannot live it. [...] you don't want them to face some of the heartbreak that comes with it. You want to protect other people, and therefore your mental wellbeing has to take second place really." (Patient 12, 59 years old, female).*

Therefore, the patients still felt alone with the disease:

> *"It's a very lonely place" (Patient 13, 32 years old).*
>
> *"I'd like to talk to the people, but [...] some things are hard" (Patient 11, 32 years old, male).*

Patients felt the need "get it off their chest":

> *"[...] not everyone needs talking therapy, but if everyone has a chance at lease to talk about it." (Patient 1, 50 years old, male).*

The patients felt like they were alone with the disease and expressed interest in being involved more closely in the management of the disease alongside the health professionals. They thought that both patients and health professionals should work together and be involved in the management of IBD alongside anxiety and/or depression:

> *"I always thought that there're two experts in the room when I go to an appointment. [...] I'm the expert in me, and they are the experts in the condition. So, I always kind of wanted that equality or taken responsibility." (Patient 1, 50 years old, male).*

This suggested that some patients were willing to be involved in self-directed interventions, where they could take responsibility for the management of their disease. However, some patients admitted that people with depression and anxiety were less likely to manage on their own:

> *"Obviously, if somebody in a really dark place with depression. They are less likely to manage everything." (Patient 3, 49 years old, male).*
>
> *"If I was in a place where psychologically I was less able,[...], then I'm going to need someone who kind of shake me and say you don't understand, but this is what you need. [...] because you wouldn't be able to do that working out." (Patient 1, 50 years old, male).*

These findings suggest the need for some support from health professionals and the need for precision medicine as each patient's needs are different. Therefore, the approach to the treatment and management of the disease should be individual. From a patient’s perspective:

> *"Each IBD patient is different because the autoimmune disease would mean different things for different people." (Patient 7, 67 years old, female).*
>
> *"Their needs form medical professionals are all slightly different." (Patient 3, 49 years old, male).*

The importance of integrated and tailored care for patients was reported by patients who for different reasons were unable to attend treatment at the hospital. A patient who suffers from IBD and social anxiety and depression refused psychological help that was offered as this required leaving the house and attending an appointment at the hospital:

> *"I've been offered a counselling, [...], but I can't, I won't walk out of the house. If [...] you could have your counselling at home because you don't want to leave the house. [...] I said no because it's bad enough when you go for your review or your tablets or [...] right now, my hands are sweating because all I want to do is get back in the car and go home."." (Patient 10, 45 years old, female).*

This patient expressed a desire to have appointments at home or at the hospital but from a collaborative/integrative care standpoint being on the same date and at the same time rather than attending different departments at different times. Further, a few patients had a fear of hospitals/doctors, which could prevent them from attending the appointments and receiving treatment:

> *"I have a real phobia of doctors, a real phobia for hospitals. The minute I know I'm driving to the hospital, my heart will go ten to the dozen, because [...] having 30 years of illness that was never diagnosed and made me feel so bad, it means it affects my trust." (Patient 12, 59 years old, female).*

One elderly patient did not want to take the medications prescribed for their depression:

> *"Doctors that I saw gave me pills for my depression. I did that for about six months but then decided that makes you so wacky. And I, don't get me wrong, I was feeling well, but sort of spaced out. So, I decided to come off them." (Patient 8, 70 years old).*

This patient wanted access to a psychological intervention to tackle his depression and chose to access this privately rather than through the NHS. Some other patients also highlighted the cost involved in IBD management:

> *"I had to retire on the ground that I can't longer work and I'm 59. I didn't choose that, but I pay for everything, I pay for my car parking, I pay for my prescriptions*..." *(Patient 12, 59 years old, female).*

This patient reported that having a team of people involved in the management of their care reduced costs as sometimes there was no agreement about prescriptions from different doctors in different departments and hospitals and that is could be avoided in an integrated care model.

Contrary to the patients' view, the health professionals felt that they gave holistic support to patients in the form of reassurance for them and their family members, talking about the medication and answering their questions:

> *"Right from the very beginning, once the patient has a diagnosis of inflammatory bowel disease then one of the IBD nurses will become involved in the patient's care, and psychological aspects are a part of the holistic care that we give, from management [of their] diseases to management of psychological aspects as well." (Female 52 years old).*

Some health professionals felt that holistic care was delivered by the team of people involved in the management of complicated IBD:

> *"I see patients in the clinic, and I also support the IBD nurses in their clinics and the IBD MDT where [...] nurses, radiologists get together to discuss the management of patients with difficult or challenging IBD." (Male 49 years old).*

Many health professionals acknowledge good cooperation between departments and services. This point was supported by good referral procedures to the other department/services and GPs:

> *"I would send them to the psychologist in the hospital. Or, if there's a more serious problem, I may refer them to a GP for an assessment to see if they are depressed." (Female, 43 years old).*

Health professionals highlighted, that despite having different experiences with referring patients for psychological help, when they did access it, they had positive outcomes:

> *"[...] when you see the patients before and after, we're lucky that we can see that in the clinic and you definitely notice a vast improvement in the patients." (Female, 53 years old).*

At the same time, health professionals acknowledge that they do not have special training in mental health assessment. The recognition of the mental health problem and the referrals rely on the personal judgment of the IBD nurse or gastroenterologist:

> *"I suppose that one of the challenges is making an assessment in the first place, but in terms of resources, the training that I had has been very, you know, learning training on the job kind of, but I have not done any formal training in my formal (speciality) education, but everything else was kind of learning through the years of experience." (Female, 52 years old).*

However, even though all health professionals reported a bidirectional link between IBD and anxiety/depression, they admitted not vigorously screening for mental health issues:

> *"...we don't currently actively pursue patients looking for any signs of anxiety and depression." (Male, 54 years old).*

Many patients understood that gastroenterology teams were not trained to deal with mental health issues and felt they should recognise the problem and refer to a specialist:

> *"[...] certainly, the gastroenterologist and specialist nurses are not equipped to support people with more severe psychological needs, and I don't think they should be. I think what they need to be skilled at is [...] refer the person to the specialist's help. So they need not to be afraid of the psychological risk of IBD" (Patient 1, 50 years old, male).*

As a result of the fragmented care received by IBD patients with anxiety and/or depression, many patients found their way of coping with the disease. Some of these coping strategies included: exercise, "pre-plan" and use distraction. These findings suggest that behavioural activation and goal setting were acceptable to patients. One of the patients said:

> *"I read a lot, so I would immerse myself in something that I really love [...]. I would walk. [...]. It's a distraction. I take my mind off it." (Patient 6, 68 years old, female).*

One of the patients did not want any external help:

> *"I'm not keen on outside interference unless that absolutely necessary. So if I thought my life..., yes I would go to the doctor, but if I just feel the kind of depression or anxiety where I know what it's caused by, you know, because I have a flare-up of the colitis that really isn't something that needs medical or psychological interference [...]. It's not something that I want to, have to involve a lot of other people with. And I can manage it easier myself, than having everybody making an issue of it [...]. I think it makes it worse. It emphasises it; it makes it more important. The more people you have talking about you: are you worrying, do you feel ok, do you feel anxious, and that makes you anxious. It's sometimes better to just look after it yourself." (Patient 6, 68 years old).*

Interestingly, the principal concern of this patient was loneliness, and this was the only patient who had no support from their family members.

One patient thought that any kind of research was very important in the management of the disease:

> *"[...] any research or anything that is going to make a difference is while worthwhile. [...] in terms of mental wellbeing not just for IBD [...]." (Patient 12, 59 years old, female).*

This was supported by another patient who, after the interview, said that the reason for taking part in this study or any other research in the future was that it might help to manage IBD if not now then for the future generations.

3.1.4 Discussion

To the author’s knowledge, this is the first qualitative study exploring patients' and health professionals' views about patients' experiences of living with IBD and comorbid anxiety and/or depression.

The bidirectional relationship between IBD and mental health

Throughout all the themes, the psychological experiences of those living with IBD and comorbid anxiety and/or depression were emphasised. Participants identified IBD's negative influence on mental health and quality of life. They also acknowledged their need for psychological support. The bidirectional relationship between IBD and mental health theme highlighted the importance of addressing both conditions in combination. In previous studies, patients with IBD have been found to have reduced quality of life and a significant level of psychological co-morbidities, including anxiety and depression, particularly during active disease (Mikocka-Walus et al., 2016b; Devlen et al., 2014; Byrne et al., 2017). The level of anxiety and depression is often high in IBD patients, and both have an overwhelming impact on QOL but also on increased levels of complications and hospitalisation (Mikocka-Walus et al., 2016b; Navabi et al., 2018; Zhang et al., 2013).

The need for health care integration

The link between IBD and mental health services was a common concern among health professionals. It was noticeable that the collaboration between psychological and IBD services differs at different hospital sites included in this study. This was supported by patients' experiences such as long waiting lists to access a psychologist and the lack of psychological resources available to them. Patients also felt that IBD nurses and gastroenterologists were not trained in delivering psychological help, but they should recognise the mental health problems in IBD patients and refer them to specialist services. This result is in line with the second European evidence-based Consensus on the diagnosis and management of Crohn's disease, which recommended: "training of gastroenterologists to integrate psychosocial factors in clinical practice" (Van Assche et al., 2010). Both health professionals and patients were aligned in their response and agreed that a team of people should care for people with IBD and comorbid anxiety and/or depression.

The recent audits (first audit n=233, second n=228), to measure prevalence, patient participation, and potential benefits to mental health and/or quality of life of integrated psychological screening and intervention model, suggested that the integrated care model is more effective than the traditional biomedical model (Lores et al., 2019). Thus, patients with IBD should be offered integrated biopsychosocial care which includes a combination of gastroenterological and psychological treatments in addition to dietary counselling and other health services as required (Van Assche et al., 2013; Van Assche et al., 2010).

In England, Improving Access to Psychological Therapies (IAPT) programme that offers psychological therapies for patients with anxiety or depression was implemented by the NHS in 2008 (Clark, 2011). The evidence from several studies suggested that there is a need to revise the method of operating of IAPT service and possibly tailoring available with IAPT programme psychological therapies to improve the outcomes (Scott, 2018; Perez et al., 2018). The recent report showed improved waiting times, referrals completion, recovery, reliable improvement and reliable recovery outcomes as the result of the IAPT use (NHS Digital, 2018). Despite this and despite of the proposed new integrated model of care for patients with a long term condition (LTC) (National Collaboration for Integrated Care and Support, 2013), it was stated that a majority of patients with common mental disorders symptoms were not receiving treatment, and an inequalities in the access to the treatment were present (McManus et al., 2016). This - with increasing demand for services - has led to increased waiting lists (BMA, 2018).

These findings are in concordance with the findings from the present study which also determined a lack of resources, a long waiting list to access a psychologist, and limited psychological support. The evidence from recent studies demonstrated that scarce healthcare resource led to increased use of self-management in the treatment of the chronic conditions, and it showed the promising result in the management of anxiety, mood disorders (Shepardson, Tapio and Funderburk, 2017; Kidd et al., 2017) and IBD (Kennedy et al., 2004). However, there are only a limited number of self-management interventions available for IBD patients requiring new robust studies in the field (Tran and Mulligan, 2018). Nevertheless, some patients with anxiety and depression, as demonstrated in the findings presented in this Chapter used a variety of self-management strategies. This is consistent with the findings from recent qualitative research on self-management for mood and anxiety where patients used variety of self-management strategies (Villaggi et al., 2015). A personalised guided self-management treatment can reduce visits to primary care and hospitals as evidenced by the RCT where patients applied a treatment protocol developed by clinicians to manage an IBD relapse (Robinson et al., 2001). Interestingly, this study also showed that prior to the trial almost 25% of the patients attempted to treat relapses themselves unguided. Therefore, guided self-management may potentially make self-treatment safer (Robinson et al., 2001). Furthermore, self-management could reduce the utilisation of the healthcare system (Barker et al., 2018), thus, possibly, could be considered in the care model of IBD patients with comorbid anxiety and/or depression.

Presently, an integrated care model is recommended for all IBD patients (Mikocka-Walus et al., 2012b). NICE also advise that IBD patients should be cared for by a multidisciplinary team of specialists with a maximum of four weeks for assessment by a specialist (NICE, 2019b). Unfortunately, this advice remains at the guidelines level and has not been applied in practice, as highlighted in the findings presented in this Chapter.

Despite receiving some support from the gastroenterology team and in some cases from the GPs, most patients felt that the NHS let them down and they were left alone with the disease. They also recognised that they did not receive holistic care, the care they received was fragmented, and they were not involved in the management of the disease. These findings revealed the need for health care integration. This theme is broadly consistent with the result from a recent survey conducted in Scotland, where participants expressed the need for a holistic care approach in the management of IBD (Schoultz, Macaden and Watson, 2016).

The NICE guidelines highlighted the importance of providing holistic, integrated care for IBD patients (NICE, 2019b). However, they predominantly focused on the management of the physical symptoms of IBD. These guidelines recommend support for psychological wellbeing in IBD. However, there is no detailed advice on the management of psychological co-morbidities in IBD. Similar to the result from the survey in Scotland, participants in the current study wanted, in addition to the IBD clinicians, integration of other specialists, including a psychologist, in their IBD care team, which would contribute to better management of the disease. Jordan et al.

(2018) also concluded that patients with IBD and anxiety and low mood wished for psychological support from a clinician specialised in the IBD knowledge, showing the need for the integration of care and better access to specialists as opposed to GP driven IBD care.

Health professionals and patients expressed the lack of psychological resources available to patients with IBD and comorbid anxiety and/or depression as a common occurence. Inadequate government funding might explain such findings. There is a need for the health professionals to actively assess for mental health problems in IBD and inform patients about the high prevalence of anxiety and depression among IBD patients and if needed to refer for psychological intervention. Furthermore, the probability of patients with mental health issues to actively seek help is reduced due to the stigma associated with the providers of psychological and psychiatric services (Corrigan, Druss and Perlick, 2014), thus the establishment of an integrated health care model with psychological services attached to current IBD services increases the probability of patients feeling able to seek psychological help. However, some hospitals unambiguously had better psychological services than others. This was also articulated by health professionals. The patients had better psychological support with shorter waiting lists to the psychologist where gastroenterology department had a gastro-psychology service with a clinical psychologist specialising in gastrointestinal diseases in place. The debate about the geographical disparity in health is not new, and the term NHS postcode lottery increasingly used (Public Health England, 2017). The access to services and the quality of care are inconsistent across the country, and their availability and sufficiency depend on where people live (Care Quality Commission, 2018).

Patients in the current study expressed a desire to be involved in the management of their disease collaboratively with health professionals and highlighted the supportive role of the family. Similarly to the current findings, the results of another recent study that examined patients' views on lived experience with Crohn's disease also emphasised the need for the collaboration between patients and health professionals in the decisions about IBD treatment (Norton et al., 2012). The importance of the supportive family role for IBD patients was identified within the current study and has been recognised by quality standards (NICE, 2019b). Furthermore, NICE also recommends, if possible, for health professionals to consider and encourage family's and friends' support and involvement in the treatment and care of IBD patients (NICE, 2019b). It has been suggested that the principal concern of IBD patients and health professionals varies considerably as patients thought that health professionals did not believe them (Fourie et al., 2018). Moreover, from patients' view non specialists health professionals had limited IBD knowledge and could not provide the information about the disease (Fourie et al., 2018). This emphasised the importance of patients' and their family's involvement in the IBD management and participation in self-directed interventions.

The assessment and management of anxiety and depression were critical to both health professionals and patients, with both groups discussing the bidirectional relationship between mental health and IBD. The implementation of new strategies in the management of IBD with the integration of psychological services could improve the course of the disease and patients' QOL (Yanartas et al., 2016; Gracie et al., 2018). Consequently, the findings from the current study suggest the need for a new way of improving accessibility to psychological help which could improve patients' QOL and relieve the pressures from NHS services. The implementation of a new mode of delivery of the psychological intervention, as an online self-directed psychological intervention, into the management of IBD patients with comorbid anxiety and/or depression could ease the access to psychological help.

The lack of awareness about the disease

Overall, the findings indicate that mental problems in IBD patients are an under-recognised health concern. Patients reported a lack of awareness of mental health issues among health professionals. Health professionals also admitted that they did not proactively look for signs of a psychological problem such as anxiety and depression in IBD patients. This could show the lack of awareness, but also perhaps, that health professionals would prefer not to find any psychological issues in IBD patients as they would have to refer patients for psychological help which is scarce. Increasing health professionals' awareness may improve the link between mental health and IBD treatment services though it will not change the problems with funding.

These findings add further weight to the conclusions from other studies suggesting the need to increase awareness about mental health in IBD among health professionals, introduce screening for these factors, and have a referral system to mental health services in place for further diagnostics and treatment (Faust et al., 2012; Mikocka-Walus et al., 2016c; Mikocka-Walus et al., 2018). Enhancing knowledge and awareness about the mental health issues faced by IBD patients among health professionals and the establishment of routine screening for anxiety and depression in IBD clinics could improve patients' referral for psychological help and in turn, could improve the management of IBD (given the “bidirectional relationship” identified). However, failing to identify the mental health problem prevents people from obtaining help and access to the best available treatments (Corrigan et al., 2014). IBD patients' QOL could be improved by increasing awareness about the disease itself and the challenges faced by patients in the management of IBD among the public and health care professionals, by increasing understanding and improving provision of services (Bray et al., 2016).

Patients felt the lack of knowledge about the disease among GPs and society. The lack of knowledge about IBD among non-specialist health professionals and public reduced patients’ ability to self-manage which has been reported in the other qualitative study (Cooper et al., 2010). The lack of awareness among non-specialist health professionals could lead to delays in diagnosis and thus in accessing care (Angelberger et al., 2009; Avedano, Lönnfors and Vermeire, 2014).

3.1.5 Implications

The findings from this study indicated a bidirectional relationship between IBD and mental health and the need for integrated care for IBD patients with comorbid anxiety and/or depression. The lack of psychological support was a significant challenge in the management of the disease. Patients and health professionals discussed the lack of psychological support for IBD patients and the lack of integrated care as a major concern for IBD patients with anxiety and/or depression. Thus, the findings indicate the need for the new provision of care for this population of patients which should be considered by the health care providers.

The lack of awareness about the disease suggests the need for implementation of activities designed to raise awareness about the disease among public and health professionals.

3.1.5.1 Future research

Future qualitative research could examine the concepts explored in this research in different geographical locations to examine the generalisability of the findings from the current study.

3.1.5.2 Strengths and Limitations of the study

The strength of this research lies in the data coding being conducted thoroughly and systematically. The research team members cross-examined the process of data collection and analysis to assure the credibility of the study. The study generated an in-depth analysis of the patients’ and health professionals’ views about the patient's experiences of living with IBD and anxiety and/or depression not possible relying on quantitative only.

This study has some potential limitations. First, the questions that were used for the interviews could have been improved by being more specifically related to the overall aims. Some questions were not clear for the participants, hence required explanation from the researcher, which in turn could have influenced the response from the participant. It is possible that patients who did not require explanation understood the questions differently. On the other hand, there were other cross-questions and prompts used to verify the information answered by the participant.

Some patients did not always answer the question with a specific focus on themselves but commented on their thoughts of other patients’ experiences and views, which might not reflect their own perspective.

Another limitation of this study is that the anxiety and depression of a few IBD patients were managed well at the time of the interview. Hence, their answers could have been different if they had suffered from acute anxiety and depression currently.

There were no difficulties in the process of recruiting health professionals to the study. However, the recruitment of the patients depended on the health professionals involved and, hence, took longer than originally anticipated. The patients who expressed interest in participating in the interview were more likely a motivated group of patients, thus demonstrating an element of the convenience sampling.

On the other hand, the study also recruited less motivated patients. One patient was observed to reject any form of outside help. They were satisfied with the management of psychological issues, which mostly consisted of distraction and were not motivated to seek outside help.

The limitations of the qualitative research design should be considered. The study examined the population of patients and health professionals in hospitals in one region of England. The rich exploration from three different sites highlighted their different perspectives, but the study findings could be tested in different geographical areas to explore if the findings differ between locations.

The study had some methodological limitations. The interview with patients took place in the hospital facilities, and some patients highlighted that they had a fear of hospitals and doctors. In other instances, patients had social anxiety and would prefer not to leave their home hence the interview had to be shortened to reduce the stress for patients. Although these patients provided very valuable data, future studies should consider a different place for the interviews, such as patients' home, cafe, or community buildings to reduce the stress on the participants. Therefore, they would be more engaged in the interviews and, perhaps, provide more in-depth data.

3.1.5.3 Conclusions

The current study gathered important data on the patients' and health professionals' views about the lived experience of patients with IBD and anxiety and/or depression. The themes of a bidirectional link between IBD and mental health, the need for integrated care for IBD patients with comorbid anxiety and/or depression, and the lack of awareness about the disease were identified. One of the main challenges that the patients faced was a lack of psychological support, thus, indicating the need for the implementation of a new, more accessible care model for this population where psychological care would be more easily available.

4 Chapter 4: Patients' and health professionals' views about online psychological interventions (PI) for inflammatory bowel disease (IBD): a qualitative exploratory study.

Chapter 3 showed that there was an extensive unsatisfied need for psychological support in IBD patients with comorbid anxiety and/or depression who received standard IBD care. The lack of resources and funding for mental health support within the NHS warrants the development of online psychological programmes. This chapter looks at the patients' and health professionals’ views about online psychological interventions (PI), including their understanding of the intervention and willingness to utilise online PI. Furthermore, this chapter reports barriers and facilitators for the implementation of the programme. A prototype of an online intervention is also proposed in this chapter. This prototype is an early illustration of the online programme, providing recommendations and some visual representation of some of its elements that could be further developed and tested in future research outside this doctoral work.

4.1 Introduction

The importance of technology in the treatment of mental health and somatic disorders is increasingly recognised (Fairburn and Patel, 2017; Kloek et al., 2017; NIMH, 2019). One of the most developed online psychological therapies is Cognitive Behavioural Therapy (CBT). Online guided CBT has been found to be as effective as face-to-face (F2F) CBT for several mental disorders (Carlbring et al., 2018). CBT delivered over the telephone and online, with minimal clinician support, could significantly improve symptoms, QOL, coping and reduce distress for patients with IBS according to an RCT (n=558) (Everitt et al., 2019). Moreover, both of these modes of CBT delivery appear to be superior to treatment as usual (TAU), with the online intervention obviously being cheaper than telephone-delivered intervention in terms of quality-adjusted life-years (QALYs) (Everitt et al., 2019). Based on the evidence of the effectiveness of CBT in IBS and considering similar mechanisms of bidirectional interaction between the brain and the gut through the gut-brain-microbiota axis in IBD and IBS (Gracie et al., 2018; Martin et al., 2018), its effectiveness could be assumed in IBD. As a result, the use of the online PI programme could be an alternative to traditional psychotherapy for selected subgroups of IBD patients and, perhaps, equally helpful as conventional psychotherapy (McCombie, 2016) while being cost-effective (McCrone et al., 2004; Nordgren et al., 2014).

The government-funded initiative, Improving Access to Psychological Therapies (IAPT) for the treatment of depression and anxiety disorders in the UK (Clark, 2011), has improved access to the services and patient Disorders of brain-gut interaction (DBGI) recovery rate (Bastiampillai et al., 2019; Leigh and Flatt, 2015). However, in recent years, there has been an increase in the prevalence of common mental health disorders in the UK population (McManus et al., 2016), thus the need for more services. Online interventions could meet the increasing demand of patients for psychological support (Andersson et al., 2019). A recent small IAPT assessment survey showed no evidence of using online psychological interventions within the current offerings (Scott, 2018). However, patients' acceptability of online PI could not be explored within this study as only one out of the 90 patients was offered but declined online PI. Thus, there is a need to investigate the effectiveness and the acceptability of online delivered PI not just for the patients, but for the health professionals as well, which will help to inform current practice.

According to a recent survey conducted in Australia (n=102), IBD patients seem to prefer online PI rather than face-to-face PI (McCombie, 2014). However, recent trials in the IBD context show that online psychotherapy is associated with high attrition which may result from the website format, therapy duration or lack of contact with a therapist (Mikocka-Walus, 2015; McCombie et al., 2016), but it is at present poorly understood. A systematic review (20 studies, 1418 participants) reported that guided internet-delivered CBT is possibly as effective as F2F CBT for some psychiatric and somatic disorders (Carlbring et al., 2018). Support from a clinician could enhance the treatment effects of online interventions for some mental health disorders, including depression and anxiety (Kenwright et al., 2005; Saddichha et al., 2014). Thus, guided online PI, with minimal clinician contact, could be considered as a therapeutic option for IBD patients with comorbid depression and anxiety.

To effectively implement the findings in a clinical environment, the effectiveness of psychological therapies should be evaluated in mixed-methods studies with a qualitative study nested within a randomised controlled trial (Midgley, Ansaldo and Target, 2014). However, there are no trials or qualitative studies conducted to date to evaluate psychotherapy in IBD patients with comorbid anxiety and/or depression.

To empower patients and health professionals and increase the likelihood of the intervention implementation, the involvement of both of these groups as equal partners in the development (co-design) of the intervention is essential (Dawda and Knight, 2017).

4.1.1 Identifying/developing theoretical evidence and the study rationale

Psychological interventions are complex multicomponent interventions. Therefore, the development of an online intervention should follow the principles of the UK Medical Research Council (MRC) framework which guide development and evaluation of complex interventions (Figure 2) (Craig et al., 2013). The present qualitative study fits within the development phase suggested by the MRC framework (Craig et al., 2013). To effectively develop, evaluate and implement the potentially effective intervention, it is necessary to identify theoretical evidence, which informs the conduct of the qualitative study. The adaptation of the online intervention to the participants' needs with regards to the intervention content and design is likely to improve the acceptability of the intervention during the feasibility/piloting and implementation phases (Craig et al., 2013).

To identify the theoretical evidence base, a comprehensive systematic review of the literature was performed and reported in Chapter 2 of this thesis. The findings from this systematic review showed insufficient evidence of an association between online CBT and most physical or mental health outcomes in IBD and IBS patients, except significantly improved gastrointestinal symptom-specific anxiety and lower symptoms induced disability (Hanlon et al., 2018). Furthermore, the findings from the review were based on the data from unselected populations (anyone with IBD) due to the lack of RCTs which would target patients who are likely to benefit from psychological interventions most, including those with poor mental health.

Recently, several studies have recommended examining the effectiveness of psychological interventions for the subgroups of IBD patients that are "in need" of psychological support (who have a high baseline IBD activity; have been recently diagnosed; are young; with comorbid psychological distress) and are more likely to benefit from the PI (Mikocka-Walus, 2015; Gracie et al., 2017; Timmer et al., 2011). However, no study to date has tested the effectiveness of the intervention for such populations. Consequently, the intention of this research was to develop a prototype online intervention for the IBD population with comorbid anxiety and/or depression, which could be tested in a future feasibility trial.

To develop a theoretical understanding of the possible process of change, it was essential to supplement existing evidence and theory with new primary research. The conduct of the qualitative study is recommended for the development of the intervention for future evaluation, or evaluation of a previously developed and/or implemented intervention (Craig et al., 2013). Therefore, there was a need to perform a qualitative exploratory study involving interviews with the selected target group of patients with IBD and comorbid anxiety and/or depression and the health professionals involved in their care.

Aim

This study aimed to develop a prototype of an online PI for IBD patients with comorbid anxiety and/or depression. The intention was to develop an online intervention that could potentially (pending future testing) be delivered by more general medical staff who provide IBD care, such as IBD nurses, NHS junior mental health workers or an NHS psychologist to reduce the clinical load of psychologists and to be as cost-effective as possible to the NHS.

The research questions were:

1. What are the participants' views on PI?
2. What are the barriers and facilitators associated with online PI for patients with IBD and anxiety/depression?
3. How can an existing online psychological intervention be modified to meet patients' and health professionals' needs?

The findings from the current study can help to adapt the existing "Tame Your Gut" online PI programme for patients with IBD developed in Australia to meet patients' needs and as a result to potentially increase adherence, improve HRQOL and decrease the cost of care for IBD patients.

4.2 Methods

The full methods are presented in Chapter 3. This section presents only the information related to the online intervention.

4.2.1 Materials

The bidirectional link between IBD and anxiety and/or depression needed to be addressed in the adaptation of the intervention. The recent systematic review that examined the effectiveness of psychological therapy in disease activity, psychological comorbidity, and QOL in IBD patients showed that a variety of PI were used for IBD patients (Gracie et al., 2017). However, only two of the included trials used an online mode of intervention delivery, and both used CBT (Mikocka-Walus, 2015; McCombie, 2016). The systematic review (Hanlon et al., 2018), reported in Chapter 2, identified nine studies that examined the effectiveness of an online PI in gastrointestinal diseases, with two of the included RCTs focusing on IBD. These were the same studies listed in the previous systematic review on psychotherapy in IBD by Gracie et al. (2017). One of these studies used the "Tame Your Gut" psychological therapy program for people living with IBD in Australia (Mikocka-Walus, 2015), the second study used a modified (8-week) version of the original 10-week "Tame Your Gut" programme (McCombie, 2016). Apart from the programme developed in Australia, to date, no other online PI programs have been available for patients living with IBD. This online intervention was useful and well received by patients (Mikocka-Walus, 2015; McCombie, 2016). Therefore, this website was chosen to serve as an example to the participants of the present study with the plan to adapt this programme to the patients' needs and the UK environment.

Before the interview, participants were asked to familiarise themselves with the "Tame Your Gut" website (TAME YOUR GUT, 2019). Participants could refer to the programme during the interview. This programme was used as an example for patients to comment on the content and visual presentation. "Tame Your Gut" (www.tameyourgut.com) is a 10-week, two hours per week program covering the following topics:

- ✔ education about IBD and CBT
- ✔ goal setting
- ✔ relaxation training (stress and relaxation)
- ✔ understanding our thinking (automatic thoughts and cognitive distortions)
- ✔ emotional well-being (cognitive restructuring)
- ✔ avoidance & IBD (exposure and overcoming avoidance)
- ✔ coping strategies
- ✔ taking responsibility (assertiveness training)
- ✔ part of the tribe -social support (relationships and communication)
- ✔ attention & distraction
- ✔ maintaining the momentum (relapse prevention for mental health problems)

The sessions include videos, audio and text materials. There are videos including a conversation between a therapist and a doctor about aetiology, symptoms and treatment of IBD. There is also a video with the dietician, who explains diet requirements for people with IBD. Some materials can be downloaded from the website and links to other relevant resources are provided.

4.2.2 Prototype development

The prototype (model) building facilitates the prediction of the interrelationships between different components of the intervention, the association between the intervention and outcomes, and can provide evidence on how the intervention proceeds (Campbell et al., 2000). The data from the developmental phase could be then used to develop a new online psychological intervention for IBD patients with comorbid anxiety and/or depression and design an appropriate trial to determine patient benefit.

4.2.2.1 Prototype enhancement

To enhance the prototype, a person-based approach to the development of digital health interventions was taken (Yardley et al., 2015). The person-based approach involves guiding principles, and qualitative research at all stages including design, development, and trial/implementation of the intervention. It is used to enhance and supplement the earlier discussed theory and evidence-based approaches suggested by the MRC framework (Craig et al., 2013; Yardley et al., 2015). Based on a person-based approach, guiding principles help guide through the intervention and make an outline of the essential aspects required to attain the intervention goals (Yardley et al., 2015). These principles were used in designing the current prototype.

4.2.2.2 Initial development of the intervention prototype - participants interviews

As the current intervention targets specific groups of patients, it is crucial to attain their views to be able to tailor the intervention to meet their requirements (NICE, 2007). To increase the effectiveness of the interventions, there is a need to combine a wide range of evidence from individual, community and population levels (NICE, 2007). Themes identified from the interviews with patients and health professionals along with the theoretical evidence were used for the development of the prototype of the online psychological intervention adapted explicitly for the needs of IBD patients with anxiety and/or depression in the UK. The fluctuating nature of IBD and anxiety/depression symptoms became apparent from the patients' and health professionals' views (discussed in Chapter 3). The fluctuating characteristic of IBD has implications for designing an online PI, which patients could use as an ongoing tool when needed. The fact that IBD affects patients’ psychological functioning during remission in the absence of inflammation (Lix et al., 2008), also suggests the continuous need for the use of this type of intervention.

4.3 Results

In the present study, 13 IBD patients with comorbid anxiety and/or depression of various ages and mix of genders were interviewed. To further tailor the specific context in which the online intervention was to be applied, 12 health professionals, who for at least two years had cared for patients with IBD, were interviewed to establish their views on online PI for IBD patients’ with comorbid anxiety and/or depression. See Chapter 3 results for detailed demographic characteristics of the participants.

4.3.1 Patients' and health professionals' perspective on online PI

Participants talked about their circumstances and described the factors which would encourage or stop them from engaging in the aspects of the online PI and how the existing "Tame Your Gut" programme could be adapted to their needs and requirements (see concept map Appendix 14). Patient responses regarding the ability to be involved in the self-directed online intervention were grouped into two major themes: 1) online psychological intervention is good, but not for everyone and 2) the existing online PI programme requires changes to the visual and contextual presentation.

4.3.1.1 Online psychological intervention is good, but not for everyone

All patients, except one, had positive attitudes towards the Internet, mobile apps and participation in an online PI. Patients were willing to participate and complete the programme irrespective of age and computer illiteracy which was suggested as a potential barrier by health professionals. However, the health professionals stated that they were uncertain about the patients' involvement, ability to facilitate and complete the self-directed online programme. The agreements and disagreements observed between practitioners and patients with regard to the participation in an online intervention are presented in Table 12. The major disagreements were about patients' participation in the programme and specific barriers for participation. Both groups agreed that the programme could increase the accessibility of psychological help and that the clinician-assisted version of the programme was preferred to the unassisted version.

The health professionals concluded that the lack of human interaction, inability to tailor the intervention to the individual needs and the online format of the treatment would prevent patients from participation. Most patients agreed that tailoring the intervention to individual needs is essential. Moreover, both the health professionals and patients strongly agreed in their responses that personal interaction is important, and that the clinician-assisted self-directed online programme would encourage patients to comply with and complete the programme.

The health professionals thought that the computer illiterate and older patients were unlikely to be involved in a self-directed online PI programme. This differed to the patients' views. For those who were in their seventies (n=2) and did not use a computer, this was not a barrier. They expressed confidence in their motivation and personal commitments with the help of their family members and encouragement from health professionals. The differences in the views were also observed regarding participation in the programme for less well-educated individuals. Health professionals thought that this group of people would opt-out of participation in the programme, while patients suggested that people could watch the videos on the programme if they were not able to read. The patients and the health professionals were equally positive about the accessibility and flexibility of the programme.

Table 12 Barriers and facilitators

Barriers and facilitators (Primary codes)	Codes	Quotations
Barriers	Both groups • not tailored to the individual • personal interaction is important Patients • not improve the wellbeing • it could feed the peoples' isolation • "stigma attached to it" • no access to the Internet • negative attitude to the Internet and mobile apps • if doesn't work for me • feed loneliness • embarrassment, the stigma attached to mental health • do not need now • repeated reminders Health professionals • busy lifestyle • not admitting the problem • the older population would not use • computer illiterate, learning difficulties, not well educated • patients "might enjoy a sick role"	*"[...] now I would not, because I didn’t think I needed, but might have done in the past." (Patient 1, 50 years old, male).* *"Online is great, but every so often you should have a forum where you see people, where you see faces, and you see hearts. Because of the sad things for a lot of IBD sufferers, it's the loneliness. [...]." (Patient 12, 59 years old, female).* *"[...] some people just don't like admitting barely that they have got the problem and like to try to manage things with their head in the sand." (Female, health professional, 53 years old).* *"[...] some people are naturally obstructive and kind of enjoy the sick role, and I think they would be harder to engage." (Female, health professional, age not indicated).* *"There isn't a reason why I wouldn't do it. Why other people not do it? Might think it is some kind of stigma attached to it. But, personally I wouldn't think that." (Patient 13, 32 years old, female).* *"I think, my consent about using for everybody, would be that it isn't flexible enough so meet the individual needs of the user." (Female, health professional, 30 years old).*

Barriers and facilitators (Primary codes)	Codes	Quotations
	• lack of motivation	
Facilitators	Both groups • positive attitude towards the Internet and mobile apps and participation in the online intervention • accessibility • flexibility • confidentiality • personal interaction (partial human contact) • tailoring intervention to individual needs • encouragement from health professionals • promotion of the programme to the patients by health professionals • family support • present the elements of the programme from a patient's perspective • patients' testimonials • "knew expected outcomes" • the programme makes the difference to patients' wellbeing • keep patients' interest in the programme • repeated reminders Patients • suitable for people with social anxiety	*"I don't use a computer[...]. I find it difficult to use a computer. [...] my wife [...] is into computers for years. [...]. I would use it. [...], my wife will make that [laughing]. Yeah, I am sure, I would" (Patient 4, 70 years old, male).* *"I would, if the IBD nurse recommended it, that would be one incentive." (Patient 1, 50 years old male).* *"[...] it allows me to choose the bits that I think would be the most helpful and for me to do it in my own time." (Patient 1, 50 years old, male).* *"[...] it may be accessible within their own time, they can do it in the evening, on the night, on the weekend, you know, they can dip in and out it, they could go back to it." (Female, health professionals, 32 years old).* *"... the chaps in my office for example where I work [...], the men were glued to the computers all the time, even in the lunch hours whereas the women took a break to talk to people about their various problems, the problems with their health, the problems with their children, the problems with their make up or whatever and I just wonder if males automatically turn to the Internet now and women may be less so and maybe that like be reflected in the website. And, I think, that men and women may handle the disease differently as well." (Patient 6, 68 years old, female).* *"I find the support from other people with IBD online invaluable" (Patient 12, 59*

Barriers and facilitators (Primary codes)	Codes	Quotations
	• there is nothing else • gender difference Health professionals • younger, more savvy	*years old, female).*
Limited role of computerised therapies	Health professionals • limited role of online PI • uncertainty about the patients' involvement and ability to facilitate and complete the self-directed online programme. • involvement in the self-directed programme - a mixed bag	*"I think it could be very useful. I think, similar to one I have it used in IAPT [Improving Access to Psychological Therapies] services. I think, if you think about a stepped care model it would probably be used, maybe for the people with a milder and off psychological problems, who might be more motivated to access it and to drive themselves to complete it independent of a facilitator or a therapist [...] as a kind of a lower level intervention for people with milder problems, but [...] a more severe mental health [...] I would feel a bit more consent, directing people to that mode of intervention. I think there is a role for computerised therapies, but I do think that it is a limited role. [...]. I think my main message would be that it isn't for everyone, and it cannot be instead of having the availability of one to one, face to face psychotherapy if needed." (Female, health professionals, 30 years old).* *"I think it depends on the symptomatology and whether they think it's um, and whether they think it is an issue for them. So, I think it is probably about the patient's selection" (Male, health professionals, 49 years old).*
Understanding of talk therapy	Both groups • a vague understanding of the talking therapy • the lack of knowledge	*"It's just talking through it. It's just talking if you've got any issues. [...]. I don't know how helpful it would be with IBD [...] I'd say more practical, doing a thing is better rather than talking." (Patient 9, 20 years old, female).* *"It won't change the symptoms, but it will change how I feel about them" (Patient 3,*

Barriers and facilitators (Primary codes)	Codes	Quotations
		49 years old, male). *"It is a therapy that involves talking to someone through your thoughts and feelings to help you manage your problems by changing the way you think and behave, like CBT." (Female, health professionals, 43 years old).*
Wish to take control of their own treatment	Patients • would like to take control of their own treatment. • would like to get health professionals support.	*"It's got to be the person's own responsibility" (Patient 2, 39 years old, male).* *"I would absolutely dearly love to take control of my own treatment. Do I have the ability? No. No, absolutely not." (Patient 12, 59 years old, female).* *"Well, I would, but I also like sound back and having specialists looking after me." (Patient 8, 70 years old, female).*
Previous experience of psychological intervention	Patients • no experience • counselling, • CBT, • hypnotherapy; • had positive outcomes • all, except one, positive attitude Health professional • no experience • only one had experience with psychological intervention.	*"[...] seeing a psychologist certainly helps [...]. It did help me." (Patient 4, 70 years old, female).* *"My experience of CBT [...] was 20 years ago. And I'm still living benefit from the kind of changing my thinking. I never knew that I could think in a different way. That's what my CBT taught me." (Patient 1, 50 years old, male).* *"My experience of it, I haven't used it personally as a user, but have used it as a staff member for working within... it gives access to psychological therapy service, so we use two computerised programmes for depression and anxiety in my role there, some experiences delivering, well assessing people of, on those, being a facilitator really to supporting people who are using those programmes." (Female health professionals,*

Barriers and facilitators (Primary codes)	Codes	Quotations
		30 years old).
Previous experience of using apps and Internet	Patients • two patients had previous (one patient had a negative attitude and one positive experience of using Internet apps for depression) • none used the apps or the Internet for IBD management. Health professionals • no experience of using apps for IBD or mental health • one health professional used for the management of mental health.	*"The app [...] for the depression. Not for IBD, but for mental health. The calming things, they're really good." (Patient 9, 20 years old, female).* *"I did try a couple of Internet apps for stress. [...] but [...] I just started irritating, [...] on the Internet you are sitting there, and you breathe in, and you breathe out, at the end you feel like saying like shut up to the app." (Patient 6, 68 years old, female).* *"I do not really have any, at all really, apart from direct people to the websites for information, but not apps or anything like this. Not really." (Female health professionals, 52 years old).* *"I [...] have used it as a staff member [...] we use two computerised programmes for depression and anxiety. [...] being a facilitator really to supporting people who are using those programmes. [...] some people it provided greater flexibility, [...], my consent about using for everybody, would be that it isn't flexible enough to meet the individual needs of the user. [...] it takes away the therapeutic relationship, which is the facilitator for change for a lot of people."*
Expectation	Patients • accept the condition • have information, • reassurance, • have a positive outlook,	*"I think that even just a short time that I've spent looking at it ["Tame Your Gut"], it makes me realise, I've got to be more positive about what I've got rather than focusing on the negatives of the IBD." "If you reduce the stress, I do believe, it would probably help your flare-ups" (Patient 5, 56 years old, female).*

Barriers and facilitators (Primary codes)	Codes	Quotations
	• improved QOL, • help flares through the management of stress • manage anxiety and stress	*"I would expect my mental outlook to change. It's the mental I have a problem with. [...] by doing this [the online psychological intervention]. I think this change my outlook... (Patient 8, 70 years old, male).*
Clinician-assisted online programme	Both groups • the personal level was important • the preferred clinician-assisted online programme • the clinician-assisted programme should be an option	*"[...] one to one relationship with somebody [...] to me was really-really important" (Patient 7, 67 years old, female).* *"The ideal way to do it would be to have your first meeting with the clinician; then after that, it would be online. So, they [..] talk you a little bit through it and to lay out and tell you what the outcomes are. [...] if you meet somebody face to face, you might reinforce the importance of it and how helpful it can be [...]" (Patient 13, 32 years old, male).* *"Either of them, [...], because text works as well." (Patient 10, 45 years old, female).* *"[...] my main consent about the computerised therapy [...], it takes away the therapeutic relationship, which is the facilitator for change for a lot of people." (Female health professionals, 30 years old).* *"[...] the clinician-assisted version would work a lot a lot better. [...] to be able to then talk about the content of what you were doing online [...] it could be at the beginning, after a month, yeah, the middle and the end, it could just be less frequent contact than what you would do in normal therapy. [...], it might help as much with the motivation to continue with the programme." (Female health professional, 30*

Barriers and facilitators (Primary codes)	Codes	Quotations
		years old). *"[...] some people like talking, it is the best way of resolving problems, and there are people who just like to get on with things [...]." (Female health professionals, 53 years old).*

4.3.1.2 The technical and visual presentation of the online programme

A concordance was observed between the health professionals and patients regarding the technical aspects and visual presentation of the online programme (see Table 13). Most of the patients and health professionals were satisfied with the format and user-friendliness of the existing programme, though some suggested the need for a mobile-friendly version.

The health professionals suggested that the intervention should have plain language (a couple of patients preferred the scientific language), bullet points, to be visually cleaner with less text, have introductory videos to each session, and use the videos with patients and health professionals, as well as offer activities to download. They proposed between three and ten sessions, of 15 min to 1-hour duration. This was to some extent in agreement with patients views, although they were more precise in their responses of what they wanted to be included in the online programme and, in particular, they wanted to see the other patients' experience, a patient forum, a and chat room. Patients also wanted to see the information about IBD itself, and various management strategies, including coping. The findings from the qualitative study on patients' lived experience with IBD and anxiety and/or depression (Chapter 3) showed the patients themselves, without acknowledging it, were using some elements of behavioural activation (BA) such as exercising, reading, and other activities in everyday life to cope with the burden of the disease. Some patients and health professionals were not sure what should be included in the online programme. Thus, a psychologist with relevant consideration of the patients' preference should develop the context of the programme.

All patient participants, except one, in the current study, expressed interest in taking part in the development of the online psychological intervention programme, indicating the likelihood of the intervention uptake. They agreed to comment on the developed programme, hence agreed to be contacted to participate in a future feasibility trial.

Table 13 Changes to the technical and visual presentation of the online programme

Primary codes	Codes	Quotations
Format and user-friendliness	Both groups - positive feedback	*"I thought it was really good, very well laid out, nice format, nice ten weeks chunks. [...]. Yeah, make sense, there is nothing over too technical, I did understand." (Patient 13, 32 years old, male).* *"[...] consistency from week to week, so [...] the layout is the same. So, if I learn on week three that was a helpful [...] then I am more likely to go to week four to that same place so it's about the consistency of appearance, so that I can learn as quickly as possible where to find where to look for the bits that would be helpful." (Patient 1, 50 years old, male).* *"...the format looks great, the way it was laid out, and there was a definite programme to follow, with different areas" (Female, 52 years old).*
Number and duration of the session	Health professionals - 3-10 sessions - 15 minutes to the 1-hour duration - should not be longer than ten weeks Patients - 3-12 sessions - 15 minutes to 1-hour duration - should not be longer than ten weeks for most patients - allow some flexibility - be able to come back to the programme if needed - online support should be	*"I feel you should do it for as long as you needed. I don't think you should set. [...] you should do stuff as long as you need [...], you should be able to come back to it, if you need [...], because with anxiety you don't know how long it's last, yeah. I find that anxiety and depression phases. You just don't know." (Patient 9, 20 years old, female).* *"I need ongoing online support that you could dip in or dip out off." (Patient 12, 59 years old, female).* *"around about 6 to 8, some patients might need less, some patients might need more and something in short bursts, probably, I don't know, 15 minutes might be suitable for some people, other patients might find that they needed a bit more." (Female, 53 years old).* *"I cannot really say. I don't have a way of judging it." (Male, 54 years old).*

Primary codes	Codes	Quotations
	ongoing.	
Text, language	Both groups - text easy to read, understandable - to use less text - more bullet points - plain language - two patients would like to see more scientific language.	*"I thought it was easy, easy to understand. I also felt that somebody with IBD probably had a lot to do with developing of it, because they really think to understand how you felt. [...] different scenarios they really seem to understand it" (Patient 5, 56 years old, female).* "*The bullet points are probably handy because it's kind of breaks down to the chunks [...]" (Patient 13, 32 years old, male).* *"It should be plain language" (Female, age not indicated).* *"it would seem quite overwhelming with long bits of text, so certainly text should be short paragraphs, maybe with bullet points to the top just so, or bullet point to the end, so once they read it, or before they read, so they know essentially what they need to get out of it. Sometimes bullet points do not have enough information." (Female, 32 years old).*
Pictures	Both groups - happy with "stress-free" pictures on the website.	*"I didn't think of that. I didn't take any notes of that, didn't really noticed." (Patient 13, 32 years old, male).* *"No, I thought, they had what they needed to have. They had a different picture for each session and things like that. So, I thought it was about right, yeah." (Patient 5, 56 years old, female).*
Colour	Both groups - happy with the website colours One patient - darker colours One health professional - less bright	*"darker colour. [...] blue or grey or black. It is the matter of to be able to see. [...] redo it." (Patient 8, 70 years old, male).* "*I think it is too bright blue, should not be yellow or red for colour blind people." (Female, health professional, 43yeaes old).*

Primary codes	Codes	Quotations
	• not yellow, red	
Video	Both groups • videos are important • to include videos with patients and health professionals • one video per session between 5 and 20 minutes • an introduction to the session's video.	*"[...] even its technology, it feels more personal. I think all session should have videos [...], it sets the tone, and it feels personal even it's probably not." (Patient 12, 59 years old, female).* *"[...] that is a very modern way of introducing topics." (Patient 1, 50 years old, male).* *"[...] a separate video for each topic, but even if it's instructions on how it could be even five bullet points [...] can be a quicker overview, and at the end, the summary again to reinforce it." (Patient 13, 32 years old, male).* *"I might give people some introduction videos, and then I might let them choose from the range." (Male, 49 years old).*
Suggestion on what to include	• anxiety and stress management • anger management • relaxation techniques • goal setting • coping strategy • the others' patients experience, testimonials • information about IBD and its treatment • programme tailoring and designed to navigate and signpost patients • not sure what should be	*"I am not a psychologist. I don't really know the full range of things that people would expect to be offered." (Patient 3, 49 years old, male).* *"[...] there should be like a chat, where you can have somebody on the other side." (Patient 10, 45 years old, female).* *"if a system was set up whereby the possible questions you had and things were there to be answered" (Patient 7, 67 years old, female).* *"if my anxiety is very bad, I am on so many different medications, that actually makes my thought process difficult. So if I am anxious and stressed, I've got these other things going on as well, so it's difficult at that point to work out what I need. Because the fatigues hit, the low mood hits and everything hits. I almost feel it's like any programme needs to be a signposting programme that can do some other thinking for you." (Patient 12, 59 years old, female).*

Primary codes	Codes	Quotations
	included in the online programme • work on mobile devices such as mobile phones and tablets • music • glossary • consistency in layout • clinician-assisted option recommendations • chat, support, focus group, forum	*" [...] a credible medical site with information about IBD itself, the actual medical information about the physical condition, progress that they were making in research about the disease, a likelihood of them ever finding the way to really control or even cure it, changes in the treatment [...]" (Patient 5, 68 years old, female).* *"[...] there should be like a chat, where you can have somebody on the other side." (Patient 10, 45 years old, female).* *"if a system was set up whereby the possible questions you had and things were there to be answered" (Patient 7, 67 years old, female).* *"I was struggling to... if I would get out my laptop, it would be fine, but because I was doing it on my phone, I was having to make a sort of to make it bigger so that I could see, what it actually is said. Then, I was having to move the page across; it makes a bit harder to read." (Patient 5, 56 years old, female)."* *"You need to ensure they do work on an I-phone or on a tablet." (Male, 42 years old).*

4.4 Discussion

To the author’s knowledge, this is the first qualitative study exploring patients' and health professionals' views, attitudes and experiences of online psychological interventions for IBD. Based on the theory and evidence from this qualitative study, a prototype of the intervention was developed.

4.4.1 Summary of the findings

The responses from the participants in the current study indicated that they welcomed the format and user-friendliness of the existing "Tame Your Gut" programme. There were similarities in the responses from the health professionals and patients about the length and number of sessions, with the agreed duration between 15 minutes and 1-hour and between 3 and 10 sessions. Most participants accepted the plain language and desired less but clearer text. This could be explained by the comorbid fatigue and the fact that patients with IBD and anxiety and/or depression are less able to process large amounts of information (Jamison, Sbrocco and Parris, 1989; van Langenberg et al., 2017; Rock et al., 2014), hence breaking it into sections and presenting as bullets point would be necessary for the programme. In addition, it was found that the videos were considered essential to the participants. They felt that the videos were more personalised than the text. Therefore, the implementation of the introductory videos that would refer directly to the participants could help with the lack of personal interaction during online sessions.

In some cases, patients wished to take part in the online programme independently, for example, when the patient did not want to leave the house. However, even a patient with a social anxiety disorder preferred a clinician-assisted version if it was accessed in their home. Similarly, the combination of other forms of assistance could be considered, for example, Skype, telephone, email, text.

Although some health professionals suggested that accessing the online programme would require a certain level of computer literacy and education, this was largely not supported by the results of the study. Patients of different ages, levels of education and computer literacy were interviewed and all of them understood the context of the existing programme and indicated that they would access the programme with the help of a clinician or family member. Further, despite the difference in access to psychological services, there were no differences observed with regards to the patients' acceptance of online PI at different hospital facilities.

Both health professionals and patients agreed that personal interaction was important. This finding is supported by the literature and also highlighted the importance of a therapeutic alliance between a patient and therapist for good treatment adherence and for some patients this alliance could be the facilitator for change (Barlow, 2014). The majority of participants in both groups recognised that encouragement from health professionals would increase compliance and completion of the online programme.

The health professionals were unsure about whether patients' would agree to access an online PI and whether patients would complete the programme. Most patients expressed interest in the programme participation and were confident about its completion. Attitudes varied and were based on the patients’ and health professionals’ responses about the provision of holistic care, as discussed in Chapter 3. Health professionals believed, despite the lack of psychological resources and the long waiting list, that they provided adequate support for their patients. Contrary to the health professionals views patients reported feeling alone with their disease. This highlights the scale of the problem that patients face and something which health professionals may underestimate. Another reason for these varied viewpoints could be that all health professionals, except one, had no previous experience of using mobile apps or the Internet for IBD or mental health management. However, this was not seen as a barrier for patients. Only two patients had experience of using mobile apps for the management of mental health. One found the intervention very useful, while the other stopped using it and had a negative experience. However, another patient had a very strong negative attitude to any form of outside help irrespective of the mode of delivery. This person’s view added richness to the perspective of other participants in the study. It is important to acknowledge that the self-directed online PI might not be an appropriate tool for the management of depression and anxiety in some IBD patients such as patients with severe depression and anxiety, patients who reject any form of psychological help or support but, perhaps, offers help to others.

Contrary to the patients’ perception, the health professionals considered the lack of patients' motivation, computer illiteracy and older age as barriers to patient participation in the online programme. Although patients did not indicate them as barriers to self-directed treatment, they did express the need for support from family members or clinicians throughout the process. It is possible that some patients had an optimistic view of the online programme as a result of a very positive outcome of F2F therapy. Therefore, they hoped for the same outcomes, but without the unnecessarily waiting list. On the other hand, a previous study exploring patients' willingness to participate in an online PI programme concluded that patients preferred the online mode of delivery compared to F2F (McCombie, 2014). However, the study was conducted in New Zealand and it is unclear if the results would translate to the UK environment.

The health professionals and patients indicated that the online programme could improve the accessibility to psychological support, avoiding a long waiting list. Therapy delivered online as part of IAPT services that provide evidence-based psychological therapies is already recommended in a stepped care model for people with anxiety disorders and depression (NICE, 2019a).

Therefore, the findings suggest that a wide range of psychological treatments for IBD patients with anxiety and/or depression could be considered instead of classical F2F therapy. It is therefore essential to explore the possibility of self-directive online PIs. This mode of delivery could widen access to the therapies (Kessler et al., 2009). On the other hand, the high dropout rate in online interventions is often experienced. A meta-analysis of data from 2,705 patients on self-guided online interventions for depression reported that such factors as a lower level of education, male gender and co-morbid anxiety significantly increased attrition risk (Karyotaki et al., 2015), although, it significantly decreases with age (Karyotaki et al., 2015). These factors suggest a necessity for some contact with the clinician to be considered during the implementation of the intervention.

4.4.2 Summary of the evidence from the previous literature in the context of the study's findings

The participants' views and suggestions formed the basis for the prototype intervention. To provide evidence-based recommendations for any future online interventions, evidence from other studies was examined to assess whether the recommendations are feasible, effective and valid. If evidence in mental health and/or gastrointestinal diseases was lacking, then evidence from other fields were utilised.

The most common patients' suggestions on what should be included in the intervention were anxiety and stress management, relaxation techniques, goal setting and coping strategies. These are part of the "Tame Your Gut" programme. This programme already demonstrated its effectiveness in improving the QOL of patients with IBD and was well received by patients in Australia and New Zealand (Mikocka-Walus, 2015; McCombie, 2016). Thus, the author discussed only the features of the programme that the patients wished to change or features that were not already included in "Tame Your Gut" but suggested by patients.

The clinician-assisted option of the PI

The most commonly reported barrier to participation in an online PI programme was the lack of personal interaction. Therefore, many participants chose the clinician-assisted option, which they thought would increase the ability to facilitate aspects of their own treatment, compliance and completion of the programme. The evidence from the literature also suggested that online psychotherapy, CBT in particular, seems to be effective when therapist-assisted, or with the addition of telephone support, or combined with F2F interventions (Kessler et al., 2009; Brabyn et al., 2016; Erbe et al., 2017; Everitt et al., 2019; Grist et al., 2019). Guided online interventions were more acceptable and offered by GPs in primary care compared to unguided interventions according to a large (n=1044) survey (Breedvelt et al., 2019). Nevertheless, some participants thought that the clinician-assisted or exclusively self-directed programmes should still be an option.

Tailoring

Patients and health professionals expressed concern about the online psychological intervention not being tailored and wished for this programme to meet each patient’s needs. “Tailored health promotion materials are any combination of information and behaviour change strategies intended to reach one specific person, based on characteristics unique to that person, related to the outcome of interest, and derived from an individual assessment” (Kreuter et al., 2000, p. 4). Tailoring engages various strategies directed on achieving more substantial outcomes (Hawkins et al., 2008). Hawkins et al. (2008) suggested that content matching, feedback and personalisation strategies help to attain the tailoring goals (Hawkins et al., 2008). Indeed, tailored online interventions appear to be more effective compared to non-tailored (Strecher, Shiffman and West, 2005; Lustria et al., 2013; De Cocker et al., 2016).

All patients in the present study had pragmatic expectations from the completion of the programme. They hoped to improve their mental health and QOL, though some thought they could have better management of IBD through the management of mental health. These expectations led to patients' suggestions on the content and format of a future intervention. Some patients and health professionals were not sure what should be included in the online programme. Thus, the context of the programme should be developed by the psychologist with the consideration of patients' preferences.

Number and duration of sessions

There is no univocal opinion on the number and duration of the online PI sessions. The majority of studies in the systematic review (Chapter 2) suggested 10-week. However, a clear link between the length of the programme and the attrition rate was not observed. On the contrary, a 6-week intervention had a higher attrition rate than some 10-week programmes (Hunt, 2009; Ljotsson, 2011). All participants in the current qualitative study agreed that the programme should not exceed 10 weeks and some suggested the need for ongoing access to the programme. The 8-week "Tame Your Gut" version of the programme was well-received by patients with IBD and it improved their QOL. Thus, an 8-week programme is recommended in the prototype of the current intervention. Any briefer intervention would not comprise all the necessary components and topics.

Videos

The importance of videos was highlighted by the participants. Patients and health professionals found videos more personal than text. This is supported by the finding of online health interventions for other mental health disorders, where patients found that communication through videos had a more personal style (Ben-Zeev et al., 2018).

The evidence from various online health interventions also showed that the information delivered through videos appeared to be more effective than the textual presentation of information, by improving patient engagement, concentration and interest (Lee, 2011; Alley et al., 2014; Soetens et al., 2014; Stanczyk et al., 2016). However, evidence from another trial suggested that for prevention of weight gain, the video format of delivery was not superior to the text format, though it depended on the patient's preferences (Walthouwer et al., 2015). Patients particularly appreciated videos with a gastroenterologist in the "Tame Your Gut" programme, which provided information about IBD. Thus, the author recommends the inclusion of these videos with permission from the author or the creation of similar videos. There is no evidence to suggest which video duration is best for this type of online intervention. Nevertheless, considering the time patients are prepared to dedicate to the intervention and their views about the videos presented in "Tame Your Gut", they should last between 5 and 20 minutes.

The repeated reminders

The participants' views about repeat reminders were divided. Nevertheless, provision of information, sending reminders, self-monitoring, reinforcement and other forms of further supervision/support could improve the effectiveness of the complex interventions for long-term conditions (Haynes, McKibbon and Kanani, 1996), thus were used during the prototype development.

A mobile-friendly version of intervention

The author also recommends having a mobile-friendly version of this intervention, to satisfy the participants' needs and thus increase the likelihood of engagement as discussed earlier. A recent mixed methods study (n=129) showed that smartphone apps are effective in improving depression symptoms (Inkster, Sarda and Subramanian, 2018). However, this study was observational and used pre-post quantitative analysis.

Forum

Patients wished to have some form of communication with other patients with similar conditions and clinicians in the format of a forum or chat room. A study in the IBS context found that an online support group of patients with similar diagnoses mainly focused on the interpretation of symptoms, disease management and on the interaction with clinicians (Coulson, 2005). Another recent study analysing 2,000 posts of online support for IBD patients during a two year period also found that the majority of patients were looking for information and emotional support (41.1% and 36.1% respectively) (Britt, 2016). Network and esteem support (type of social support directed at improving peoples' believe in themselves) or encouragement were considered less important (14.2% and 14.3% respectively) (Britt, 2016). A qualitative study examining a community online social support also found that information about IBD was one of the major themes (Nehasil, 2015). This raises concerns as to whether patients were looking for answers about disease symptoms and management from other patients and the quality of responses they received. Patients could possibly be satisfied with the testimonials in the proposed intervention, which were highly valued by patients and health professionals in the present qualitative study, and the harmful information could be moderated in this format. It emerged from an ethnographic study of patients with cystic fibrosis that a forum was a useful tool not just to share information and emotions but to improve interactions with health professionals (Kirk, 2016). The forum option could be considered and its feasibility tested in a future feasibility trial.

4.4.3 Recommendations and real-world implementation

Therefore, based on the findings from the present study and evidence from the previous literature in the context of the study's findings described in the section above, the following recommendations for the future interventions and how these recommendations can be implemented in the real world are provided.

4.4.3.1 Recommendations

Table 14 Recommendations

Primary codes	Comments
Format and user-friendliness	✓ have consistency in the layout
Number and duration of the session	✓ 8-week programme approximately of 1-hour duration ✓ after the completion patients should be able to come back to the programme if needed, to have ongoing online support
Text, language	✓ reduce text by introducing bullet points with the link to more detailed text ✓ use plain language with the link to the scientific resources, articles
Pictures	✓ have "stress-free" pictures on the website.
Colour	✓ use similar colour schemes to the "Tame Your Gut"
Video	✓ inclusion of videos into each session between 5 and 20 minutes with an introduction video to each session as essential. ✓ to include videos with health professionals and patients
Suggestion on what to include	✓ anxiety and stress management ✓ anger management ✓ relaxation techniques ✓ goal setting ✓ coping strategy ✓ the others' patients experience, testimonials ✓ information about IBD and its treatment ✓ programme tailoring ✓ mobile-friendly version ✓ glossary ✓ clinician-assisted option ✓ chat/forum

4.4.3.2 The real-world implementation of the PI

4.4.3.2.1 Tailoring

To tailor the current online intervention, patients will be required to complete a pre-test before the start of the programme and at the end of it. The pre-test will contain questionnaires to measure the levels of distress and HRQOL. A short version of questionnaires is recommended to reduce the burden on patients as they reported that numerous questions put them off using interventions. After the completion of this online intervention programme, patient' outcomes could be assessed. Based on the results and depending on the chosen option (entirely self-directed or clinician-assisted), patients could receive an individualised message with the patient's name to complement them on the completion of part of the programme and suggesting the return to the programme, if needed, as they will have unlimited free access after completion. In the event of no improvement or worsening of the outcomes, patients will receive a telephone call from a clinician, in addition to the massage, to encourage attending a high-intensity therapy (step 3 of the stepped care model).

Based on the answers to the questions during the pre-test, through tailored matrices, the programme design will allow participants to choose automatically from the database the appropriate response text using if-then principles (Dijkstra and De Vries, 1999). Use of algorithms complicate the development of the online PI (Hawkins et al., 2008). Nevertheless, feedback technology appears to reduce symptom severity in patients with depression and anxiety at risk of poor response to treatment (Delgadillo et al., 2018) and was found to be effective in symptom reduction for patients with fibromyalgia (Collinge, Yarnold and Soltysik, 2013).

The programme could be developed in collaboration with a programmer or using existing software for developing behavioural interventions, for instance, the LifeGuide Community Website (Williams, Yardley and Wills, 2013).

To further tailor this online intervention, the following personalisation strategies might be used: identification, raising the expectation of customisation and contextualisation (Kelders et al., 2012).

- ✓ Identification (patients' names will be appearing at the screen as he/she logs in to the programme; the patient name will be used at all forms of communication and feedback) (see Appendix 17-20).
- ✓ Raising expectations of customisation (explicit declaration of tailoring, for instance, use of "welcome to YOUR online psychological intervention programme", "designed for YOU" (see Appendix 15-17).

- ✓ Contextualisation (to increase enthusiasm for processing the information, attention and interest, the intervention will address both the IBD and mental health (anxiety and depression); this would be relevant to the patients' context). Furthermore, at the top of each website page there should be a bar, which would show which percentage of the online intervention programme a patient had completed. Patients will also be able to participate in the forum to communicate with patients suffering from a similar condition as some of the participants highlighted the need for it in the interviews (see Appendix 19-20).

Patients desired the intervention to be tailored to their level of anxiety and/or depression. However, as discussed above this online intervention is a low-intensity intervention (step 2 of the stepped care model) and patients referred to the intervention should have the same or similar levels of needs (sub-threshold depressive symptoms or mild to moderate depression and/or anxiety).

Moreover, over the past decade, the efforts of many scientists have been directed at the development of the treatment protocols applicable across various mental illness diagnosis, without tailoring to the specific disorder, the so-called transdiagnostic treatment protocols (Sauer-Zavala et al., 2017). The idea is based on the principle that emotional disorders have common causal mechanisms (Sauer-Zavala et al., 2017). The recent evidence demonstrates the effectiveness of transdiagnostic treatments for reducing anxiety and depression (Norton and Barrera, 2012; Newby et al., 2015; Barlow et al., 2017). The transdiagnostic approach also showed greater usefulness compared to other approaches for patients with multiple comorbid anxiety, depression or other psychological distresses (Craske, 2012; Norton and Roberge, 2017). Taking into account the high comorbidity rate of these psychological disorders, the transdiagnostic treatment offers a personalised approach during the selection of individual treatments (Craske, 2012; Brown et al., 2001).

4.4.3.2.2 Adherence and behavioural outcomes

Adherence to interventions during implementation in the health care settings and consequently, the intervention outcomes, is lower than during a trial (Beintner, Jacobi and Taylor, 2014). Therefore, it is essential to design the intervention programme that has a mechanism in place which maximises adherence by encouraging patients to engage with the intervention (Cugelman, Thelwall and Dawes, 2011). A recent systematic review that looked at the adherence concept in e-health concluded that the main measure of adherence is the actual use of technology and consists of the time spent online, number of completed activities, and active interaction with the intervention, rather than completion of the whole programme (Sieverink, Kelders and van Gemert-Pijnen, 2017).

Despite the varied responses about the repeated reminders in the present study, the reminders as well as the programme design that requires logging in should encourage the use of the programme and enable the providers to monitor participants. Provision of information, sending reminders, self-monitoring, reinforcement and other forms of further supervision/support could improve the effectiveness of complex interventions for long-term conditions (Haynes et al., 1996), thus were used during the model development.

Open access websites have lower attrition, and higher dropout rates compared to the online interventions where participants enrolled in the intervention (Christensen, Griffiths and Farrer, 2009). Therefore, adherence to the intervention would be increased if the participants logged in to the programme and got repeat reminders (Christensen et al., 2009). The participants should receive an invitation letter to the programme (see an example in Appendix 15) and an automatic reminder email or a telephone text message (the patient's preferred option) at the beginning of each week (see an example in Appendix 16).

Table 15 provides proposed steps of the patients care during participation in the programme. If the patient did not login to the programme during the subsequent two weeks, the health professional would make a follow-up telephone call to encourage the patient's participation. At the same time, the additional telephone support should be provided, or if there is a need and indication for more intensive care during this time, the person could step up in the stepped care model.

The delivery of the programme would require some basic training for a clinician in the context in which it was to be implemented, and their minimal contact with the patients would have to be further tailored during the development of the programme.

Table 15 Proposed steps to improve adherence to the intervention

Step	Time scale	Action
1	Before the start of the programme	An invitation letter to the programme with login details
2	The beginning of each programme week	An automatic reminder email or a telephone text message
3	Two weeks no log in	A follow-up telephone call from the clinician to encourage and support
4	If there is an indication for more intensive care during the phone call (step 3), person can be moved to more intensive care, face-to-face CBT.	

It has been found that as intervention length increases the dropout rate increases whereas the reverse was found with adherence (Christensen et al., 2009). The patients and health professionals' views about the number and duration of the session in the current study varied. However, they agreed that it should allow for some flexibility but should not exceed ten sessions of between 15 minutes to 1-hour duration. Two previous studies that used ten and eight weeks of the "Tame Your Gut" programme had high dropout rates (Mikocka-Walus, 2015; McCombie, 2016). Therefore, the author aimed to develop the intervention to be as short as possible at the same time as making sure that it could achieve the expected outcomes. The eight weeks programme was considered optimal, as any shorter then it would not be able to deliver all the necessary topics.

The design of the intervention can be enhanced by understanding the factors involved in achieving the desired behavioural outcomes. Fogg (2009) created a behaviour model where they showed how components such as ability, motivation, and triggers are cooperating in achieving the target behaviour (Figure 26). By addressing main aspects of motivation such as patients' devotion to the goal and their ability to self-direct the intervention could increase adherence to the intervention (Swann et al., 2010). Highly motivated patients appear to benefit more from low-intensity interventions (Joice et al., 2011). Therefore, patients with a different level of motivation should maybe be dealt with differently (Swann et al., 2010). Health professionals involved in the delivery of such low-intensity interventions are crucial as adherence to the online interventions highly depends on the encouragement of compliance from a clinician in addition to the specific technology tools used (Joice et al., 2011; Kelders et al., 2012).

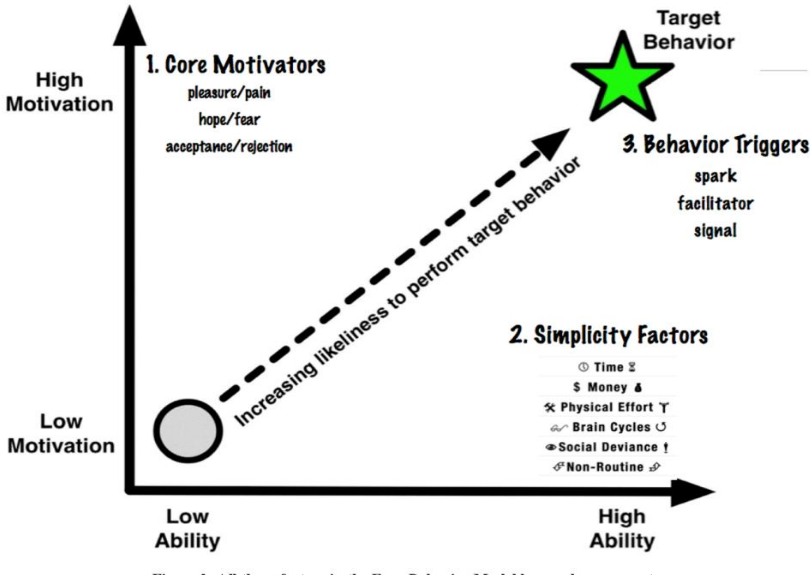


Figure 26 Three factors with subcomponents in the Fogg Behavior Model (Fogg, 2009).

This can be applied to the current psychological interventions by altering the level of support for different patients and was supported by findings from the current qualitative study. For instance, motivated patients would have an option to enter an exclusively self-directed online programme themselves or have a clinician-assisted alternative. Less motivated patients could enter a clinician-assisted version and have a telephone or additional email support. However, it is essential for both this group of patients to be reassessed after the programme. This would encourage patients to comply with and complete the programme and assess the need for moving a step up to more intensive care if this programme did not achieve the objectives.

4.4.3.2.3 Considering and maximising the likelihood of intervention uptake

Stepped care model/embedding the intervention

The National Institute for Health and Clinical Excellence (NICE) framework organises psychological therapy services for the treatment of some common mental health disorders in a structure of stepped care (Table 16) to archive the best patient-reported outcome measures (PROMS) with the least intrusive and most effective intervention (NICE, 2019a). If the initial intervention were found to be non beneficial to the patient, they should be offered an intervention from the subsequent step (NICE, 2019a).

This stepped care model ensures that more patients can access the appropriate services as a part of the UK's Improving Access to Psychological Therapies (IAPT) programme (NICE, 2019a). A stepped-care model appears to be more effective for the treatment of subthreshold depression and/or anxiety than usual care (van't Veer-Tazelaar et al., 2009). This model also achieves more effective use of high-intensity intervention and is possibly cost-effective (Boyd, Baker and Reilly, 2019).

Table 16 Stepped-care model: a combined summary for common mental health disorders

Staff	The focus of the intervention	Nature of the intervention
Step 3: High-intensity service	Persistent subthreshold depressive symptoms or mild to moderate depression that has not responded to a low-intensity intervention; initial presentation of moderate or severe depression; GAD with marked functional impairment or that has not responded to a low-intensity intervention; moderate to severe panic disorder; OCD with moderate or severe functional impairment; PTSD.	Depression: CBT, IPT, behavioural activation, behavioural couples therapy, counselling*, short-term psychodynamic psychotherapy*, antidepressants, combined interventions, collaborative care**, self-help groups. GAD: CBT, applied relaxation, drug treatment, combined interventions, self-help groups. Panic disorder: CBT, antidepressants, self-help groups. OCD: CBT (including ERP), antidepressants, combined interventions and case management, self-help groups. PTSD: Trauma-focused CBT, EMDR, drug treatment. All disorders: Support groups, befriending, rehabilitation programmes, educational and employment support services; referral for further assessment and interventions.
Step 2: Low-intensity service	Persistent subthreshold depressive symptoms or mild to moderate depression; GAD; mild to moderate panic disorder; mild to moderate OCD; PTSD (including people with mild to moderate PTSD)	Depression: Individual facilitated self-help, computerised CBT, structured physical activity, group-based peer support (self-help) programmes**, non-directive counselling delivered at home†, antidepressants, self-help groups. GAD and panic disorder: Individual non-facilitated and facilitated self-help, psychoeducational groups, self-help groups. OCD: Individual or group CBT (including ERP), self-help groups.

		PTSD: Trauma-focused CBT or EMDR. All disorders: Support groups, educational and employment support services; referral for further assessment and interventions.
Step 1: Primary care/IAPT service	All disorders – known and suspected presentations of common mental health disorders.	All disorders: Identification, assessment, psychoeducation, active monitoring; referral for further assessment and interventions.

Step 2 of this care model is a low-intensity intervention for treating depression and anxiety disorders usually delivered by psychological well-being practitioners (PWPs) (NCCMH, 2019).

Computerised and internet-delivered CBT is considered as a suitable treatment alternative and approved by IAPT at this step (NICE, 2019a). Therefore, the proposed intervention was considered as step 2 low-intensity intervention and could be used and integrated into the pathway for IAPT services. Therefore, online psychological intervention could be used in the first instance and in case of no response to this intervention, patients could be moved to a higher-intensity psychotherapy of step 3 services. As these services provide a protocol-driven path, an implementation of the current intervention for IBD patients with comorbid anxiety and/or depression into IAPT would maximise the likelihood of the intervention uptake. However, this implies health professionals' awareness about the existence of an online programme.

4.4.3.2.3.1 Collaborative care

The online intervention can only be successfully implemented when it engages the collaboration between the targeted users, in the present case IBD patients with comorbid anxiety and/or depression, clinicians, researchers, software developers, and policy-makers (Pagliari, 2007) and the implementation of the collaborative care models for patients with depression emerge to be the most cost-effective (Joice et al., 2011). The codes and themes that came through patients and health professionals' data in the current study also illustrated an important role of collaborative and integrated care.

Patients' role

To improve the implementation of the intervention in future and empower patients, their involvement in the evaluation phase of the intervention is essential (Craig et al., 2013) and is desired by patients in this study.

Health professionals' role

At an early stage of the development of an intervention, it is vital to take into consideration who will deliver the intervention and in which settings. The complete version of the online psychological intervention is intended to be delivered by more general medical staff who provide IBD care, such as IBD nurses, NHS junior mental health workers, trained coaches (psychological wellbeing practitioners), social workers, professional counsellors, PWPs, but who would have access to psychological advice from a psychologist if and when required. The NHS psychologist also could refer patients to the programme to have minimal contact with patients instead of usual treatment involving regular face-to-face sessions that would reduce the workload of psychologists and could be cost-effective to the NHS.

The finding from the current study demonstrated the importance for patients of the health professionals' encouragement. At the same time, they would like to take control of their own treatment with the clinicians' support. This can be facilitated with an improved relationship between health professionals and patients. Nurses play a crucial role in the encouragement of patients to be actively involved in their own treatment and make sure that patients benefit from safe, quality care (Norton et al., 2012).

The nurse-led services are fundamental for IBD care (Armuzzi et al., 2018; O'Connor et al., 2013) and a holistic approach to IBD care in the integrated care model involves a shift from essential to enhanced care by IBD nurses (Kemp et al., 2018). A recent systematic and meta-analysis of RCTs showed the effectiveness of the care delivered by nurse management of depression in a variety of long term health conditions, but the authors could not conclude on it's the cost-effectiveness (Ekers et al., 2013). However, several recent studies show nurse-led services, including telephone support, can significantly improve the quality of care and reduce the cost of care (Bager, 2014; Squires, Boal and Naismith, 2016; Taylor et al., 2016; Correal et al., 2019). Patients in the current study also highlighted the importance of support from IBD nurses. Thus, the current intervention could be designed to be delivered by nurses or NHS junior mental health workers, psychological wellbeing practitioners (PWPs), or NHS psychologist with limited human contact.

However, in practice, non-specialist nurses or other health care practitioners could face some challenges during the delivery of the programme as shown in the study on delivering psychological intervention for patients with chronic fatigue syndrome/myalgic encephalomyelitis (Peters et al., 2011). The study concluded that being a beginner in delivering therapy, engaging patients, emotions, and the intricacy of the setting could lead to a possible strain between the therapist and patient (Peters et al., 2011). The negative impact that the intervention had on nurses could be overcome by regular supervision (Webster, Ekers and Chew-Graham, 2016). However, the proposed psychological intervention is aimed at IBD patients with subthreshold, mild or moderate depression and anxiety, hence determines the selection process prior engagement in the programme and referral of severe cases to the specialists before assigning to the programme. The online mode of delivery minimises the contact with the providers, thus reduce the emotional burden on them. From the evidence of the current qualitative study, it is predicted that for the implementation of the online interventions at least one nurse, PWP or psychotherapist is required per site. This assumption was based on the currently available services for this population. However, a feasible and acceptable number of health professionals delivering the intervention per a set number of patients could be defined in a future study.

The current online psychological intervention could be delivered through various settings, including outpatient, hospital-based and therapeutic communities. The IBD patients with comorbid anxiety and/or depression can use the online psychological interventions in a wide range of locations: clinics, hospitals, homes and other facilities. The only requirement for the use of this intervention is access to the Internet.

4.4.3.2.3.2 Confidentiality, security and ethical concerns about online interventions

The internet assists implementation of the online interventions but, conversely, personal privacy could be breached during its use. Therefore, privacy and ethical concerns have to be taken into account during the development of the intervention by following the e-Health Code of Ethics (e-Health Ethics, 2000). This assumes the patients, and the providers of the intervention are aware of the potential risks that could arise during the application of the online intervention (e-Health Ethics, 2000) and information about a possible breach of confidentiality should be given to patients (Manhal-Baugus, 2001).

Online interventions bring some ethical advantages: they are more accessible and flexible, help to avoid the stigma, show psychologists' consideration of patients who cannot access services and their attempt to progress professionally by expanding expertise in the new format (Dever Fitzgerald et al., 2010). Despite security and confidentiality concerns, the majority of long-term condition patients have confidence in the online interventions and believe that these risks do not exceed gained returns (Hale and Kvedar, 2014).

4.4.3.2.4 Determining measures for clinical outcomes

A logic model (Figure 27) was adapted from the Better Care Fund (NHS England, 2015) and the draft of a logic model for integrating mental health into chronic disease prevention and health promotion. (Lando et al., 2006). It guides you through the process of design, development, evaluation and implementation of the intervention and helps with interpreting the result (NHS England, 2015). This model could be further modified during a feasibility trial. However, it is important to determine the outcomes at the beginning of the intervention development rather than "retrospectively fitting them to a predetermined and funded set of activities or interventions" (NHS England, 2015).

System outcomes are reflected in the Impact section of Figure 27. Additionally, to the health and wellbeing outcomes, and the effective use of resources, system outcomes included improved experience in care (England, Butler and Gonzalez, 2015). Being a part of a stepped care model suggested online psychological intervention would be directed to achieving both, the system outcomes by improving access to psychological therapies and the personal outcomes for the patients as a result of using an online psychological intervention (van't Veer-Tazelaar et al., 2009; Clark, 2011).

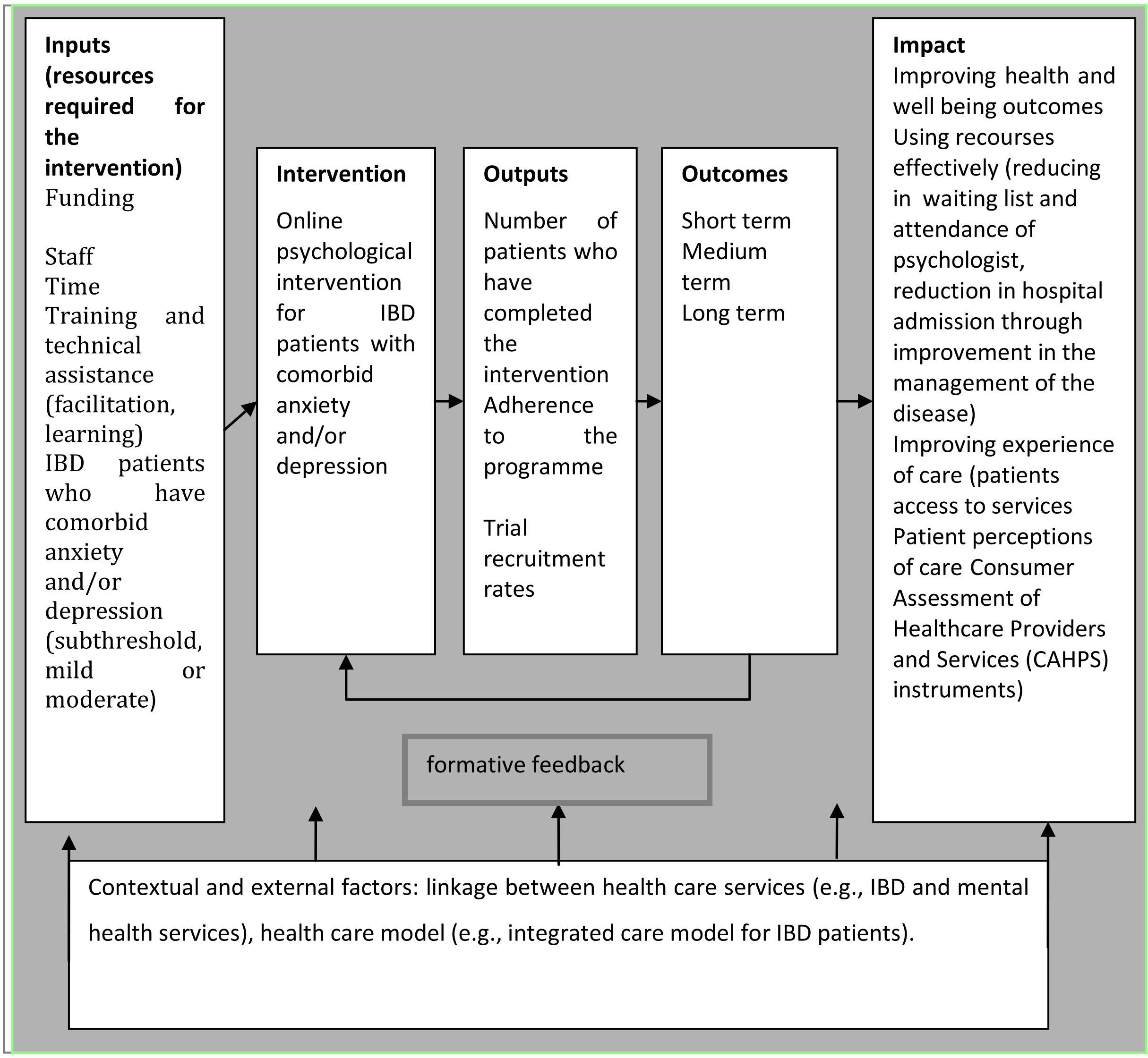


Figure 27 Logic model modified from the Better Care Fund (NHS England, 2015).

Personal level outcomes

At the personal level, the intervention should improve anxiety, depression and QOL. The disease activity and any other related outcomes could also be assessed. Suggested health outcomes and measures at a personal level as a result of participation in the current psychological intervention could be:

1) Mental health outcomes

Rates of anxiety and depression and/or mean levels of anxiety and depression

Rates of anxiety, depression, level of stress and coping in patients assessed using validated screening scales such as the Hospital Anxiety and Depression Scale (HADS), the Patient Health Questionnaire (PHQ9), the State-Trait Anxiety Inventory (STAI), Generalised Anxiety Disorder Assessment (GAD-7), the Depression Anxiety Stress Scales (DASS), the Revised Social Readjustment Rating Scale (RSRRS), the IBD Stages of Change Coping Questionnaire (IBDSCCQ), the Perceived Stress Scale (PSS), the Brief COPE, the CORE /CORE – 10 (Clinical Outcomes in Routine Evaluation).

2) HRQoL

Health-related quality of life assessed using validated screening scales such as the (SF-36) and IBDQ. Work and Social Adjustment Scale (WSAS) to measure of social functioning.

3) Disease activity outcomes

The remission rate in patients with IBD.

Disease activity assessed using well-established scales or tests (the Crohn's Disease Activity Index (CDAI) for those with CD or the Simple Clinical Colitis Activity Index (SCCAI) for those with UC, faecal calprotectin; blood parameters (C-reactive protein (CRP), Haemoglobin (Hb), platelet, White Cell Count (WCC), haematocrit).

4) Any related outcomes

(E.g. reduced time off work or school, sick leave, hospitalisation (frequency and length), pain, adverse events, adherence to the intervention programme, trial withdrawal and attrition during feasibility trial). A result of a recent study showed that 9.3 % of 558 pooled participants reported some adverse events related to the online interventions for mental disorders (Rozental et al., 2015). Therefore, any adverse outcomes should be reported, as they could deteriorate patients' health and as a result reduce the cost-effectiveness of the intervention (Joice et al., 2011).

Patients should be assessed at the last session to measure short term outcomes and at 12 and 24 months after the intervention for long term outcomes.

4.4.4 Implications

The findings from this study indicate that IBD patients with comorbid anxiety and/or depression are open to the participation in self-directed online PI, suggesting its implementation in the current management of IBD. The intervention designed to meet the patient needs could be tested in future trials. If successful, online intervention could be integrated into the management of IBD with comorbid anxiety and/or depression. The provision of online psychological help could be considered as part of the holistic care for this population. Furthermore, it could reduce long waiting lists to a psychologist and take the burden from the overstretched NHS resources and, potentially, reduce the cost of care.

Patients and health professionals discussed the lack of psychological support for IBD patients and the lack of integrated care as a major concern for IBD patients with anxiety and/or depression (reported in Chapter 3). The integration of online intervention may fill this gap. Furthermore, the online mode of delivery could improve the accessibility of the intervention, as all participants considered this as a significant advantage of the programme. Additionally, as some participants reported that IBD symptoms and anxiety, including social anxiety, made them housebound, as a result, they missed the appointments. Therefore, the online mode of delivery intervention would increase the accessibility of help for this group of people, who would not be reached during conventional management of the disease, hence reducing inequality in care.

It is estimated that the approximate annual NHS cost for UC was £3,084 per patient and £6,156 for CD, although, the cost could increase dramatically during relapses (Ghosh and Premchand, 2015). The cost-effectiveness of the online delivered interventions is debatable. The recently published study shows that the online delivered CBT for depression was as cost-effective as treatment as usual and had similar health outcomes (Holst et al., 2018). However, this study was conducted between 2010 and 2014 in Sweden, and its findings may not apply to the NHS settings in the UK. Furthermore, it is anticipated that the cost of usual care might have increased compared to an online intervention since the study was conducted. Therefore, the implementation of the programme and its cost-effectiveness should be explored in a future study.

4.4.5 Strengths and limitations of the study

The strength of this study have been discussed in Chapter 3. The methodological and design limitations were already discussed in chapter 3 and are applicable here.

Further, even though prior to the study, all participants received the recruitment pack with the glossary, the majority of participants did not read it. As a result, they had a vague understanding of the talk therapy term, and this might have influenced their answers. As an example, one patient thought that talk therapy is "just talking", and wanted more "practical things", but after the explanation, they changed the perception. All participants were asked to familiarise themselves with the "Tame Your Gut" website prior to the interview/focus group. However, many participants did not do this. For these participants, the website was available during the interview. However, this could be considered to mirror usual practice, as patients in real life may decide on the participation in the programme in similar circumstances.

Health professionals and patients received the link to the "Tame Your Gut" website and the glossary of terms prior to the interview. However, some patients were recruited during the IBD clinic and interviewed immediately after a short familiarisation with the study’s purpose, consent and a brief explanation of the terminology. These patients were able to access the website during the interview and navigate around it when answering the questions. Future studies could specify the time required for the participants' familiarisation with the online intervention. The patients who expressed interest in doing the interview instantly, possibly, were a more motivated group of patients and could have more positive attitudes toward an online PI.

On the other hand, the study also recruited less motivated patients. One patient was observed to reject any form of outside help. They were satisfied with the management of psychological issues, which mostly consisted of distraction, were not motivated to seek outside help and had a negative attitude towards an online PI.

The agreement between the health professionals and patients that the online programme can increase the accessibility of psychological help and that clinician-assisted version of the programme was preferred increases the confidence of this study’s findings and the expectation for the implementation of the online programme into the management of the disease in this population of patients.

4.4.6 Future research

To broaden the findings from this study, future research needs to consider designing better alternatives to the presently scarce psychological treatments. This prototype should be used in the development of the complete online programme and its efficacy tested in a future feasibility trial.

The online psychological intervention should be tested in mixed-methods analysis to enhance effectiveness, feasibility and acceptability for the implementation in future. The mediators and moderators of intervention effectiveness and cost-effectiveness should also be explored. Furthermore, future research should determine if the self-directed online PI directed on anxiety and depression is useful in the management of patients' IBD symptoms.

4.5 Conclusions

The current study gathered important data on the patients' and health professionals' perception (feasibility and acceptability) of an online PI programme for IBD. The findings suggested that patients, in general, had a positive attitude towards the online PI and were willing to participate in the programme. This differed from the health professionals' views, as they were unsure about the patients' participation.

The patients' and health professionals' comments about the existing "Tame Your Gut" programme formed a basis for the development of a prototype of an online PI for IBD patients with comorbid anxiety and/or depression. The inclusion of the online PI intervention could improve the accessibility to the psychological help and, as a result, enhance integrated care.

5 Discussion

This chapter summarises the main findings of the present PhD project and their implications for research and practice, discussing study strengths and limitations, policy, clinical and research recommendations and providing the overall conclusion.

5.1 Main findings

This thesis made an original contribution to the research knowledge in three ways. Firstly, it demonstrated that there is insufficient evidence on the effectiveness of the online psychological therapy for mental and physical outcomes in gastrointestinal diseases, IBD and IBS specifically and the need to investigate it further. Secondly, the results of the qualitative study showed that there is a need for the integrated care for patients with IBD and comorbid anxiety and/or depression, particularly regarding the provision of psychological help. The findings also demonstrated that patients had a positive attitude towards online psychological intervention. Thirdly, based on theoretical evidence and patients' and health professionals' views, the project provided the recommendations (the prototype) for the online psychological intervention for patients with IBD and anxiety and/or depression. However, this prototype was explicitly developed for this population, and the generalisability of these recommendations for the other IBD patients "in need" (patients who have a high baseline IBD activity; have been recently diagnosed; are young; with comorbid psychological distress) requires further research. Moreover, a complete intervention would require further investigation of patients', health professionals' and stakeholders' views about the finished product in a new qualitative study to improve its implementation.

This PhD project was informed by the MRC framework for designing complex interventions. The key findings of this thesis are discussed in line with the following specific aims:

1. To gather theoretical evidence on the effectiveness of the online psychological therapy in gastrointestinal diseases.
2. To investigate patients' with IBD and comorbid anxiety and/or depression and their service providers' views about the lived experiences of these patients.

3. To investigate participants' views about online psychological intervention and provide the recommendation for the online psychological intervention for patients with IBD and comorbid anxiety and/or depression.

The use of online interventions in health, including the use of these interventions in mental health, has increased rapidly (Hill et al., 2017; Maples-Keller et al., 2017; Fodor et al., 2018). Several systematic reviews and meta-analyses have demonstrated that online psychotherapy is effective for treatment of anxiety and depression, convenient, flexible, confidential, acceptable, accessible, and more cost-effective compared to face-to-face therapy (Andrews et al., 2010; Richards and Richardson, 2012; Andrews and Williams, 2015; Musiat and Tarrier, 2014).

The data on the effectiveness of online interventions in IBD are generally limited and thus to learn about its usefulness a decision was made to review the relevant literature in the context of gastrointestinal illness in general (i.e. including all gastrointestinal conditions and not just IBD). To the author's knowledge, this was the first systematic review of its kind. The review showed that there is insufficient evidence to demonstrate the effectiveness of online CBT to manage mental and physical outcomes in gastrointestinal diseases, including IBS and IBD – data for only these two conditions were identified (Chapter 2).

The previous systematic review on the effectiveness of psychotherapy in IBD, not limited to the online mode of delivery, showed that psychotherapies, CBT in particular, are effective in improving QOL and depression in patients with IBD (Gracie et al., 2017). The authors of this review suggested investigating its effectiveness in patients with IBD and comorbid psychological distress, as this group is likely to benefit more from psychotherapy than the unselected patients with IBD included in the currently available trials (Gracie et al., 2017).

A difference in the findings between Gracie et al. (2017) and the current review likely stems from the present review's focus on online interventions. It is possible that for psychotherapy to work in this context, human contact is necessary – it is unclear for now what is the minimum amount of contact with a therapist for psychotherapy to be effective. While online therapies offer clear advantages of time and cost savings, future interventions may need to examine hybrid models which involve both a therapist and online components. Furthermore, engagement in therapy, a high attrition rate and low adherence to treatment typical for the online interventions could potentially be improved by providing support of a clinician or technician (Musiat and Tarrier, 2014; Gilbody et al., 2017).

The main message from the current systematic review was that the evidence on the usefulness of online psychological interventions in gastroenterology, and IBD specifically, is scarce. There is a need for more robust trials of psychotherapy in IBD, going beyond exclusively online solutions and with a particular focus on the selected subgroup of patients with IBD that are in need of psychotherapy such as those with anxiety and depression.

The advantages of online interventions, the recommendations from the previous review (Gracie et al., 2017) and the studies of online psychological interventions in IBD identified during the current systematic review (Mikocka-Walus et al., 2015; Mikocka-Walus et al., 2016a) confirmed the rationale for the present project: to develop a prototype of the programme for patients with IBD and comorbid anxiety and/or depression which could be tested in a future feasibility trial. Following the MRC framework, after the systematic review a qualitative exploratory study investigating patients' with IBD and comorbid anxiety and/or depression and their service providers' views about the lived experiences of these patients was performed (Chapter 3). To the author's knowledge, this was the first qualitative study of its kind. The basis for the selection of this group of patients was the recommendation from the previous systematic review (Gracie et al., 2017), as well as a high level of anxiety and depression comorbid with IBD and their impact on the disease management that was reported in previous research (Mikocka-Walus et al., 2016b; Navabi et al., 2018).

The participants' views about the lived experience were investigated to identify any gaps and difficulties in the management of the disease in this population and, as a result, increase understanding of how the provision of psychological services could be improved and to confirm the need for psychological interventions (Chapter 3).

The main message from this qualitative study was that patients with IBD and comorbid anxiety and/or depression do not get adequate psychological help. Because of the bidirectional links between IBD and mental health, there is a need to treat both at the same time (Chapter 3) (Gracie et al., 2018). There is a further need to increase awareness of IBD, a need for the implementation of the integrated model of care and more accessible psychological interventions into the routine management of patients with IBD and anxiety and/or depression. The online or partly online self-directed psychological intervention could be one such solution.

This qualitative study also collected data on patients' and health professionals' views about future psychological interventions, which together with the theoretical evidence, lay the foundation for the modelling prototype of an online intervention for those with IBD and co-morbid anxiety/depression (Chapter 4). Only one online intervention for people with IBD called "Tame Your Gut" (TAME YOUR GUT, 2019) has been developed and tested to date (Mikocka-Walus, 2015; McCombie, 2016). Therefore, the "Tame Your Gut" programme was used as an example for the participants in this qualitative study to comment on the features of this intervention so it could be adapted to the patients' needs.

The main message of this qualitative study was that self-directed online psychological interventions are accepted as an alternative to F2F therapy, an accessible option of delivering psychological help for patients with IBD and anxiety and/or depression, and are well-received by patients. The existing "Tame Your Gut" online psychological intervention for patients with IBD requires changes to adapt it to this population's needs and the UK environment (the intervention was originally designed in Australia). The proposed recommendations (discussed in detail in Chapter 4) could be implemented into the online intervention and its effectiveness evaluated in future trials.

5.2 Implications for policy and practice

The present work highlights the need for further trials on the effectiveness of online psychotherapy in IBD with comorbid anxiety/depression. It further showed a lack of awareness about the mental health comorbidity in IBD and IBD itself among the public and non-specialist health professionals, GPs specifically, which in turn affects patients' mental health and QOL. Data from another qualitative study showed that lack of awareness and knowledge about IBD among non-specialist health professionals and the public could reduce patients' ability to self-manage (Cooper et al., 2010), which is an essential part of the integrated model of care. The lack of public awareness and embarrassment could lead to the patients concealing their IBD diagnosis (Fourie et al., 2018). Thus, the surrounding community might be unaware about the patients' IBD and, as a result, this could lead to discrimination at work or study due to frequent and extended sick leave (Avedano et al., 2014). The psychological wellbeing of patients could be improved by increasing awareness about the disease and developing support in the education sector and workplace. Consequently, by increasing awareness about the disease among health professionals and society, the improvement in the patients' QOL could be achieved (Bray et al., 2016). There is a clear need for the implementation of national and community level activities designed to raise awareness of IBD and mental health among patients, public and health professionals. These activities could include developing a resource guide for the health professionals on screening for signs of anxiety and depression, and on IBD symptoms for none IBD specialist health professionals; publication of articles in peer-reviewed journals and local newspapers; organising the workshops and interactive educational sessions for the patients and health professionals; development and distribution of newsletters and educational leaflets on the topic among patients and wider public; creating partnerships between media and the healthcare providers to increase awareness about IBD through radio and television; and a variety of campaigns (e.g. annual IBD walks) run by patient organisations such as Crohn's & Colitis UK. The leading role in the increasing awareness of IBD belongs to scientific research, the results of which can subsequently be used to inform the above activities (Long et al., 2008). These activities showed their usefulness in raising disease awareness in other healthcare fields (Long et al., 2008; Ueland, Hornung and Greenwald, 2006; Zielinski et al., 2006; Bero et al., 1998). However, a passive distribution of the materials through papers, conferences and lectures may not be sufficient to change the behaviour of health professionals in decision making about the disease management compared to the interactive activities (Bero et al., 1998). Including more information about IBD and its mental health comorbidities in the clinical curriculum for GPs could improve diagnostics and early treatment of the disease.

Despite the fact that an integrated model of care with a multidisciplinary team of specialists is recommended for all IBD patients (Mikocka-Walus et al., 2012b; NICE, 2019b), it is not implemented widely in practice and the findings of the current work indicated the need for integration of care to address anxiety and/or depression comorbid with IBD specifically. Lack of psychological support was commonly reported. Therefore, at the hospital trusts level, improving the provision of care is required, and at the national level, it is necessary for policymakers to take into consideration the barriers for its implementation and the mechanisms of overcoming these barriers. Development and introduction of an alternative provision of care such as self-management online psychotherapy, may improve access to psychological help, reduce the long waiting lists to a psychologist and, potentially, reduce the cost of care under overstretched NHS resources.

5.3 Strengths and limitations

The main strength of this project was that it followed the development phase of the MRC framework for complex interventions. It was important to follow this framework as it has a phased approach which allows the researcher to determine to which stage the study belongs, to effectively plan and design the research, evaluate and implement the results (Campbell et al., 2000; Craig et al., 2013). The MRC framework had a significant impact on the research and is a valuable tool for the development, evaluation and implementation of the complex interventions (Campbell et al., 2000; Craig et al., 2013; Moore et al., 2014; De Silva et al., 2014). This framework has been applied effectively in the development of the complex interventions in other health fields (Furness et al., 2018; Bobrow et al., 2018; Lakshman et al., 2014). There are other frameworks for the development of the complex interventions available (Bartholomew et al., 2001; Glasgow, Vogt and Boles, 1999; Green and Kreuter, 1999; Pagliari, 2007), but they to some extent include stages of MRC framework what makes it the most inclusive and, thus, the most practical framework.

However, the project unavoidably has some limitations. The main drawback is that there was no experimental component to this project and the prototype has not been tested. Originally, there was an intention to develop the final product of the online intervention and conduct a feasibility trial to test its effectiveness. However, it was not feasible within the scope of this PhD project due to the delays in obtaining the research passport for the primary researcher, accessing the hospital sites and slow recruitment of patients to the qualitative study.

The systematic review used a rigorous methodology with meta-analyses to increase the statistical power and followed the strict protocol registered on PROSPERO. Nevertheless, the findings of the systematic review were inconclusive due to the small number of studies, warranting new research on the subject. The sources of significant heterogeneity between included studies and the presence of publication bias also could not be investigated due to a small number of studies included in the meta-analysis. There were also limitations in the individual studies such as short-term follow up, a high risk of performance and detection bias, inconsistency in the reporting outcomes.

The strength of the qualitative study was applying triangulation principles, the coding of the data was conducted in a thorough and systematic way, and the process was cross-examined by the other research team members to increase the credibility and validity of the results. Moreover, this study was conducted across several hospital sites, which allowed for achieving richness and diversity of the data.

Based on the theoretical evidence gathered prior to this qualitative study, the author focused on the selected population with IBD who had comorbid anxiety and/or depression. The gender variation was also crucial for this population to explore the difference in perceptions of online interventions. The evidence shows that there are gender differences in preferences between traditional and technology-assisted interventions (Kim, Choo and Ranney, 2014) and the acceptability of online psychological interventions (Campbell et al., 2015). No differences in the views between the genders were however observed in the current study.

The diverse ages of the participants were also essential to identify if their behaviour towards the Internet and technology differed. There are controversies with regards to the internet behaviours of the older population (Wagner, Hassanein and Head, 2010). Some evidence suggested the use of internet, e-mail or text messages is limited in older adults (over 65 years old) (Morrell, Mayhorn and Bennett, 2000; Gell et al., 2013), particularly the use of online health interventions by those who likely to gain benefit from them (Gell et al., 2013), whereas other studies suggested that online interventions are effective in older adults (Choi, Kong and Jung, 2012). Furthermore, the uptake of online interventions by an older adult could be enhanced with encouragement, support and use of specially designed technology training for this population (Wagner et al., 2010; Vaportzis, Clausen and Gow, 2017). These findings correlated with the patients' view from the current study where old patients did not consider their age or knowledge of the technology as a barrier for participation in the programme but required support from family members or clinicians.

The qualitative study also had some potential limitations. Its sample size was limited to a specific group of patients, patients with IBD and comorbid anxiety and/or depression in one region of England, and this limits its generalisability to other patients' with IBD in other regions. However, this was a purposely selected sample to develop the intervention prototype for this specific group of patients. The data collection was at the hospital facilities. However, putting patients in a less stressful environment during the interviews could, perhaps, engage them more in the conversation and provide more in-depth data.

The majority of the participants did not familiarise themselves with the glossary or the "Tame Your Gut" programme prior interview. However, for these participants, the terminology was explained, and the website was available during the interviews. This was a pragmatic approach, which reflected the circumstances in which participants would make decisions about the online programme. The familiarisation time could be specified in future studies. Another limitation of this study was the inclusion of patients based on patient case notes and clinician’s evaluations. Specified levels of anxiety and depression on validated scales as inclusion criteria could benefit future studies.

5.4 Recommendations

The limited number of online psychological interventions in gastrointestinal diseases, particularly IBD, identified in the systematic review, suggests the need for more robust trials to investigate its effectiveness. Future research should address the limitations of the existing studies by lengthening the follow-up period over 12 months, be consistent in presenting outcomes in the format facilitating meta-analysis (n, means, SD or mean difference with associated 95% confidence intervals), use allocation concealment during randomisation and use blinding of outcome assessors (the assessors could be masked to therapy).

A high attrition level reported in the online interventions could be reduced by the introduction of the booster sessions, which also could help to maintain the effect of the psychotherapy (Beck and Beck, 2011; Gearing et al., 2013), thus should be considered during the design of the future interventions.

The studies that met the inclusion criteria in the systematic review examined the effectiveness of CBT only. Thus, there is a need to test the effectiveness of other types of online interventions in gastrointestinal diseases. A systematic review by Gracie et al. (2017) confirmed CBT to be the most commonly used and most effective psychotherapy type in IBD to date (Gracie et al., 2017). However, other types of psychological therapy also were beneficial (Ford et al., 2014; Gracie et al., 2017) for QOL and reduction of depression in IBD (Gracie et al., 2017) and IBS (Ford et al., 2014), thus should be considered while designing future online interventions. One of the psychological interventions that could be considered is behavioural activation (BA), the effectiveness of which for depression is comparable to CBT (Jacobson et al., 1996; Richards et al., 2016). Moreover, BA was more cost-effective and could be delivered by NHS junior mental health workers not requiring specialised training in psychotherapies (Richards et al., 2016), which is fundamental due to the constrained resources in the NHS. Furthermore, the previous systematic reviews, not limited to the online mode of delivery, demonstrated the effectiveness of various psychological therapies delivered in-person or through telephone in IBS and IBD, including CBT (Ford et al., 2014; Gracie et al., 2017). The level of effectiveness of the intervention may depend on the mode of its delivery, suggesting the need for designing online psychotherapy programs where the effectiveness can be enhanced by human contact which was considered during the development of the current prototype of the online intervention. However, a recent study showed that the combination of face-to-face with online intervention for anxiety and depression did not increase effectiveness, led to more treatment sessions and as a result was less cost-effective than the standard treatment (Kenter et al., 2015). However, these data came from an observational study and not an RCT thus could be subject to various types of bias for example selection bias. Furthermore, the study had online intervention in addition to the face-to-face, whereas future studies should develop online interventions as a substitute for face-to-face with limited human contact.

The current systematic review can be updated in the future with the availability of more studies assessing online psychological interventions in gastrointestinal diseases, as it used a robust methodology and comprehensive search strategy. The most important recommendation resulting from the qualitative study is that the online psychological intervention should be co-designed by the patients, researches and other stakeholders to enhance effectiveness, feasibility and acceptability of its implementation.

Moreover, future qualitative studies could examine patients’ and health professionals' views about online psychological interventions for patients with IBD and comorbid anxiety and or depression in different geographical locations of the UK to explore the generalisability of the findings from the current study. Furthermore, the view about online psychological interventions should be assessed for other subgroups of patients with IBD who are likely to benefit from psychological interventions: patients, who have been recently diagnosed, are young and have high baseline IBD activity (Gracie et al., 2017; Mikocka-Walus, 2015).

The recruitment process could be improved in future qualitative studies. The recruitment of patients in the current qualitative study depended on the collaborators’ level of involvement and interest in the study and was easier at some hospital sites than at others. The collaborators could not provide the data on how many patients who had been approached were not interested in the study participation. Thus, the difficulties in the recruitment could be explained by either patients' low interest in the study or because collaborators were not approaching the potential patient's participants. Using more network contacts and opening the recruitment process at several sites simultaneously could increase recruitment. Furthermore, participants could be recruited online, for instance through Crohn's and Colitis UK website or the University where the researchers are based (recruiting the students and staff members with IBD). This would expand the area of recruitment, would require only the University ethical approval and would avoid unnecessary waiting time for the NHS ethical approval, obtaining the research passport and site access, however, may result in few recruits as IBD is not very common.

Online psychological interventions should be tested in mixed-methods analyses (O'Cathain, Murphy and Nicholl, 2007; Campbell et al., 2000). Therefore, the feasibility trial on the effectiveness of the intervention that is developed based on the current prototype should be supported by new qualitative research. This could be done with the same patients and health professionals, as they agreed to comment on the finished intervention product, to see if the intervention met their requirements and needs. Engagement and work in partnership with health care providers, patients, PPI and policy-makers are becoming increasingly important in health care research (Banner et al., 2019; Graham et al., 2006). Some authors call this approach an experience-based co-design (Dawda and Knight, 2017). This methodology is based not only on patients' perceptions, attitudes, needs and views, but combines the user-centred orientation (experience base), also called a Design Thinking, and collaborative change process (co-design) (Altman, Huang and Breland, 2018; Dawda and Knight, 2017). Consequently, patients and healthcare professionals work on improving the intervention as equal partners (co-designers) (Dawda and Knight, 2017). This would empower patients, public members, and stakeholders to become active participants in the development of the intervention that they will implement/use in the future.

5.5 Conclusion

The theoretical evidence from the broader literature and patients' and health professionals' comments about the existing "Tame Your Gut" programme formed a basis for the development of a modelling prototype of an online PI for IBD patients with comorbid anxiety and/or depression. The intervention based on this prototype could be tested in a future trial. The productive collaborations between patients, stakeholders and researchers in co-designing of an online psychological intervention and its implementation into integrated care of patients with IBD and comorbid anxiety and/or depression, and other "in need" patients with IBD that are likely to benefit from psychological interventions, will be the key to broaden the knowledge in the field and to improve wellbeing of those with IBD.

Appendixes

Appendix 1 Search result in Ovid MEDLINE(R) Epub Ahead of Print

Ovid MEDLINE(R) Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present

Searches	Results
exp Psychotherapy/	173930
exp Adaptation, Psychological/	113018
(psychotherap* or (behavior* adj2 therap*) or (behaviour* adj2 therap*) or cognitive therap* or psychological intervention* or psychological adaptation or systematic desensitiz* or systematic desensitis*).ti,ab.	58369
(Cognitive problem-solving skills training or characteranalyti* or character-analyti* or client-centered or client-centred or coherence therap* or contemplative therap* or conversational therap*).ti,ab.	1242
exp Problem Solving/	22986
Patient-Centered Care/	14436
(problem-solving adj2 training).ti,ab.	307
((coping or cope or copes or coped) adj2 (skill* or behavior* or behaviours or train*)).ti,ab.	4659
(core energetic* or core process*).ti,ab.	492
(dialectical behavio?r therap* or DBT).ti,ab.	2007
(Dreamwork or Dyadic or DDP).ti,ab.	7092
(expressive therap* or Desensiti* reprocessing or Desensiti* re-processing or Emotional Freedom Techni* or EFT or encounter group* or Experient* Dynamic or Existential therap* or exposure response prevent* therap* or (Eye Movement Desensitization adj2 Reprocessing) or EMDR).ti,ab.	1224
(goal setting or Gestalt* or Group Analy* or Milieu Therap* or milieutherap* or group-based therap* or group-based treatment* or group-based intervention).ti,ab.	11001
(hakomi or holistic or holotropic or humanistic or human givens or hypnos* or hypnot* or hypno-therap*).ti,ab.	37593
(interaction therap* or interperson* therap* or inter-personal therap* or IPT).ti,ab.	2240
(meditati* or mindfulness* or MBSR or morita therap*).ti,ab.	6824
Mind-Body Therapies/	782
(body mind or mind-body therap* or Radix therap* or pulsing or body-oriented psychotherap* or IBP or postural integration or integrative body psychotherap* or Pesso Boyden system psychomotor or lifespan Integration or Rubenfeld synergy or Reichian).ti,ab.	3716
(multimodal* therap* or multi-modal* therap* or multi-theoreti* or multitheoreti*).ti,ab.	4543
(relaxation therapy or tai ji or therapeutic touch or yoga).ti,ab.	4121
(object* relation* or objectrelation*).ti,ab.	1715
Neurolinguistic programming/	77
(family constellation* or family therapy or family coping or family coping impairment or (family inventory adj (life events or changes)) or compromised family coping or parent education or (ineffective management adj3 therapeutic families regimen) or family support or family involvement or family coping inventory or family centered	16441

care or family care or altered family coping or critical care family needs inventory or psychoeducation or (adolescent coping orientation adj2 problem experiences) or feminist therap* or functional analytic or Freudian or family-based intervention* or internal family systems model or parent-child interact* or parent-training program* or peer support group*).ti,ab.	
(psychoanaly* or psycho-analyti* or psychodynamic or psycho-dynamic).ti,ab.	17205
Counseling/	32029
(counsel?ing or directive counsel?ing or motivational interviewing or distance counsel?ing or (pastoral adj (care or counsel* or therap*))).ti,ab.	77337
reality therap*.ti,ab.	82
(rebirthing or re-birthing or relationship counsel* or reprogram* or re-program* or breathwork).ti,ab.	16760
Psychotherapy, Rational-Emotive/	189
(rational emoti* or Reiki or REBT or rational living therap* or RLT or sensorimotor psychotherap*).ti,ab.	566
Acupuncture/	1454
acupuncture.ti,ab.	17792
Self Care/	28644
(self care or self help or self relationship or sponsorship or self-manag* or selfmanag* or self-talk).ti,ab.	33374
(SHEN or social support* or social therap* or social care or social problem skills train* or psychoeducation or psychology social or social support).ti,ab.	37287
(spiritual therap* or prayer or holistic care or Sophia-analys).ti,ab.	2943
(thought field therap* or transactional* or trans-actional* or transperson* or trans-person* or twelve-step program* or vegetotherap* or vegeto-therap*).ti,ab.	1968
(relational-cultural or MCT or (multicultural adj (counsel?ing or therapy))).ti,ab.	4709
1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38	592816
exp Digestive System Diseases/	1538482
(digestive system diseases or biliary tract diseases or digestive system abnormalities or digestive system fistul* or gastrointestinal diseases or oesophag* diseases or esophag* diseases or oesophagit* or esophagit* or gastrit* or enterit* or gastroenterit* or intestinal diseases or colit* or enterocolit* or proctit* or proctocolit* or rectal diseases or IBD or inflammatory bowel diseases or Crohn disease or ulcerative colit* or diverticul* or achalasia cardiae or megaesophagus or megaoesophagus or achlorhydria or Barrett esophagus or Barrett oesophagus or deglutition disorder* or duodenogastric reflux or eructation or esophag* fistul* or esophag* motility disorder* or oesophag* motility disorder* or oesophag* diverticul* or oesophag* fistula or esophageal achalasia or oesophageal achalasia or gastric dilatation or reflux esophagitis or reflux oesophagitis or gastroesophag* reflux or gastro-esophageal reflux disease or gastro-oesophageal reflux disease or gastropares* or liver diseases or pancreatic diseases or postgastrectomy syndrom* or stomach diseases or stomach diverticul* or Zollinger-Ellison syndrome).ti,ab.	220432
(gastrit* adj2 (chronic superficial or chronic atrophic or atrophy or unspecified or antral or fundal or Helicobacter pylori associated or giant hypertrophic or granulomatous or alcoholic)).ti,ab.	2687
gastroptosis.ti,ab.	49
(ulcer adj2 (peptic or duodenal or gastroduodenal or gastrojejunal or gastrocolic or gastrointestinal or jejunal or marginal or intestine or anus or rectum or gastric or stomach or pylorus or esophagus or oesophagus)).ti,ab.	44516

pylorospasm.ti,ab.	111
(hourglass contraction adj stomach).ti,ab.	0
hemorrhoid*.ti,ab.	3875
proctalgia fugax.ti,ab.	112
(psychogenic adj2 (diarrhoea or dyspepsia or intestinal disorders)).ti,ab.	1
(neurogenic bowel or neurogenic bowel dysfunction).ti,ab.	207
(liver diseases or liver cirrhosis or (drug-induced liver injury adj chronic) or fatty liver or liver failure or hepatitis chronic or liver cirrhosis or ((liver diseases or fatty liver or liver cirrhosis or hepatitis) adj2 alcoholic)).ti,ab.	72102
((chronic or alcoholic) adj pancreatitis).ti,ab.	13603
(cholangitis or cholestasis or gallbladder diseases or postcholecystectomy syndrome).ti,ab.	24882
pancreatic steatorrhoea.ti,ab.	34
postcholecystectomy syndrome.ti,ab.	330
(spasm adj2 (sphincter adj3 Oddi)).ti,ab.	27
(gallstone adj2 (disease or pancreatitis)).ti,ab.	3052
(fistula adj2 ((rectum adj skin) or anal or rectal or anorectal or stomach or duodenum or gastrocolic or gastrojejunocolic)).ti,ab.	1775
enteroptosis.ti,ab.	12
(dyspepsia adj2 (nervous or neurotic or psychogenic or heartburn)).ti,ab.	106
(dyspepsia adj2 (nervous or neurotic or psychogenic or heartburn)).ti,ab.	106
((dyskinesia adj esophagus) or (dyskinesia adj oesophagus) or corkscrew esophagus or corkscrew oesophagus or diffuse esophageal spasm or diffuse oesophageal spasm or (spasm adj esophagus) or (spasm adj oesophagus)).ti,ab.	434
(allergic adj2 (gastroenteritis or colitis)).ti,ab.	151
(functional gastrointestinal disorder* or FGID*).ti,ab.	1641
irritable bowel syndrome.ti,ab.	10325
40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56 or 57 or 58 or 59 or 60 or 61 or 62 or 63 or 64 or 65	1628977
exp Telecommunications/	75705
Internet/	60255
Computer Communication Networks/	13144
Text Messaging/	1463
(online or on-line or internet or telemedicine or telecommunication or computeri?ed or computer-assisted or (computer adj2 assisted)).ti,ab.	221899
website*.ti,ab.	18149
(e-health or ehealth).ti,ab.	2866
(etherap* or e-therapy).ti,ab.	361
(electronic mail or electronic-mail or text messag*).ti,ab.	2957
67 or 68 or 69 or 70 or 71 or 72 or 73 or 74 or 75	337709
39 and 66 and 76	387

Appendix 2 Search result in British Nursing Index ProQuest

British Nursing Index ProQuest 19/02/2017

((SU.EXACT.EXPLODE("Computer Networks") OR SU.EXACT.EXPLODE("Technology In Health Care") OR SU.EXACT("Information Technology")) OR ab(("online" OR "on-line" OR "internet" OR "telemedicine" OR "telecommunication" OR "computeri?ed" OR "computer-assisted" OR ("computer" NEAR/2 "assisted")) OR ("website*") OR ("e-health" OR "health") OR ("etherap*" OR "e-therapy") OR ("electronic mail" OR "electronic-mail" OR "text messag*"))) AND (ab(ab(("digestive system diseases" OR "biliary tract diseases" OR "digestive system abnormalities" OR "digestive system fistul*" OR "gastrointestinal diseases" OR "oesophag* diseases" OR "esophag* diseases" OR "oesophagit*" OR "esophagit*" OR "gastrit*" OR "enterit*" OR "castroenterit*" OR "intestinal diseases" OR "colit*" OR "enterocolit*" OR "proctit*" OR "proctocolit*" OR "rectal diseases" OR "ibid" OR "inflammatory bowel diseases" OR "croon disease" OR "ulcerative colit*" OR "diverticul*" OR "achaenia cardiac" OR "oesophagus" OR "oesophagus" OR "achlorhydria" OR "Barrett esophagus" OR "Barrett oesophagus" OR "deglutition disorder*" OR "digastric reflux" OR "eructation" OR "esophag* fistul*" OR "esophag* motility disorder*" OR "oesophag* motility disorder*" OR "oesophag* diverticul*" OR "oesophag* fistula" OR "esophageal achaenia" OR "oesophageal achaenia" OR "gastric dilatation" OR "reflux esophagitis" OR "reflux oesophagitis" OR "castroesophag* reflux" OR "castro-esophageal reflux disease" OR "castro-oesophageal reflux disease" OR "castropares*" OR "liver diseases" OR "pancreatic diseases" OR "postgastrectomy syndrom*" OR "stomach diseases" OR "stomach diverticul*" OR "bollinger-Ellison syndrome") OR ("gastrit*" PRE/2 ("chronic superficial" OR "chronic atrophic" OR "atrophy" OR "unspecified" OR "antral" OR "poundal" OR "Helicobacter pylori associated" OR "giant hypertrophic" OR "granulomatous" OR "alcoholic")) OR ("proptosis") OR ("ulcer" PRE/2 ("peptic" OR "duodenal" OR "astrodome" OR "jejunal" OR "astrocytic" OR "gastrointestinal" OR "jejunal " OR "marginal" OR "intestine" OR "anus" OR "rectum" OR "gastric" OR "stomach" OR "pylorus" OR "esophagus" OR "oesophagus")) OR ("pylorus") OR ("hourglass contraction" NEAR/4 "stomach") OR ("hemorrhoid*") OR ("nostalgia fugal") OR ("psychogenic" PRE/2 ("diarrhoea" OR "dyspepsia" OR "intestinal disorders")) OR ("neurogenic bowel" OR "neurogenic bowel dysfunction") OR ("liver diseases" OR "liver cirrhosis" OR ("drug-induced liver injury" NEAR/1 "chronic") OR "fatty liver" OR "liver failure" OR "hepatitis chronic" OR "liver cirrhosis" OR (("liver diseases" OR "fatty liver" OR "liver cirrhosis" OR "hepatitis") PRE/2 "alcoholic")) OR (("chronic" OR "alcoholic") NEAR/1 "pancreatitis") OR ("cholangitis" OR "homeostasis" OR "gallbladder diseases" OR "cholecystectomy syndrome") OR ("pancreatic steatorrhoea") OR ("cholecystectomy syndrome") OR ("spasm" PRE/2 ("sphincter" PRE/3 "odds")) OR ("gallstone" NEAR/2 ("disease" OR "pancreatitis")) OR ("fistula" PRE/2 (("rectum" NEAR/1 "skin") OR "anal" OR "rectal" OR "anorectal" OR "stomach" OR "duodenum" OR "astrocytic" OR "castrojejunocolic")) OR ("enterostomies") OR ("dyspepsia" PRE/2 ("nervous" OR "neurotic" OR "psychogenic" OR "heartburn")) OR (("dyskinesia" NEAR/1 "esophagus") OR ("dyskinesia" NEAR/1 "oesophagus") OR "corkscrew esophagus" OR "corkscrew oesophagus" OR "diffuse esophageal spasm" OR "diffuse oesophageal spasm" OR ("spasm" NEAR/1 "esophagus") OR ("spasm" NEAR/1 "oesophagus")) OR ("allergic" NEAR/2 ("gastroenteritis" OR "colitis")) OR ("functional gastrointestinal disorder*" OR "FGID*") OR ("irritable bowel syndrome") OR ("inflammatory bowel diseases"))) OR SU.EXACT.EXPLODE("Gastrointestinal System and Disorders")) AND ((SU.EXACT.EXPLODE("Psychotherapy") OR SU.EXACT.EXPLODE("Crisis

Intervention") OR SU.EXACT.EXPLODE("Alternative Therapies") OR SU.EXACT.EXPLODE("Creative Therapy") OR SU.EXACT.EXPLODE("Counselling") OR SU.EXACT("Self Care") OR SU.EXACT("Personal Care") OR SU.EXACT.EXPLODE("Patients : Education") OR SU.EXACT("Self Help Groups") OR SU.EXACT.EXPLODE("Biofeedback")) OR ab(("psychotherap*" OR ("behavior* NEAR/2 therap*") OR ("behaviour* NEAR/2 therap*") OR "cognitive therap*" OR "psychological intervention*" OR "psychological adaptation" OR "systematic desensitiz*" OR "systematic desensitis*") OR ("cognitive problem-solving skills training" OR "characteranalyti*" OR "character-analyti*" OR "client-centered" OR "client-centred" OR "coherence therap*" OR "contemplative therap*" OR "conversational therap*") OR ("problem-solving NEAR/2 training") OR (("coping" OR "cope" OR "copes" OR "coped") NEAR/2 ("skill*" OR "behavio?r*" OR "train*")) OR ("core energetic*" OR "core process*") OR ("dialectical behavio?r therap*" OR "debt") OR ("dreamworld" OR "Dyadic" OR "dip") OR ("expressive therap*" OR "Desensiti* reprocessing" OR "Desensiti* re-processing" OR "Emotional Freedom Techni*" OR "EFT" OR "encounter group*" OR "Experient* Dynamic" OR "Existential therap*" OR "exposure response prevent* therap*" OR ("Eye Movement Desensitization NEAR/2 Reprocessing") OR "emir") OR ("goal setting" OR "Gestalt*" OR "Group Analy*" OR "Milieu Therap*" OR "milieutherap*" OR "group-based therap*" OR "group-based treatment*" OR "group-based intervention") OR ("hakim" OR "holistic" OR "aeolotropic" OR "humanistic" OR "human givens" OR "hypnos*" OR "hypnot*" OR "hypno-therap*") OR ("interaction therap*" OR "interperson* therap*" OR "inter-personal therap*" OR "apt") OR ("meditati*" OR "mindfulness*" OR "maer" OR "morita therap*") OR ("body mind" OR "mind-body therap*" OR "Radix therap*" OR "pulsing" OR "body-oriented psychotherap*" OR "imp" OR "postural integration" OR "integrative body psychotherap*" OR "gesso hoyden system psychomotor" OR "lifespan Integration" OR "rosenfeld synergy" OR "Reichian") OR ("multimodal* therap*" OR "multi-modal* therap*" OR "multi-theoreti*" OR "multitheoreti*") OR ("relaxation therapy" OR "tai jib" OR "therapeutic touch" OR "yoga") OR ("object* relation*" OR "objectrelation*") OR ("family constellation*" OR "family therapy" OR "family coping" OR "family coping impairment" OR ("family inventory NEAR/1 " life events OR changes ") OR " compromised family coping " OR " parent education " OR (" ineffective management " NEAR/3 " therapeutic families regimen ") OR " family support " OR " family involvement " OR " family coping inventory " OR " family centered care " OR " family care " OR " altered family coping " OR " critical care family needs inventory " OR " coeducation " OR (" adolescent coping orientation " NEAR/2 " problem experiences ") OR " feminist therap* " OR " functional analytic " OR " Freudian " OR " family-based intervention* " OR " internal family systems model " OR " parent-child interact* " OR " parent-training program* " OR " peer support group* ") OR (" psychoanaly* " OR " psycho-analyti* " OR " psychodynamic " OR " psycho-dynamic ") OR (" counsel?ing " OR " directive counsel?ing " OR " motivational interviewing " OR " distance counsel?ing " OR (" pastoral " NEAR/1 (" care " OR " counsel* " OR " therap* "))) OR (" reality therap* ") OR (" rebirthing " OR " re-birthing " OR " relationship counsel* " OR " reprogram* " OR " re-program* " OR " breathwork ") OR (" rational emoti* " OR " Reiki " OR " rebs " OR " rational living therap* " OR " rut " OR " sensorimotor psychotherap* ") OR (" acupuncture ") OR (" self care " OR " self help " OR " self relationship " OR " sponsorship " OR " self-manag* " OR " selfmanag* " OR " self-talk ") OR (" SHEN " OR " social support* " OR " social therap* " OR " social care "

OR " social problem skills train* " OR " coeducation " OR " psychology social " OR " social support ") OR (" spiritual therap* " OR " prayer " OR " holistic care " OR " Sophia-analyse ") OR (" thought field therap* " OR " transactional* " OR " trans-actional* " OR " transperson* " OR " trans-person* " OR " twelve-step program* " OR " vegetotherap* " OR " vegeto-therap* ") OR (" relational-cultural " OR " mot " OR (" multiculturaL NEAR/4 ("counsel?ing" OR "therapy")))))
116

Appendix 3 Search result in CINAHL Plus

CINAHL Plus search 19/02/2017			
Search Terms	Search Options	Actions	
S83	S80 AND S81 AND S82	Search modes - Boolean/Phrase	(284)
S82	S70 OR S71 OR S72 OR S73 OR S74 OR S75 OR S76 OR S77 OR S78 OR S79	Search modes - Boolean/Phrase	(153,280)
S81	S42 OR S43 OR S44 OR S45 OR S46 OR S47 OR S48 OR S49 OR S50 OR S51 OR S52 OR S53 OR S54 OR S55 OR S56 OR S57 OR S58 OR S59 OR S60 OR S61 OR S62 OR S63 OR S64 OR S65 OR S66 OR S67 OR S68 OR S69	Search modes - Boolean/Phrase	(181,107)
S80	S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16 OR S17 OR S18 OR S19 OR S20 OR S21 OR S22 OR S23 OR S24 OR S25 OR S26 OR S27 OR S28 OR S29 OR S30 OR S31 OR S32 OR S33 OR S34 OR S35 OR S36 OR S37 OR S38 OR S39 OR S40 OR S41	Search modes - Boolean/Phrase	(354,048)
S79	TI (electronic mail OR electronic-mail OR text messag*) OR AB (electronic mail OR electronic-mail OR text messag*)	Search modes - Boolean/Phrase	(5,114)
S78	TI (etherap* OR e-therapy) OR AB (etherap* OR e-therapy)	Search modes - Boolean/Phrase	(82)
S77	TI (e-health OR ehealth) OR AB (e-health OR ehealth)	Search modes - Boolean/Phrase	(1,692)
S76	TI website* OR AB website*	Search modes - Boolean/Phrase	(8,025)
S75	TI (online OR on-line OR internet OR telemedicine OR telecommunication OR computeri#ed OR computer-assisted OR (computer N2 assisted)) OR AB (online OR on-line OR internet OR telemedicine OR telecommunication OR computeri#ed OR computer-assisted OR (computer N2 assisted))	Search modes - Boolean/Phrase	(113,382)
S74	MH Telemedicine	Search modes - Boolean/Phrase	(6,573)
S73	MH Computer Communication Networks	Search modes -	(2,540)

		Boolean/Phrase	
S72	MH Internet	Search modes - Boolean/Phrase	(36,891)
S71	MH Text Messaging	Search modes - Boolean/Phrase	(958)
S70	MH Electronic Mail	Search modes - Boolean/Phrase	(4,900)
S69	TI (functional gastrointestinal disorder* OR FGID*) OR AB (functional gastrointestinal disorder* OR FGID*)	Search modes - Boolean/Phrase	(356)
S68	TI (allergic N2 (gastroenteritis OR colitis)) OR AB (allergic N2 (gastroenteritis OR colitis))	Search modes - Boolean/Phrase	(16)
S67	TI ((dyskinesia N esophagus) OR (dyskinesia N oesophagus) OR corkscrew esophagus OR corkscrew oesophagus OR diffuse esophageal spasm OR diffuse oesophageal spasm OR (spasm N esophagus) OR (spasm N oesophagus)) OR AB ((dyskinesia N esophagus) OR (dyskinesia N oesophagus) OR corkscrew esophagus OR corkscrew oesophagus OR diffuse esophageal spasm OR diffuse oesophageal spasm OR (spasm N esophagus) OR (spasm N oesophagus))	Search modes - Boolean/Phrase	(34)
S66	TI (dyspepsia N2 (nervous OR neurotic OR psychogenic OR heartburn)) OR AB (dyspepsia N2 (nervous OR neurotic OR psychogenic OR heartburn))	Search modes - Boolean/Phrase	(20)
S65	TI enteroptosis OR AB enteroptosis	Search modes - Boolean/Phrase	(0)
S64	TI f#ecal# incontinence OR AB f#ecal# incontinence	Search modes - Boolean/Phrase	(1,215)
S63	TI (fistula N3 ("rectum to skin" OR anal or rectal OR anorectal OR stomach OR duodenum OR gastrocolic OR gastrojejunocolic)) OR AB (fistula N3 ("rectum to skin" OR anal or rectal OR anorectal OR stomach OR duodenum OR gastrocolic OR gastrojejunocolic))	Search modes - Boolean/Phrase	(158)
S62	TI (functional N3 (diarrhoea OR (disorders N stomach) OR dyspepsia OR indigestion)) OR AB (functional N3 (diarrhoea OR (disorders N stomach) OR dyspepsia OR indigestion))	Search modes - Boolean/Phrase	(391)
S61	TI (gallstone N2 (disease OR pancreatitis)) OR AB (gallstone N2 (disease OR pancreatitis))	Search modes - Boolean/Phrase	(301)
S60	TI spasm N2 "sphincter of Oddi") OR AB spasm N2 "sphincter of Oddi")	Search modes - Boolean/Phrase	(6)
S59	TI postcholecystectomy syndrome OR AB postcholecystectomy syndrome	Search modes - Boolean/Phrase	(12)

S58	TI pancreatic steatorrhoea OR AB pancreatic steatorrhoea	Search modes - Boolean/Phrase	(1)
S57	TI (cholangitis OR cholestasis OR gallbladder diseases OR postcholecystectomy syndrome) OR AB (cholangitis OR cholestasis OR gallbladder diseases OR postcholecystectomy syndrome)	Search modes - Boolean/Phrase	(1,822)
S56	TI ((chronic OR alcoholic) N pancreatitis) OR AB ((chronic OR alcoholic) N pancreatitis)	Search modes - Boolean/Phrase	(22)
S55	TI (liver diseases OR liver cirrhosis OR (drug-induced liver injury N chronic) OR fatty liver OR liver failure OR hepatitis chronic OR liver cirrhosis OR ((liver diseases OR fatty liver OR liver cirrhosis OR hepatitis) N2 alcoholic)) OR AB (liver diseases OR liver cirrhosis OR (drug-induced liver injury N chronic) OR fatty liver OR liver failure OR hepatitis chronic OR liver cirrhosis OR ((liver diseases OR fatty liver OR liver cirrhosis OR hepatitis) N2 alcoholic))	Search modes - Boolean/Phrase	(13,080)
S54	TI (neurogenic bowel OR neurogenic bowel dysfunction) OR AB (neurogenic bowel OR neurogenic bowel dysfunction)	Search modes - Boolean/Phrase	(152)
S53	TI (psychogenic N2 (diarrhoea OR dyspepsia OR intestinal disorders)) OR AB (psychogenic N2 (diarrhoea OR dyspepsia OR intestinal disorders))		(444)
S52	TI (psychogenic N2 (diarrhoea OR dyspepsia OR intestinal disorders)) OR AB (psychogenic N2 (diarrhoea OR dyspepsia OR intestinal disorders))	Search modes - Boolean/Phrase	(0)
S51	TI proctalgia fugax OR AB proctalgia fugax	Search modes - Boolean/Phrase	(11)
S50	TI hemorrhoid* OR AB hemorrhoid*	Search modes - Boolean/Phrase	(434)
S49	TI hourglass contraction N stomach OR AB hourglass contraction N stomach		(3)
S48	TI hourglass contraction N stomach OR AB hourglass contraction N stomach	Search modes - Boolean/Phrase	(0)
S47	TI pylorospasm OR AB pylorospasm	Search modes - Boolean/Phrase	(3)
S46	TI (ulcer N2 (peptic OR duodenal OR gastroduodenal OR gastrojejunal OR gastrocolic OR gastrointestinal OR jejunal OR marginal OR intestine OR anus OR rectum or gastric OR stomach OR pylorus or esophagus OR oesophagus)) OR AB (ulcer N2 (peptic OR duodenal OR gastroduodenal OR gastrojejunal OR gastrocolic OR gastrointestinal OR jejunal OR marginal OR intestine OR anus OR rectum or gastric OR	Search modes - Boolean/Phrase	(2,279)

	stomach OR pylorus or esophagus OR oesophagus))		
S45	TI gastroptosis OR AB gastroptosis	Search modes - Boolean/Phrase	(2)
S44	TI (gastrit* N2 (chronic superficial OR chronic atrophic OR atrophy OR unspecified OR antral OR fundal OR Helicobacter pylori associated OR giant hypertrophic OR granulomatous OR alcoholic)) OR AB (gastrit* N2 (chronic superficial OR chronic atrophic OR atrophy OR unspecified OR antral OR fundal OR Helicobacter pylori associated OR giant hypertrophic OR granulomatous OR alcoholic))	Search modes - Boolean/Phrase	(123)
S43	TI (digestive system diseases OR biliary tract diseases OR digestive system abnormalities OR digestive system fistul* OR gastrointestinal diseases OR oesophag* diseases OR esophag* diseases OR oesophagit* OR esophagit* OR gastrit* OR enterit* OR gastroenterit* OR intestinal diseases OR colit* OR enterocolit* OR proctit* OR proctocolit* OR rectal diseases OR IBD OR inflammatory bowel diseases OR Crohn disease OR ulcerative colit* OR diverticul* OR achalasia cardiae OR megaesophagus OR megaoesoph ...	Search modes - Boolean/Phrase	(28,258)
S42	MH Digestive System Diseases+	Search modes - Boolean/Phrase	(168,039)
S41	TI (relational-cultural OR MCT OR (multicultural N (counsel#ing OR therapy)) OR AB (relational-cultural OR MCT OR (multicultural N (counsel#ing OR therapy)))	Search modes - Boolean/Phrase	(479)
S40	TI (thought field therap* OR transactional* OR trans-actional* OR transperson* OR trans-person* OR twelve-step program* OR vegetotherap* OR vegeto-therap*) OR AB (thought field therap* OR transactional* OR trans-actional* OR transperson* OR trans-person* OR twelve-step program* OR vegetotherap* OR vegeto-therap*)	Search modes - Boolean/Phrase	(1,241)
S39	TI (spiritual therap* OR prayer OR holistic care OR Sophia-analys) OR AB (spiritual therap* OR prayer OR holistic care OR Sophia-analys)	Search modes - Boolean/Phrase	(4,131)
S38	TI (SHEN OR social support* OR social therap* OR social care OR social problem skills train* psychoeducation OR psychology social OR social support) OR AB (SHEN OR social support* OR social therap* OR social care OR social problem skills train* psychoeducation OR psychology social OR social support)	Search modes - Boolean/Phrase	(31,255)

S37	TI (self care OR self help OR self relationship OR sponsorship OR self-manag* OR selfmanag* OR self-talk) OR AB (self care OR self help OR self relationship OR sponsorship OR self-manag* OR selfmanag* OR self-talk)	Search modes - Boolean/Phrase	(28,843)
S36	MH Self Care	Search modes - Boolean/Phrase	(27,249)
S35	TI acupuncture OR AB acupuncture	Search modes - Boolean/Phrase	(8,280)
S34	MH Acupuncture	Search modes - Boolean/Phrase	(9,856)
S33	TI (rational emoti* OR Reiki or REBT OR rational living therap* OR RLT OR sensorimotor psychotherap*) OR AB (rational emoti* OR Reiki or REBT OR rational living therap* OR RLT OR sensorimotor psychotherap*)	Search modes - Boolean/Phrase	(481)
S32	TI (rebirthing OR re-birthing OR relationship counsel* OR reprogram* OR re-program* OR breathwork) OR AB (rebirthing OR re-birthing OR relationship counsel* OR reprogram* OR re-program* OR breathwork)	Search modes - Boolean/Phrase	(1,203)
S31	TI reality therap* OR AB reality therap*	Search modes - Boolean/Phrase	(371)
S30	TI (counsel#ing OR directive counsel#ing OR motivational interviewing OR distance counsel#ng OR (pastoral N (care OR counsel* OR therap*))) OR AB (counsel#ing OR directive counsel#ing OR motivational interviewing OR distance counsel#ng OR (pastoral N (care OR counsel* OR therap*)))	Search modes - Boolean/Phrase	(28,200)
S29	MH Counseling	Search modes - Boolean/Phrase	(21,155)
S28	TI (psychoanaly* OR psycho-analyti* OR psychodynamic OR psycho-dynamic) OR AB (psychoanaly* OR psycho-analyti* OR psychodynamic OR psycho-dynamic)	Search modes - Boolean/Phrase	(2,238)
S27	TI (family constellation* OR family therapy OR family coping OR family coping impairment OR (family inventory N (life events OR changes)) OR compromised family coping OR parent education OR (ineffective management N3 therapeutic families regimen) OR family support OR family involvement OR family coping inventory OR family centered care OR family care OR altered family coping OR critical care family needs inventory OR psychoeducation OR (adolescent coping orientation N2 problem experiences) OR f ...	Search modes - Boolean/Phrase	(31,729)

S26	TI (object* relation* OR objectrelation*) OR AB (object* relation* OR objectrelation*)	Search modes - Boolean/Phrase	(7,961)
S25	TI (relaxation therapy OR tai ji OR therapeutic touch OR yoga) OR AB (relaxation therapy OR tai ji OR therapeutic touch OR yoga)	Search modes - Boolean/Phrase	(4,058)
S24	TI (multimodal* therap* OR multi-modal* therap* OR multi-theoreti* OR multitheoreti*) OR AB (multimodal* therap* OR multi-modal* therap* OR multi-theoreti* OR multitheoreti*)	Search modes - Boolean/Phrase	(871)
S23	TI (body mind OR mind-body therap* OR Radix therap* OR pulsing OR body-oriented psychotherap* OR IBP OR postural integration OR integrative body psychotherap* OR Pesso Boyden system psychomotor OR lifespan Integration OR Rubenfeld synergy OR Reichian) OR AB (body mind OR mind-body therap* OR Radix therap* OR pulsing OR body-oriented psychotherap* OR IBP OR postural integration OR integrative body psychotherap* OR Pesso Boyden system psychomotor OR lifespan Integration OR Rubenfeld synergy OR ...	Search modes - Boolean/Phrase	(2,984)
S22	MH Mind Body techniques	Search modes - Boolean/Phrase	(2,161)
S21	TI (meditati* OR mindfulness* OR MBSR OR morita therap*) OR AB (meditati* OR mindfulness* OR MBSR OR morita therap*)	Search modes - Boolean/Phrase	(4,152)
S20	TI (interaction therap* OR interperson* therap* or inter-personal therap* OR IPT) OR AB (interaction therap* OR interperson* therap* OR inter-personal therap* OR IPT)	Search modes - Boolean/Phrase	(1,959)
S19	TI (hakomi OR holistic or holotropic OR humanistic OR human givens OR hypnos* OR hypnot* OR hypno-therap*) OR AB (hakomi OR holistic OR holotropic or humanistic OR human givens OR hypnos* OR hypnot* OR hypno-therap*)	Search modes - Boolean/Phrase	(14,025)
S18	TI (goal setting OR gestalt* OR group analy* OR Milieu therap* OR milieutherap* OR group-based therap* OR group-based treatment* OR group-based intervention) OR AB (goal setting OR gestalt* OR group analy* OR Milieu therap* OR milieutherap* OR group-based therap* OR group-based treatment* OR group-based intervention)	Search modes - Boolean/Phrase	(25,319)
S17	TI (expressive therap* or desensiti* reprocessing or desensiti* re-processing or emotional freedom techni* or EFT or encounter group* or experient* dynamic or	Search modes - Boolean/Phrase	(839)

	existential therap* or exposure response prevent* therap* or ("eye movement desensitization and reprocessing") or EMDR) OR AB (expressive therap* or desensiti* reprocessing or desensiti* re-processing or emotional freedom techni* or EFT or encounter group* or experient* dynamic or existential therap* or exposure response prevent* therap ...		
S16	TI (dreamwork or dyadic or DDP) OR AB (dreamwork or dyadic or DDP)	Search modes - Boolean/Phrase	(1,603)
S15	(TI dialectical behavio#r therap* OR DBT) OR (AB dialectical behavio#r therap* OR DBT)	Search modes - Boolean/Phrase	(427)
S14	(TI core energetic* OR core process*) OR (AB core energetic* OR core process*)	Search modes - Boolean/Phrase	(647)
S13	AB (coping OR cope OR copes OR coped) N2 (skill* OR behavior* OR behaviours OR train*)	Search modes - Boolean/Phrase	(2,408)
S12	TI (coping OR cope OR copes OR coped) N2 (skill* OR behavior* OR behaviours OR train*)	Search modes - Boolean/Phrase	(543)
S11	AB problem solving N2 training	Search modes - Boolean/Phrase	(138)
S10	TI problem solving N2 training	Search modes - Boolean/Phrase	(43)
S9	AB problem-solving N2 training	Search modes - Boolean/Phrase	(135)
S8	TI problem-solving N2 training	Search modes - Boolean/Phrase	(43)
S7	MH Patient centered care	Search modes - Boolean/Phrase	(19,539)
S6	MH Problem Solving+	Search modes - Boolean/Phrase	(8,998)
S5	AB cognitive problem-solving skills training OR characteranalyti* OR character-analyti* OR client-centered OR client-centred OR coherence therap* OR contemplative therap* OR conversational therap*	Search modes - Boolean/Phrase	(1,173)
S4	TI cognitive problem-solving skills training OR characteranalyti* OR character-analyti* OR client-centered OR client-centred OR coherence therap* OR contemplative therap* OR conversational therap*	Search modes - Boolean/Phrase	(1,165)
S3	AB psychotherap* OR (behavior* N2 therap*) OR (behaviour* N2 therap*) OR cognitive therap* OR psychological intervention* OR psychological adaptation OR systematic desensitiz* OR systematic desensitis*	Search modes - Boolean/Phrase	(56,373)

S2	TI psychotherap* OR (behavior* N2 therap*) OR (behaviour* N2 therap*) OR cognitive therap* OR psychological intervention* OR psychological adaptation OR systematic desensitiz* OR systematic desensitis*	Search modes - Boolean/Phrase	(55,676)
S1	MH Psychotherapy+	Search modes - Boolean/Phrase	(132,030)

Appendix 4 Search result in Cochrane

Cochrane
Search Name: GASTRO
Date Run: 19/02/17
Description:
ID Search Hits

#1 MeSH descriptor: [Psychotherapy] explode all trees 19988

#2 MeSH descriptor: [Adaptation, Psychological] explode all trees 4684

#3 (psychotherap* or (behavior* near/2 therap*) or (behaviour* near/2 therap*) or cognitive near therap* or "psychological intervention*" or "psychological adaptation" or systematic near desensiti?*):ti,ab 14078

#4 "cognitive problem-solving skills training":ti,ab 2

#5 ((characteranalyti* or character-analyti*) or client-centered or client-centred or (coherence near therap*) or (contemplative next therap*) or (conversational next therap*)):ti,ab 170

#6 MeSH descriptor: [Problem Solving] explode all trees 1384

#7 MeSH descriptor: [Patient-Centered Care] this term only 456

#8 (problem-solving near/2 training):ti,ab 186

#9 ((coping or cope or copes or coped) near/2 (skill* or behavio?r* or train*)):ti,ab 825

#10 (core next energetic* or core next process*):ti,ab 4

#11 (dialectical next behavio?r next therap* or DBT):ti,ab 157

#12 (Dreamwork or Dyadic or DDP):ti,ab 577

#13 (expressive next therap* or Desensiti* next reprocessing or Desensiti* next re-processing or Emotional next Freedom next Techni* or EFT or encounter next group* or Experient* next Dynamic or Existential next therap* or exposure near response near prevent* near therap* or (Eye next Movement next Desensitization near/2 Reprocessing) or EMDR):ti,ab 301

#14 (goal near setting or Gestalt* or Group near Analy* or Milieu next Therap* or milieutherap* or group-based near therap* or group-based near treatment* or group-based near intervention):ti,ab 14353

#15 (hakomi or holistic or holotropic or humanistic or human next givens or hypnos* or hypnot* or hypno-therap*):ti,ab 3575

#16 (interaction next therap* or interperson* next therap* or inter-personal next therap* or IPT):ti,ab 494

#17 (meditati* or mindfulness* or MBSR or morita next therap*):ti,ab 2101

#18 MeSH descriptor: [Mind-Body Therapies] explode all trees 5361

#19 (body next mind or mind-body next therap* or Radix next therap* or pulsing or body-oriented near psychotherap* or IBP or postural near integration or integrative next body next psychotherap* or Pesso next Boyden next system next psychomotor or lifespan near Integration or Rubenfeld next synergy or Reichian):ti,ab 230

#20 (multimodal* near therap* or multi-modal* near therap* or multi-theoreti* or multitheoreti*):ti,ab 398

#21 (relaxation near therapy or tai ji or therapeutic next touch or yoga):ti,ab 1882

#22 (object* next relation* or objectrelation*):ti,ab 56

#23 MeSH descriptor: [Neurolinguistic Programming] this term only 9

#24 (family near constellation* or family next therapy or family next coping or "family coping impairment" or (family next inventory near (life next events or changes)) or compromised next family next coping or parent next education or ((ineffective next management) near/3 (therapeutic next families next regimen)) or family next support or family next involvement or family next coping next inventory or family next centered next care or family next care or altered next family next coping or critical next care next family next needs next inventory or psychoeducation or ((adolescent next coping next orientation) near/2 (problem next experiences)) or feminist next therap* or functional next analytic or Freudian or family-based next intervention* or internal next family next systems model or parent-child next interact* or parent-training near program* or peer next support next group*):ti,ab 2126

#25 (psychoanaly* or psycho-analyti* or psychodynamic or psycho-dynamic):ti,ab 570

#26 MeSH descriptor: [Counseling] this term only 3626

#27 (counsel?ing or directive counsel?ing or motivational next interviewing or distance next counsel?ing or (pastoral near (care or counsel* or therap*))):ti,ab 3811

#28 reality therap*:ti,ab 615

#29 (rebirthing or re-birthing or relationship next counsel* or reprogram* or re-program* or breathwork):ti,ab 112

#30 (rational next emoti* or Reiki or REBT or rational next living next therap* or RLT or sensorimotor near psychotherap*):ti,ab 165

#31 MeSH descriptor: [Acupuncture] this term only 164

#32 acupuncture:ti,ab 7809

#33 MeSH descriptor: [Self Care] this term only 3661

#34 (self next care or self next help or self next relationship or sponsorship or self-manag* or selfmanag* or self-talk):ti,ab 6756

#35 (SHEN or social next support* or social next therap* or social next care or social next problem next skills next train* or psychoeducation or psychology near social or social next support):ti,ab 3712

#36 (spiritual next therap* or prayer or holistic care or Sophia-analys):ti,ab 244

#37 (thought next field next therap* or transactional* or trans-actional* or transperson* or trans-person* or twelve-step near program* or vegetotherap* or vegeto-therap*):ti,ab 88

#38 (relational-cultural or MCT or (multicultural near (counsel?ing or therapy))):ti,ab 588

#39 #1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25 or #26 or #27 or #28 or #29 or #30 or #31 or #32 or #33 or #34 or #35 or #36 or #37 or #38 74967

#40 MeSH descriptor: [Digestive System Diseases] explode all trees 43191

#41 (digestive next system next diseases or biliary next tract next diseases or digestive next system next abnormalities or digestive next system next fistul* or gastrointestinal next diseases or oesophag* next diseases or esophag* next diseases or oesophagit* or esophagit* or gastrit* or enterit* or gastroenterit* or intestinal next diseases or colit* or enterocolit* or proctit* or proctocolit* or rectal next diseases or IBD or inflammatory next bowel next diseases or Crohn next disease or ulcerative next colit* or diverticul* or achalasia near cardiae or megaesophagus or megaoesophagus or achlorhydria or Barrett near esophagus or Barrett near oesophagus or deglutition next disorder* or duodenogastric near reflux or eructation or esophag* fistul* or esophag* next motility next disorder* or oesophag* next motility next disorder* or oesophag* near diverticul* or oesophag* near fistula or esophageal near achalasia or oesophageal near achalasia or gastric near dilatation or reflux near esophagitis or reflux near oesophagitis or gastroesophag* near reflux or gastro-esophageal neat reflux next disease or gastro-oesophageal next reflux next disease or gastropares* or liver near diseases or pancreatic near diseases or postgastrectomy next syndrom* or stomach near diseases or stomach near diverticul* or Zollinger-Ellison near syndrome):ti,ab 10690

#42 (gastrit* near/2 (chronic next superficial or chronic next atrophic or atrophy or unspecified or antral or fundal or Helicobacter next pylori next associated or giant near hypertrophic or granulomatous or alcoholic)):ti,ab 214

#43 gastroptosis:ti,ab 13

#44 (ulcer near/2 (peptic or duodenal or gastroduodenal or gastrojejunal or gastrocolic or gastrointestinal or jejunal or marginal or intestine or anus or rectum or gastric or stomach or pylorus or esophagus or oesophagus)):ti,ab 5004

#45 pylorospasm:ti,ab 0

#46 (hourglass next contraction near stomach):ti,ab 0

#47 hemorrhoid*:ti,ab 625

#48 proctalgia next fugax:ti,ab 2

#49 (psychogenic near/2 (diarrhoea or dyspepsia or intestinal near disorders)):ti,ab 0

#50 (neurogenic near bowel or neurogenic next bowel next dysfunction):ti,ab 21

#51 (liver near diseases or liver near cirrhosis or (drug-induced next liver next injury near chronic) or fatty next liver or liver near failure or hepatitis near chronic or liver near cirrhosis or ((liver next diseases or fatty next liver or liver next cirrhosis or hepatitis) near/2 alcoholic)):ti,ab 9993

#52 ((chronic or alcoholic) near pancreatitis):ti,ab 476
#53 (cholangitis or cholestasis or gallbladder near diseases or postcholecystectomy near syndrome):ti,ab 868
#54 pancreatic near steatorrhoea:ti,ab 15
#55 postcholecystectomy near syndrome:ti,ab 8
#56 (spasm near/2 (sphincter near/3 Oddi)):ti,ab 5
#57 (gallstone near/2 (disease or pancreatitis)):ti,ab 190
#58 (fistula near/2 ((rectum near skin) or anal or rectal or anorectal or stomach or duodenum or gastrocolic or gastrojejunocolic)):ti,ab 87
#59 (dyspepsia near/2 (nervous or neurotic or psychogenic or heartburn)):ti,ab 24
#60 ((dyskinesia near esophagus) or (dyskinesia near oesophagus) or corkscrew near esophagus or corkscrew near oesophagus or diffuse next esophageal next spasm or diffuse next oesophageal next spasm or (spasm near esophagus) or (spasm near oesophagus)):ti,ab 12
#61 (allergic near/2 (gastroenteritis or colitis)):ti,ab 9
#62 (functional next gastrointestinal next disorder* or FGID*):ti,ab 140
#63 irritable next bowel next syndrome:ti,ab 1809
#64 inflammatory next bowel next diseases:ti,ab 139
#65 #40 or #41 or #42 or #43 or #44 or #45 or #46 or #47 or #48 or #49 or #50 or #51 or #52 or #53 or #54 or #55 or #56 or #57 or #58 or #59 or #60 or #61 or #62 or #63 or #64 58565
#66 MeSH descriptor: [Telecommunications] explode all trees 4904
#67 MeSH descriptor: [Internet] this term only 2832
#68 MeSH descriptor: [Computer Communication Networks] this term only 73
#69 MeSH descriptor: [Text Messaging] this term only 388
#70 (online or on-line or internet or telemedicine or telecommunication or computeri?ed or computer-assisted or (computer near/2 assisted)):ti,ab 14933
#71 website*:ti,ab 1656
#72 (e-health or ehealth):ti,ab 250
#73 (etherap* or e-therapy):ti,ab 80
#74 (electronic near mail or electronic-mail or text near messag*):ti,ab 863
#75 #66 or #67 or #68 or #69 or #70 or #71 or #72 or #73 or #74 20837
#76 #39 and #65 and #75 91

Appendix 5 Search result in Health Management Information Consortium

HMIC Health Management Information Consortium 1979 to November 2016

(Run 19/02/2017)

	Searches	Results
1	exp psychotherapy/	1875
2	(psychotherap* or (behavior* adj2 therap*) or (behaviour* adj2 therap*) or cognitive therap* or psychological intervention* or psychological adaptation or systematic desensitiz* or systematic desensitis*).ti,ab.	1229
3	(cognitive problem-solving skills training or characteranalyti* or character-analyti* or client-centered or client-centred or coherence therap* or contemplative therap* or conversational therap*).ti,ab.	164
4	exp Problem solving/	225
5	exp patient centred care/	1234
6	(problem-solving adj2 training).ti,ab.	10
7	((coping or cope or copes or coped) adj2 (skill* or behavior* or behaviours or train*)).ti,ab.	137
8	(core energetic* or core process*).ti,ab.	6
9	(dialectical behavio?r therap* or DBT).ti,ab.	11

10	(Dreamwork or Dyadic or DDP).ti,ab.	42
11	(expressive therap* or Desensiti* reprocessing or Desensiti* re-processing or Emotional Freedom Techni* or EFT or encounter group* or Experient* Dynamic or Existential therap* or exposure response prevent* therap* or (Eye Movement Desensitization and Reprocessing) or EMDR).ti,ab.	9
12	(goal setting or Gestalt* or Group Analy* or Milieu Therap* or milieutherap* or group therap* or group-based therap* or group-based treatment* or group-based intervention).ti,ab.	327
13	exp Hypnosis/	14
14	(hakomi or holistic or holotropic or humanistic or human givens or hypnos* or hypnot* or hypno-therap*).ti,ab.	1303
15	(interaction therap* or interperson* therap* or inter-personal therap* or IPT).ti,ab.	23
16	(meditati* or mindfulness* or MBSR or morita therap*).ti,ab.	79
17	exp complementary medicine/	1402
18	(body mind or mind-body therap* or Radix therap* or pulsing or body-oriented psychotherap* or IBP or postural integration or integrative body psychotherap* or Pesso Boyden system psychomotor or lifespan Integration or Rubenfeld synergy or Reichian).ti,ab.	11
19	(multimodal* therap* or multi-modal* therap* or multi-theoreti* or multitheoreti*).ti,ab.	6
20	exp Relaxation therapy/	39
21	(relaxation therapy or tai ji or therapeutic touch or yoga).ti,ab.	39
22	(object* relation* or objectrelation*).ti,ab.	8
23	exp Neurolinguistic programming/	29
24	(family constellation* or family therapy or family coping or family coping impairment or (family inventory adj (life events or changes)) or compromised family coping or parent education or (ineffective management adj3 therapeutic families regimen) or family support or family involvement or family coping inventory or family centered care or family care or altered family coping or critical care family needs inventory or psychoeducation or (adolescent coping orientation adj2 problem experiences) or feminist therap* or functional analytic or Freudian or family-based intervention* or internal family systems model or parent-child interact* or parent-training program* or peer support group*).ti,ab.	1107
25	(psychoanaly* or psycho-analyti* or psychodynamic or psycho-dynamic).ti,ab.	180
26	exp Counselling/	1473
27	(counsel?ing or directive counsel?ing or motivational interviewing or distance counsel?ing or (pastoral adj (care or counsel* or therap*))).ti,ab.	2911
28	reality therap*.ti,ab.	2
29	(rebirthing or re-birthing or relationship counsel* or reprogram* or re-program* or breathwork).ti,ab.	10
30	(rational emoti* or Reiki or REBT or rational living therap* or RLT or sensorimotor psychotherap*).ti,ab.	13
31	acupuncture.ti,ab.	170
32	Self care/	257
33	(self care or self help or self relationship or sponsorship or self-manag*	2435

	or selfmanag* or self-talk).ti,ab.	
34	(SHEN or social support* or social therap* or social care or social problem skills train* or psychoeducation or psychology social or social support).ti,ab.	9414
35	(spiritual therap* or prayer or holistic care or Sophia-analys).ti,ab.	194
36	(thought field therap* or transactional* or trans-actional* or transperson* or trans-person* or twelve-step program* or vegetotherap* or vegeto-therap*).ti,ab.	98
37	(relational-cultural or MCT or (multicultural adj (counsel?ing or therapy))).ti,ab.	4
38	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37	22617
39	exp Digestive System Diseases/	2975
40	(digestive system diseases or biliary tract diseases or digestive system abnormalities or digestive system fistul* or gastrointestinal diseases or oesophag* diseases or esophag* diseases or oesophagit* or esophagit* or gastrit* or enterit* or gastroenterit* or intestinal diseases or colit* or enterocolit* or proctit* or proctocolit* or rectal diseases or IBD or inflammatory bowel diseases or Crohn disease or ulcerative colit* or diverticul* or achalasia cardiae or megaesophagus or megaoesophagus or achlorhydria or Barrett esophagus or Barrett oesophagus or deglutition disorder* or duodenogastric reflux or eructation or esophag* fistul* or esophag* motility disorder* or oesophag* motility disorder* or oesophag* diverticul* or oesophag* fistula or esophageal achalasia or oesophageal achalasia or gastric dilatation or reflux esophagitis or reflux oesophagitis or gastroesophag* reflux or gastro-esophageal reflux disease or gastro-oesophageal reflux disease or gastropares* or liver diseases or pancreatic diseases or postgastrectomy syndrom* or stomach diseases or stomach diverticul* or Zollinger-Ellison syndrome).ti,ab.	266
41	(gastrit* adj2 (chronic superficial or chronic atrophic or atrophy or unspecified or antral or fundal or Helicobacter pylori associated or giant hypertrophic or granulomatous or alcoholic)).ti,ab.	0
42	gastroptosis.ti,ab.	0
43	(ulcer adj2 (peptic or duodenal or gastroduodenal or gastrojejunal or gastrocolic or gastrointestinal or jejunal or marginal or intestine or anus or rectum or gastric or stomach or pylorus or esophagus or oesophagus)).ti,ab.	78
44	pylorospasm.ti,ab.	0
45	(hourglass contraction adj stomach).ti,ab.	0
46	hemorrhoid*.ti,ab.	0
47	proctalgia fugax.ti,ab.	0
48	(psychogenic adj2 (diarrhoea or dyspepsia or intestinal disorders)).ti,ab.	0
49	(neurogenic bowel or neurogenic bowel dysfunction).ti,ab.	0
50	(liver diseases or liver cirrhosis or (drug-induced liver injury adj chronic) or fatty liver or liver failure or hepatitis chronic or liver cirrhosis or ((liver diseases or fatty liver or liver cirrhosis or hepatitis) adj2 alcoholic)).ti,ab.	98
51	((chronic or alcoholic) adj pancreatitis).ti,ab.	8
52	(cholangitis or cholestasis or gallbladder diseases or postcholecystectomy syndrome).ti,ab.	7

53	pancreatic steatorrhoea.ti,ab.	0
54	postcholecystectomy syndrome.ti,ab.	0
55	(spasm adj2 "sphincter of Oddi").ti,ab.	0
56	(gallstone adj2 (disease or pancreatitis)).ti,ab.	8
57	(functional adj3 (diarrhoea or (disorders adj stomach) or dyspepsia or indigestion)).ti,ab.	2
58	(fistula adj3 ("rectum to skin" or anal or rectal or anorectal or stomach or duodenum or gastrocolic or gastrojejunocolic)).ti,ab.	0
59	f?ecal? incontinence.ti,ab.	37
60	enteroptosis.ti,ab.	0
61	(dyspepsia adj2 (nervous or neurotic or psychogenic or heartburn)).ti,ab.	1
62	(dyspepsia adj2 (nervous or neurotic or psychogenic or heartburn)).ti,ab.	1
63	((dyskinesia adj esophagus) or (dyskinesia adj oesophagus) or corkscrew esophagus or corkscrew oesophagus or diffuse esophageal spasm or diffuse oesophageal spasm or (spasm adj esophagus) or (spasm adj oesophagus)).ti,ab.	0
64	(allergic adj2 (gastroenteritis or colitis)).ti,ab.	0
65	(functional gastrointestinal disorder* or FGID*).ti,ab.	3
66	Inflammatory Bowel Diseases/	0
67	39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56 or 57 or 58 or 59 or 60 or 61 or 62 or 63 or 64 or 65 or 66	3210
68	exp telecommunications/	697
69	exp internet/	1295
70	exp telemedicine/	1248
71	(online or on-line or internet or telemedicine or telecommunication or computeri?ed or computer-assisted or (computer adj2 assisted)).ti,ab.	6026
72	website*.ti,ab.	3637
73	(e-health or ehealth).ti,ab.	229
74	(etherap* or e-therapy).ti,ab.	0
75	(electronic mail or electronic-mail or text messag*).ti,ab.	157
76	68 or 69 or 70 or 71 or 72 or 73 or 74 or 75	10719
77	38 and 67 and 76	2

Appendix 6 Search result in PsycINFO

PsycINFO 1806 to February Week 2 2017 (Run 19/02/2017)

Searches	Results
exp Psychotherapy/	197148
(psychotherap* or (behavior* adj2 therap*) or (behaviour* adj2 therap*) or cognitive therap* or psychological intervention* or psychological adaptation or systematic desensitiz* or systematic desensitis*).ti,ab.	130371
(cognitive problem-solving skills training or characteranalyti* or character-analyti* or client-centered or client-centred or coherence therap* or contemplative therap* or conversational therap*).ti,ab.	2548

exp problem solving/	41735
Client Centered Therapy/	2897
(problem-solving adj2 training).ti,ab.	853
((coping or cope or copes or coped) adj2 (skill* or behavior* or behaviours or train*)).ti,ab.	8566
(core energetic* or core process*).ti,ab.	403
(dialectical behavio?r therap* or DBT).ti,ab.	1510
(dreamwork or dyadic or DDP).ti,ab.	11311
(expressive therap* or desensiti* reprocessing or desensiti* re-processing or emotional freedom techni* or EFT or encounter group* or experient* dynamic or existential therap* or exposure response prevent* therap* or (eye movement desensitization adj3 reprocessing) or EMDR).ti,ab.	3425
(goal setting or gestalt* or group analy* or Milieu therap* or milieutherap* or group therap* or group-based therap* or group-based treatment* or group-based intervention).ti,ab.	28885
(hakomi or holistic or holotropic or humanistic or human givens or hypnos* or hypnot* or hypno-therap*).ti,ab.	39760
(interaction therap* or interperson* therap* or inter-personal therap* or IPT).ti,ab.	1859
(meditati* or mindfulness* or MBSR or morita therap*).ti,ab.	12973
Mind body therapy/	130
(body mind or mind-body therap* or Radix therap* or pulsing or body-oriented psychotherap* or IBP or postural integration or integrative body psychotherap* or Pesso Boyden system psychomotor or lifespan Integration or Rubenfeld synergy or Reichian).ti,ab.	1399
(multimodal* therap* or multi-modal* therap* or multi-theoreti* or multitheoreti*).ti,ab.	471
(relaxation therapy or tai ji or therapeutic touch or yoga).ti,ab.	2661
(object* relation* or objectrelation*).ti,ab.	8317
Neurolinguistic programming/	222
(family constellation* or family therapy or family coping or family coping impairment or (family inventory adj (life events or changes)) or compromised family coping or parent education or (ineffective management adj3 therapeutic families regimen) or family support or family involvement or family coping inventory or family centered care or family care or altered family coping or critical care family needs inventory or psychoeducation or (adolescent coping orientation adj2 problem experiences) or feminist therap* or functional analytic or Freudian or family-based intervention* or internal family systems model or parent-child interact* or parent-training program* or peer support group*).ti,ab.	41085
(psychoanaly* or psycho-analyti* or psychodynamic or psycho-dynamic).ti,ab.	86908
Counseling/	21116
(counsel?ing or directive counsel?ing or motivational interviewing or distance counsel?ing or (pastoral adj (care or counsel* or therap*))).ti,ab.	75039
reality therap*.ti,ab.	773
(rebirthing or re-birthing or relationship counsel* or reprogram* or re-program* or breathwork).ti,ab.	768
(rational emoti* or Reiki or REBT or rational living therap* or RLT or sensorimotor psychotherap*).ti,ab.	2385
Acupuncture/	1275
acupuncture.ti,ab.	1672

Self Care/	3868
(self care or self help or self relationship or sponsorship or self-manag* or selfmanag* or self-talk).ti,ab.	23453
(SHEN or social support* or social therap* or social care or social problem skills train* or psychoeducation or psychology social or social support).ti,ab.	46467
(spiritual therap* or prayer or holistic care or Sophia-analys).ti,ab.	2901
(thought field therap* or transactional* or trans-actional* or transperson* or trans-person* or twelve-step program* or vegetotherap* or vegeto-therap*).ti,ab.	8863
(relational-cultural or MCT or (multicultural adj (counsel?ing or therapy))).ti,ab.	1823
1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36	543752
exp digestive system disorders/	11402
(digestive system diseases or biliary tract diseases or digestive system abnormalities or digestive system fistul* or gastrointestinal diseases or oesophag* diseases or esophag* diseases or oesophagit* or esophagit* or gastrit* or enterit* or gastroenterit* or intestinal diseases or colit* or enterocolit* or proctit* or proctocolit* or rectal diseases or IBD or inflammatory bowel diseases or Crohn disease or ulcerative colit* or diverticul* or achalasia cardiae or megaesophagus or megaoesophagus or achlorhydria or Barrett esophagus or Barrett oesophagus or deglutition disorder* or duodenogastric reflux or eructation or esophag* fistul* or esophag* motility disorder* or oesophag* motility disorder* or oesophag* diverticul* or oesophag* fistula or esophageal achalasia or oesophageal achalasia or gastric dilatation or reflux esophagitis or reflux oesophagitis or gastroesophag* reflux or gastro-esophageal reflux disease or gastro-oesophageal reflux disease or gastropares* or liver diseases or pancreatic diseases or postgastrectomy syndrom* or stomach diseases or stomach diverticul* or Zollinger-Ellison syndrome).ti,ab.	2309
(gastrit* adj2 (chronic superficial or chronic atrophic or atrophy or unspecified or antral or fundal or Helicobacter pylori associated or giant hypertrophic or granulomatous or alcoholic)).ti,ab.	6
gastroptosis.ti,ab.	0
(ulcer adj2 (peptic or duodenal or gastroduodenal or gastrojejunal or gastrocolic or gastrointestinal or jejunal or marginal or intestine or anus or rectum or gastric or stomach or pylorus or esophagus or oesophagus)).ti,ab.	863
pylorospasm.ti,ab.	3
(hourglass contraction adj stomach).ti,ab.	0
hemorrhoid*.ti,ab.	34
proctalgia fugax.ti,ab.	4
(psychogenic adj2 (diarrhoea or dyspepsia or intestinal disorders)).ti,ab.	0
(neurogenic bowel or neurogenic bowel dysfunction).ti,ab.	8
(liver diseases or liver cirrhosis or (drug-induced liver injury adj chronic) or fatty liver or liver failure or hepatitis chronic or liver cirrhosis or ((liver diseases or fatty liver or liver cirrhosis or hepatitis) adj2 alcoholic)).ti,ab.	913
((chronic or alcoholic) adj pancreatitis).ti,ab.	87
(cholangitis or cholestasis or gallbladder diseases or postcholecystectomy syndrome).ti,ab.	75
pancreatic steatorrhoea.ti,ab.	0
postcholecystectomy syndrome.ti,ab.	0
(spasm adj2 (sphincter adj3 Oddi)).ti,ab.	0
(gallstone adj2 (disease or pancreatitis)).ti,ab.	18
(fistula adj2 ((rectum adj skin) or anal or rectal or anorectal or stomach or	10

duodenum or gastrocolic or gastrojejunocolic)).ti,ab.	
enteroptosis.ti,ab.	0
(dyspepsia adj2 (nervous or neurotic or psychogenic or heartburn)).ti,ab.	12
(dyspepsia adj2 (nervous or neurotic or psychogenic or heartburn)).ti,ab.	12
((dyskinesia adj esophagus) or (dyskinesia adj oesophagus) or corkscrew esophagus or corkscrew oesophagus or diffuse esophageal spasm or diffuse oesophageal spasm or (spasm adj esophagus) or (spasm adj oesophagus)).ti,ab.	2
(allergic adj2 (gastroenteritis or colitis)).ti,ab.	0
(functional gastrointestinal disorder* or FGID*).ti,ab.	194
irritable bowel syndrome.ti,ab.	1258
38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56 or 57 or 58 or 59 or 60 or 61 or 62 or 63	13767
exp Telecommunications/	15053
Internet/	26294
Computer Mediated Communication/	4937
Text Messaging/	430
(online or on-line or internet or telemedicine or telecommunication or computeri?ed or computer-assisted or (computer adj2 assisted)).ti,ab.	98899
website*.ti,ab.	9265
(e-health or ehealth).ti,ab.	837
(electronic mail or electronic-mail or text messag*).ti,ab.	1842
65 or 66 or 67 or 68 or 69 or 70 or 71 or 72	124631
37 and 64 and 73	56

Appendix 7 Search result in PubMed

PubMed 19/02/2017

(("telecommunications"[MeSH Major Topic]) AND "digestive system diseases"[MeSH Major Topic]) AND "telecommunications"[MeSH Major Topic]

Result 435

Appendix 8 Search result in Embase

Embase 1974 to 2017 February 17 (search run 19/02/2017)

	Searches	Results
1	exp Psychotherapy/	231545
2	Psychoanalysis/	34885
3	Color therapy/	106
4	Crisis intervention/	6236
5	Horticultural therapy/	59
6	exp Adaptive behavior/	53151
7	(psychotherap* or (behavior* adj2 therap*) or (behaviour* adj2 therap*) or cognitive therap* or psychological intervention* or psychological adaptation or systematic desensitiz* or systematic desensitis*).ti,ab.	83209

8	(Cognitive problem-solving skills training or characteranalyti* or character-analyti* or client-centered or client-centred or coherence therap* or contemplative therap* or conversational therap*).ti,ab.	1661
9	exp Problem Solving/	32957
10	(problem-solving adj2 training).ti,ab.	436
11	((coping or cope or copes or coped) adj2 (skill* or behavior* or behaviours or train*)).ti,ab.	6142
12	(core energetic* or core process*).ti,ab.	549
13	(dialectical behavio?r therap* or DBT).ti,ab.	2689
14	(dreamwork or dyadic or DDP).ti,ab.	8407
15	(expressive therap* or desensiti* reprocessing or desensiti* re-processing or emotional freedom techni* or EFT or encounter group* or experient* dynamic or existential therap* or exposure response prevent* therap* or (eye movement desensitization adj2 reprocessing) or EMDR).ti,ab.	1858
16	(goal setting or gestalt* or group analy* or Milieu therap* or milieutherap* or group-based therap* or group-based treatment* or group-based intervention).ti,ab.	15555
17	(hakomi or holistic or holotropic or humanistic or human givens or hypnos* or hypnot* or hypno-therap*).ti,ab.	47083
18	(interaction therap* or interperson* therap* or inter-personal therap* or IPT).ti,ab.	2823
19	(meditati* or mindfulness* or MBSR or morita therap*).ti,ab.	9083
20	Alternative medicine/	43480
21	(body mind or mind-body therap* or Radix therap* or pulsing or body-oriented psychotherap* or IBP or postural integration or integrative body psychotherap* or Pesso Boyden system psychomotor or lifespan Integration or Rubenfeld synergy or Reichian).ti,ab.	4745
22	(multimodal* therap* or multi-modal* therap* or multi-theoreti* or multitheoreti*).ti,ab.	6463
23	(relaxation therapy or tai ji or therapeutic touch or yoga).ti,ab.	5559
24	(object* relation* or objectrelation*).ti,ab.	2470
25	Kinesiotherapy/	28294
26	Psychophysiology/	19708
27	Meditation/	6075
28	(family constellation* or family therapy or family coping or family coping impairment or (family inventory adj (life events or changes)) or compromised family coping or parent education or (ineffective management adj3 therapeutic families regimen) or family support or family involvement or family coping inventory or family centered care or family care or altered family coping or critical care family needs inventory or psychoeducation or (adolescent coping orientation adj2 problem experiences) or feminist therap* or functional analytic or Freudian or family-based intervention* or internal family systems model or parent-child interact* or parent-training program* or peer support group*).ti,ab.	21749
29	(psychoanaly* or psycho-analyti* or psychodynamic or psycho-dynamic).ti,ab.	25218
30	Counseling/	74219
31	(counsel?ing or directive counsel?ing or motivational interviewing or distance counsel?ing or (pastoral adj (care or counsel* or therap*))).ti,ab.	104544
32	reality therap*.ti,ab.	136
33	(rebirthing or re-birthing or relationship counsel* or reprogram* or re-	22365

	program* or breathwork).ti,ab.	
34	(rational emoti* or Reiki or REBT or rational living therap* or RLT or sensorimotor psychotherap*).ti,ab.	864
35	Acupuncture/	36872
36	acupuncture.ti,ab.	25964
37	Self Care/	45720
38	(self care or self help or self relationship or sponsorship or self-manag* or selfmanag* or self-talk).ti,ab.	43956
39	(SHEN or social support* or social therap* or social care or social problem skills train* or psychoeducation or psychology social or social support).ti,ab.	45847
40	(spiritual therap* or prayer or holistic care or Sophia-analys).ti,ab.	3475
41	(thought field therap* or transactional* or trans-actional* or transperson* or trans-person* or twelve-step program* or vegetotherap* or vegeto-therap*).ti,ab.	2412
42	(relational-cultural or MCT or (multicultural adj (counsel?ing or therapy))).ti,ab.	7050
43	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42	782271
44	exp digestive system disease/	2730701
45	(digestive system diseases or biliary tract diseases or digestive system abnormalities or digestive system fistul* or gastrointestinal diseases or oesophag* diseases or esophag* diseases or oesophagit* or esophagit* or gastrit* or enterit* or gastroenterit* or intestinal diseases or colit* or enterocolit* or proctit* or proctocolit* or rectal diseases or IBD or inflammatory bowel diseases or Crohn disease or ulcerative colit* or diverticul* or achalasia cardiae or megaesophagus or megaoesophagus or achlorhydria or Barrett esophagus or Barrett oesophagus or deglutition disorder* or duodenogastric reflux or eructation or esophag* fistul* or esophag* motility disorder* or oesophag* motility disorder* or oesophag* diverticul* or oesophag* fistula or esophageal achalasia or oesophageal achalasia or gastric dilatation or reflux esophagitis or reflux oesophagitis or gastroesophag* reflux or gastro-esophageal reflux disease or gastro-oesophageal reflux disease or gastropares* or liver diseases or pancreatic diseases or postgastrectomy syndrom* or stomach diseases or stomach diverticul* or Zollinger-Ellison syndrome).ti,ab.	300016
46	(gastrit* adj2 (chronic superficial or chronic atrophic or atrophy or unspecified or antral or fundal or Helicobacter pylori associated or giant hypertrophic or granulomatous or alcoholic)).ti,ab.	3584
47	gastroptosis.ti,ab.	41
48	(ulcer adj2 (peptic or duodenal or gastroduodenal or gastrojejunal or gastrocolic or gastrointestinal or jejunal or marginal or intestine or anus or rectum or gastric or stomach or pylorus or esophagus or oesophagus)).ti,ab.	49504
49	pylorospasm.ti,ab.	116
50	(hourglass contraction adj stomach).ti,ab.	0
51	hemorrhoid*.ti,ab.	5236
52	proctalgia fugax.ti,ab.	151
53	(psychogenic adj2 (diarrhoea or dyspepsia or intestinal disorders)).ti,ab.	1
54	(neurogenic bowel or neurogenic bowel dysfunction).ti,ab.	342

55	(liver diseases or liver cirrhosis or (drug-induced liver injury adj chronic) or fatty liver or liver failure or hepatitis chronic or liver cirrhosis or ((liver diseases or fatty liver or liver cirrhosis or hepatitis) adj2 alcoholic)).ti,ab.	107715
56	((chronic or alcoholic) adj pancreatitis).ti,ab.	19440
57	(cholangitis or cholestasis or gallbladder diseases or postcholecystectomy syndrome).ti,ab.	34632
58	pancreatic steatorrhoea.ti,ab.	39
59	postcholecystectomy syndrome.ti,ab.	318
60	(spasm adj2 (sphincter adj3 Oddi)).ti,ab.	34
61	(gallstone adj2 (disease or pancreatitis)).ti,ab.	3981
62	(fistula adj2 ((rectum adj skin) or anal or rectal or anorectal or stomach or duodenum or gastrocolic or gastrojejunocolic)).ti,ab.	2502
63	enteroptosis.ti,ab.	7
64	(dyspepsia adj2 (nervous or neurotic or psychogenic or heartburn)).ti,ab.	182
65	((dyskinesia adj esophagus) or (dyskinesia adj oesophagus) or corkscrew esophagus or corkscrew oesophagus or diffuse esophageal spasm or diffuse oesophageal spasm or (spasm adj esophagus) or (spasm adj oesophagus)).ti,ab.	605
66	(allergic adj2 (gastroenteritis or colitis)).ti,ab.	197
67	(functional gastrointestinal disorder* or FGID*).ti,ab.	2672
68	irritable bowel syndrome.ti,ab.	15988
69	44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56 or 57 or 58 or 59 or 60 or 61 or 62 or 63 or 64 or 65 or 66 or 67 or 68	2779657
70	Mass communication/	13441
71	Reminder System/	2198
72	Text messaging/	2652
73	Computer network/	13511
74	Telehealth/	4063
75	Telecommunication/	31736
76	Internet/	96675
77	(online or on-line or internet or telemedicine or telecommunication or computeri?ed or computer-assisted or (computer adj2 assisted)).ti,ab.	282240
78	website*.ti,ab.	25402
79	(e-health or ehealth).ti,ab.	3168
80	(etherap* or e-therapy).ti,ab.	429
81	(electronic mail or electronic-mail or text messag*).ti,ab.	3568
82	70 or 71 or 72 or 73 or 74 or 75 or 76 or 77 or 78 or 79 or 80 or 81	398934
83	43 and 69 and 82	1206

Appendix 9 Excluded studies

1	2011	Online behavioural therapy may help some IBS patients	http://www.magonlinelibrary.com/doi/pdf/10.12968/gasn.2011.9.5.8a	Summary of the other study, which is already included in the review
2	(Cross and	Integration of Telemedicine Into Clinical Gastroenterology and	http://www.sciencedirect.com/science/	ISD

	Kane, 2017)	Hepatology Practice	article/pii/S1542356516306681	
3	(Dorn, 2015)	Development and pilot testing of an integrated, web-based self-management program for irritable bowel syndrome (IBS)	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5317252/	ISD
4	(Everitt et al., 2015)	Assessing Cognitive behavioural Therapy in Irritable Bowel (ACTIB): protocol for a randomised controlled trial of clinical-effectiveness and cost-effectiveness of therapist delivered cognitive behavioural therapy and web-based self-management in irritable bowel syndrome in adults	http://bmjopen.bmj.com/content/bmjopen/5/7/e008622.full.pdf	Protocol of the trial
5	(Hommel, 2015)	The Telehealth Enhancement of Adherence to Medication (TEAM) in pediatric IBD trial: Design and methodology	http://www.sciencedirect.com/science/article/pii/S1551714415300094	Protocol of the trial
6	(Krier, 2011)	Potential use of telemedicine to provide outpatient care for inflammatory bowel disease	http://www.nature.com/ajg/journal/v106/n12/full/ajg2011329a.html	II
7	(Ljotsson et al., 2011c)	Long-term follow-up of internet-delivered exposure and mindfulness based treatment for irritable bowel syndrome	http://www.sciencedirect.com/science/article/pii/S0005796710002238	Inappropriate comparator (IC) crossover trials, control group had online CBT intervention after post treatment assessment.
8	(Ljotsson et al., 2013a)	Prediction of symptomatic improvement after exposure-based treatment for irritable bowel syndrome	http://bmcgastroenterol.biomedcentral.com/articles/10.1186/1471-230X-13-160	Assessed predictors of treatment outcome in 2 other studies, already included
9	(Ljotsson et al., 2013b)	Mechanisms of change in an exposure-based treatment for irritable bowel syndrome	https://www.ncbi.nlm.nih.gov/pubmed/23750460	Identifying mediators of already included study
10	(Ljotsson et al., 2014)	Provoking symptoms to relieve symptoms: a randomized controlled dismantling study of exposure therapy in irritable bowel syndrome	http://www.sciencedirect.com/science/article/pii/S000579671400014X	Inappropriate comparator (IC) Both arms included online delivered CBT (ICBT and without systematic exposure CBT (ICBT-WE))
11	(Silberbogen, 2012)	A telehealth intervention for veterans on antiviral treatment for the hepatitis C virus	https://www.ncbi.nlm.nih.gov/pubmed/22662730	II (participants received the brief telephone intervention, not online)

Appendix 10 PRISMA Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	
Risk of bias in individual studies	12	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.	
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	
Synthesis of results	14	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.	

Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	

Appendix 11 Topic guide for the focus group

Agenda and discussion topics for the focus group

Duration of the session - 90 minutes

Timetable

1) *0-5 minutes: Seating positions and informed consent checks*
2) *5-10 minutes: Introduction points*
3) *10-40 minutes: Session one - Reviewing management of comorbid IBD and impact of IBD on wellbeing, quality of life*

4) *40-50 minutes: break for refreshments*
5) *50-80 minutes: Session two - Reviewing CBT role in management of IBD alongside depression and/or anxiety and exploring attitudes towards proposed online programme*
6) *80-90 minutes: Summarise session and thank participants*

1. Seating positions and informed consent checks
2. Introduction points

- Introduce the research and thanks for taking part
- Remind the group that participation is voluntary and that they are free to leave at any time
- Talk about the purpose of the focus group and how the information will be used
- Set the ground rules for the group (only one person speaks at a time; give everyone equal chance to participate in the discussion; respect the opinions of others; do not put down or criticise others' comments; have the right to disagree during the discussion, respect the privacy of others in the group by not repeating what is discussed outside of the focus group)
- Introduce the structure of the session
- Introduce the discussion topics
- Any questions?

3. Session one - Reviewing management of comorbid IBD

- Discuss the impact of IBD on QoL and wellbeing in general. Discuss that if wellbeing is affected for a long time, anxiety and depression may develop. Discuss challenges in managing IBD alongside depression and/or anxiety; how mental disorders impacts on IBD and IBD impacts on mental health?
- Discuss who should have responsibility for the management of IBD in people with depression and/or anxiety (gastroenterologists, nurses, psychologists or patients should play a role in managing IBD alongside a mental disorder themselves?). Discuss the patient's ability and wish to take control of their own treatment.
- Discuss medical, nursing or other care patients currently receive for their mental health (e.g. GP, mental health nurse, psychologist, and family, voluntary organisations, paid care) and which help was the most useful for management of IBD.

4. Break
5. Session two - Reviewing PIs role in the management of IBD alongside depression and/or anxiety and exploring attitudes towards proposed online programme

- Discuss the role of talk therapy in managing IBD (a short explanation will be provided of what talk or talking or psychotherapy is). Discuss what is the role of talk therapy in IBD treatment and how could talk therapy help manage IBD and how it is relevant to them.

- Discuss what experience of using internet or mobile apps for IBD management or for mental health the patients have and their thoughts and feeling about the online talk therapy programme.
- Discuss what should be included in this online programme; the lengths and how many of online session should be; should it be self-directed or delivered with their doctor/nurse/other health professionals assistance; how user-friendly with regards to the content and format this programme is (format, colour, language, lay out; ease of use) and how this programme can be improved (i.e., should be added more videos, if so what length 5 -10 min, less text, more bullet points text). (Prior the focus group the participants will receive the link to the already developed online PI in Australia, as an example: http://www.tameyourgut.com/. This will be modified and adapted to the UK environment and participants need in the future feasibility trial).
- Discuss their expectation from this programme (what outcomes they expect to change and what they would like to change); the reasons for using or not using this programme; their confidence that they will comply with and complete the online therapy; what will encourage patients to complete this programme?
- Ask if there is anything else they would like to share that we haven't discussed.

6. Close session

Appendix 12 Topic guide for the interview with health professionals

1. Background information, role

For gastroenterologist

- Can you describe the role you play in supporting patients with IBD?
- At what point do you tend to become involved in supporting patients with their IBD? (E.g. diagnosis, management, complications).
- Are you involved in signposting patients, or referring them to other services for their IBD or mental health? If so, can you tell me about this?
- If you noticed that an IBD patient suffers from anxiety and/or depression would you refer him/her to a mental health specialist or would you deal with this yourself? If yourself, how would you approach that?
- What do patients think when you suggest referring them for psychological intervention?

For psychologists

- Can you describe the role you play in supporting patients with IBD to manage their mental health?
- At what point do you tend to become involved in supporting patients with their mental health? (E.g. diagnosis, management, complications).
- How patients accept their mental health disorder diagnosis?
- Are you involved in signposting patients, or referring them to other services for their mental health? If so, can you tell me about this?

For nurses

- Can you describe the role you play in supporting patients with IBD?

- At what point do you tend to become involved in supporting patients with their IBD? (E.g. diagnosis, management, complications).
- What do patients think when you suggest referring them for psychological intervention?

2. IBD management

- What do you think are the challenges to managing IBD with comorbid depression and/or anxiety? (Prompts – motivation, adherence, lack of psychological help).
- How many practitioners should care for people with IBD and mental health disorder comorbidity? Is this right?
- Do you think that patients have been helped by referral on to psychological services?
- How do you think a mental disorder impacts on IBD?
- Do you think that a mental health disorder impacts of a patient's ability to manage their IBD?
- How do you think IBD impacts on mental health?
- Do you think that IBD impacts on a patient's ability to manage their mental health?

2. Psychological interventions and mode of delivery

For gastroenterologist and nurses

- Can you tell me, please, what is a talk therapy or psychotherapy? (Short explanation will be provided if a person has different understanding or does not know the meaning).
- What is your experience of using internet or mobile apps for IBD management or for mental health? Explore attitudes and views on this.
- How likely do you think IBD patients would agree to be involved in self-directed online programme?
- How confident are you that IBD patients will comply with and complete the online programme?
- How many sessions and of what duration should be included in an online psychotherapy programme?
- Why would IBD patients use or not use this programme?
- What will encourage patients to complete this programme?
- What are your thoughts on providing exclusively online programme as compared to clinician-assisted programme?

For psychologists

- What is the role of psychotherapy or talk therapy in IBD management?
- What is your experience of using internet or mobile apps for mental health management? Explore attitudes and views on this.
- How confident are you that IBD patients will comply with and complete the online therapy?
- How many sessions and of what duration should be included in an online psychotherapy programme?
- Why would IBD patients use or not use this programme?
- What will encourage patients to complete this programme?
- What are your thoughts on providing exclusively online psychotherapy as compared to clinician or therapist-assisted psychotherapy?

3. Improving online psychological intervention programme

- How user-friendly with regards to the content and format this programme is? What do you think should be included? (Prior the interview the participants will receive the link to the already developed online psychological intervention in Australia, as an example: http://www.tameyourgut.com/, which will be modified and adapted to the UK environment and participants need in the future feasibility trial).
- How this programme can be improved? (Prompts –format, colour, language, and lay out, more information presented in short videos, rather than text, how many minutes maximum video should be to not lose patients interest).
- Is there anything else you would like to share that we haven’t asked about?

Appendix 13 Concept map on patients' with IBD and anxiety and/or depression lived experiences

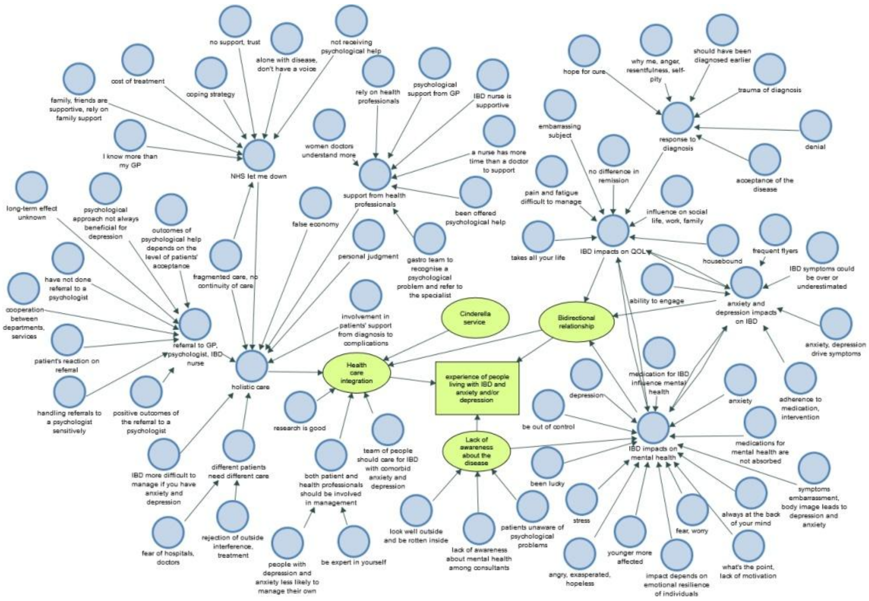


Figure 28 Concept map on patients with IBD and comorbid anxiety and/or depression lived experiences

Appendix 14 Concept map on patients' and health professionals' view about patients' participation in the online psychological intervention

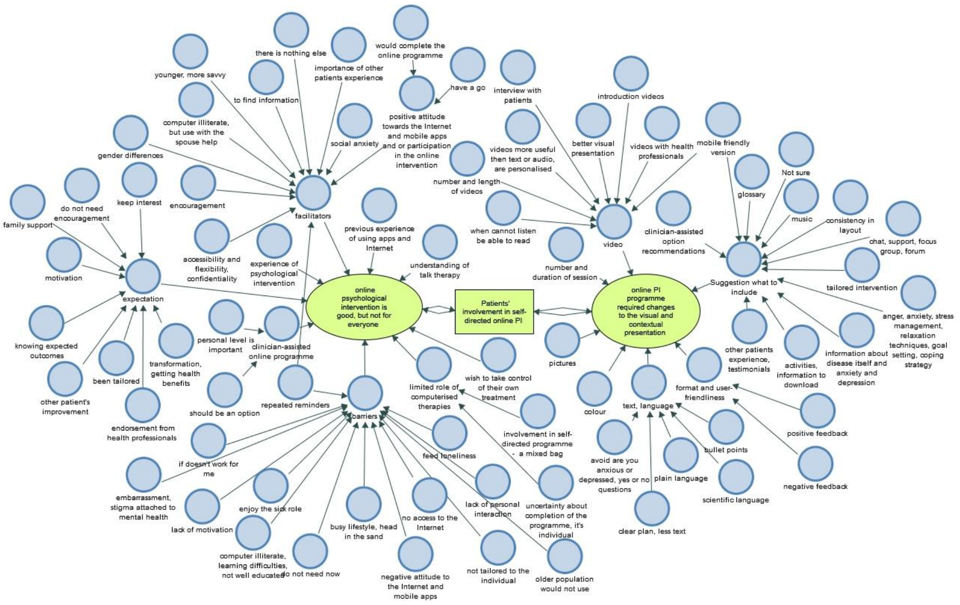


Figure 29 Concept map on patients' and health professionals' view about patients' participation in the online psychological intervention

Appendix 15 The invitation letter

Dear (name of the participant),

Welcome to your online psychological intervention programme.

During this programme, you can learn how to improve your mood, reduce stress and anxiety and thus a quality of life with the help of this short (8 weeks) online psychological intervention programme. Each week in the programme includes 2 to 3 sessions, approximately one hour length. The programme includes videos, text materials and activities for you learning a specific skill to enable you to control and improve your mood and anxiety.

You will learn to:

- ✓ *understand psychological interventions and learn specific skills for managing anxiety and low mood*
- ✓ *learn how to use this knowledge in your own everyday lives to relieve the burden of negative emotions and IBD.*

After the completion of this programme you will have unlimited access to it, so it can be used when you need it.

Your link to access the course is below, but before you get started we have some important summary information and tips to share.

Programme length

CBT for IBD people with anxiety/depression online programme will run for eight weeks. Each week, a new materials for that week's will be released. At the end of the eight weeks you will be able to go back to all of the course materials for unlimited time.

Session lengths

We encourage you to dedicate at least 1 hour per week for the programme. The interactive forum will be available for you all the time through with the other IBD patients who have similar symptoms and you will be able to sent a questions to the clinician. However, you might not get the response straight away, such as the member of our team will review questions on a weekly bases. If you have an urgent question contact your IBD nurse or GP.

Get started

Select one of the links below to start your course:

I already have an online psychological programme account

I have an account, but forgot my password

I'm new -create an account

We hope you enjoy and your programme will be useful!

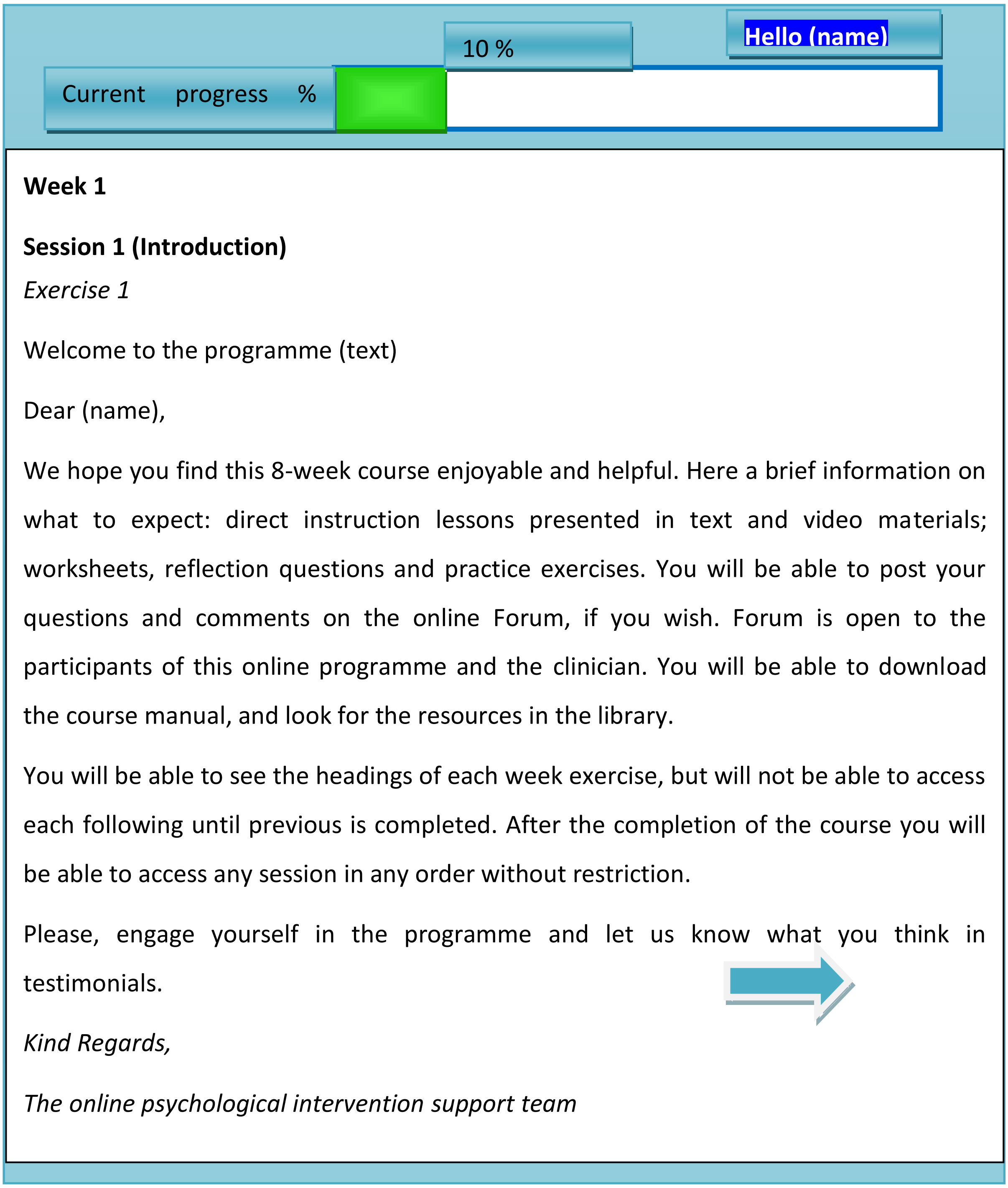
Kind Regards,

The online psychological intervention support team

Appendix 16 The repeated reminder letter

***Dear (name of the participant)**,*
*Welcome to **Week** (week number) of your online psychological intervention programme.*
Your personal link to access the programme is below. Here the summary of what will be covered this week.
This Week 1** - **Introduction to the programme
Overview of the whole programme
Goal setting
Psychological help for IBD
Recognising stress and symptom and dealing with stress
Get started
Select one of the links below to start your course.
link to the programme:
I already have an online psychological programme account
I have an account, but forgot my password
I'm new -create an account
We hope you enjoy your programme!
Kind Regards,
The online psychological intervention support team

Appendix 17 Example of personalisation on the screen and communication



Week 1

Session 1 (Introduction)

Exercise 1

Welcome to the programme (text)

Dear (name),

We hope you find this 8-week course enjoyable and helpful. Here a brief information on what to expect: direct instruction lessons presented in text and video materials; worksheets, reflection questions and practice exercises. You will be able to post your questions and comments on the online Forum, if you wish. Forum is open to the participants of this online programme and the clinician. You will be able to download the course manual, and look for the resources in the library.

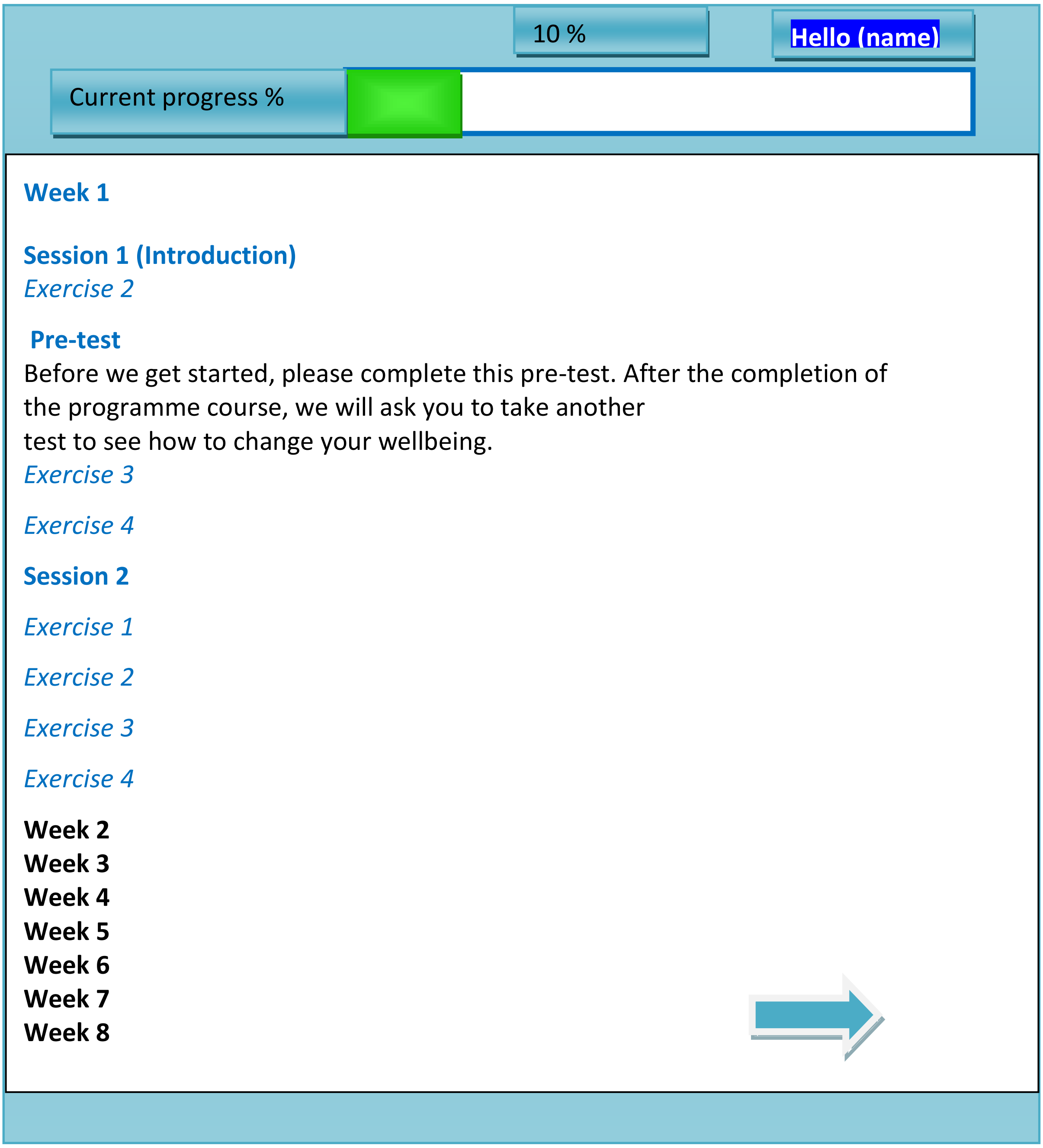
You will be able to see the headings of each week exercise, but will not be able to access each following until previous is completed. After the completion of the course you will be able to access any session in any order without restriction.

Please, engage yourself in the programme and let us know what you think in testimonials.

Kind Regards,

The online psychological intervention support team

Appendix 18 Example of consistency of appearance of the screen



Week 1

Session 1 (Introduction)
Exercise 2

Pre-test
Before we get started, please complete this pre-test. After the completion of the programme course, we will ask you to take another test to see how to change your wellbeing.
Exercise 3

Exercise 4

Session 2

Exercise 1

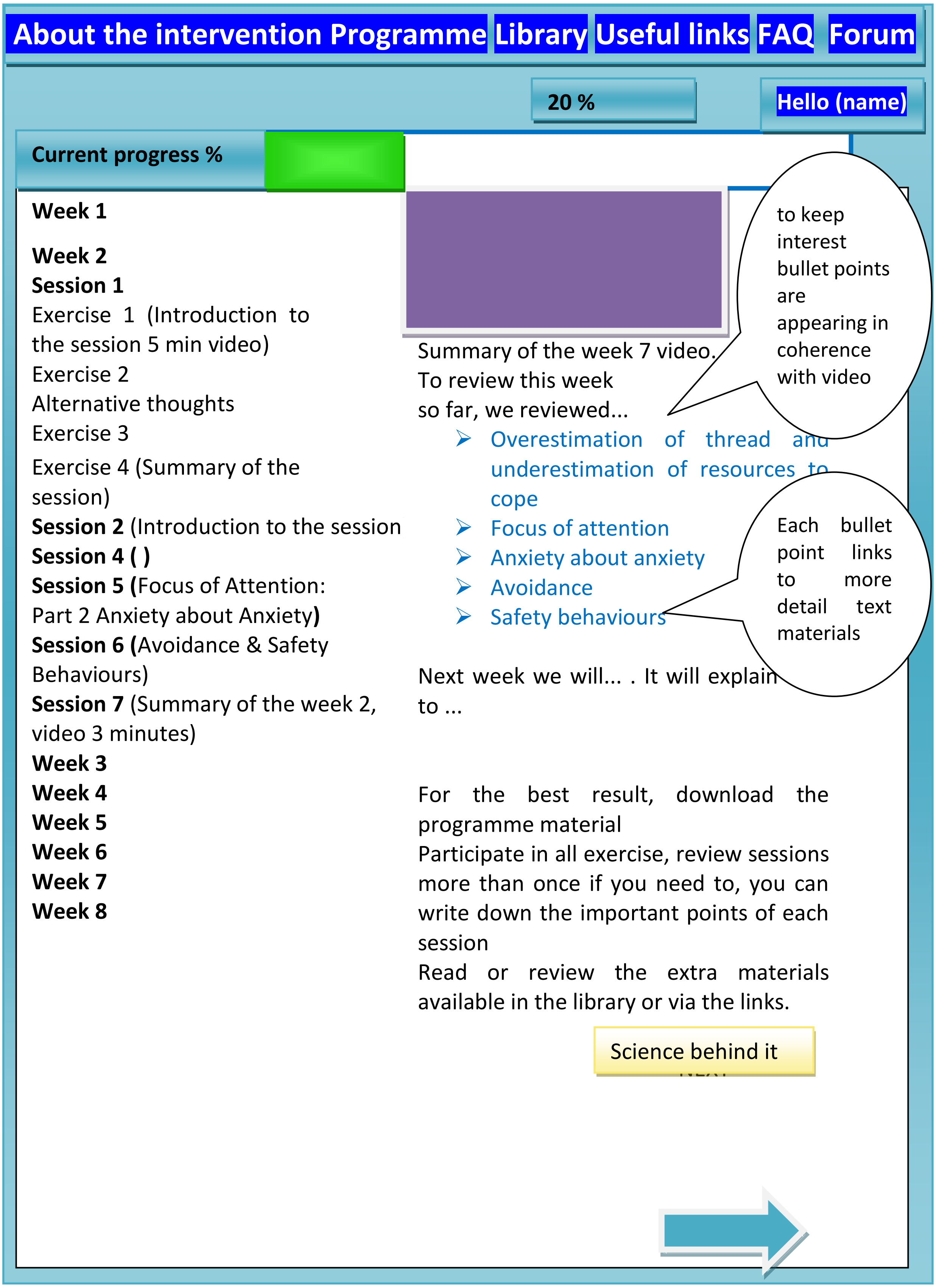
Exercise 2

Exercise 3

Exercise 4

Week 2
Week 3
Week 4
Week 5
Week 6
Week 7
Week 8

Appendix 19 Example of consistency of appearance of the screen and presentation of text in bullet points



About the intervention Programme | Library | Useful links | FAQ | Forum

20 %

Hello (name)

Current progress %

Week 1

Week 2
Session 1
Exercise 1 (Introduction to the session 5 min video)
Exercise 2
Alternative thoughts
Exercise 3
Exercise 4 (Summary of the session)
Session 2 (Introduction to the session
Session 4 ( )
Session 5 (Focus of Attention: Part 2 Anxiety about Anxiety**)**
Session 6 (Avoidance & Safety Behaviours)
Session 7 (Summary of the week 2, video 3 minutes)
Week 3
Week 4
Week 5
Week 6
Week 7
Week 8

Summary of the week 7 video.
To review this week so far, we reviewed...

- Overestimation of thread and underestimation of resources to cope
- Focus of attention
- Anxiety about anxiety
- Avoidance
- Safety behaviours

Next week we will... . It will explain to ...

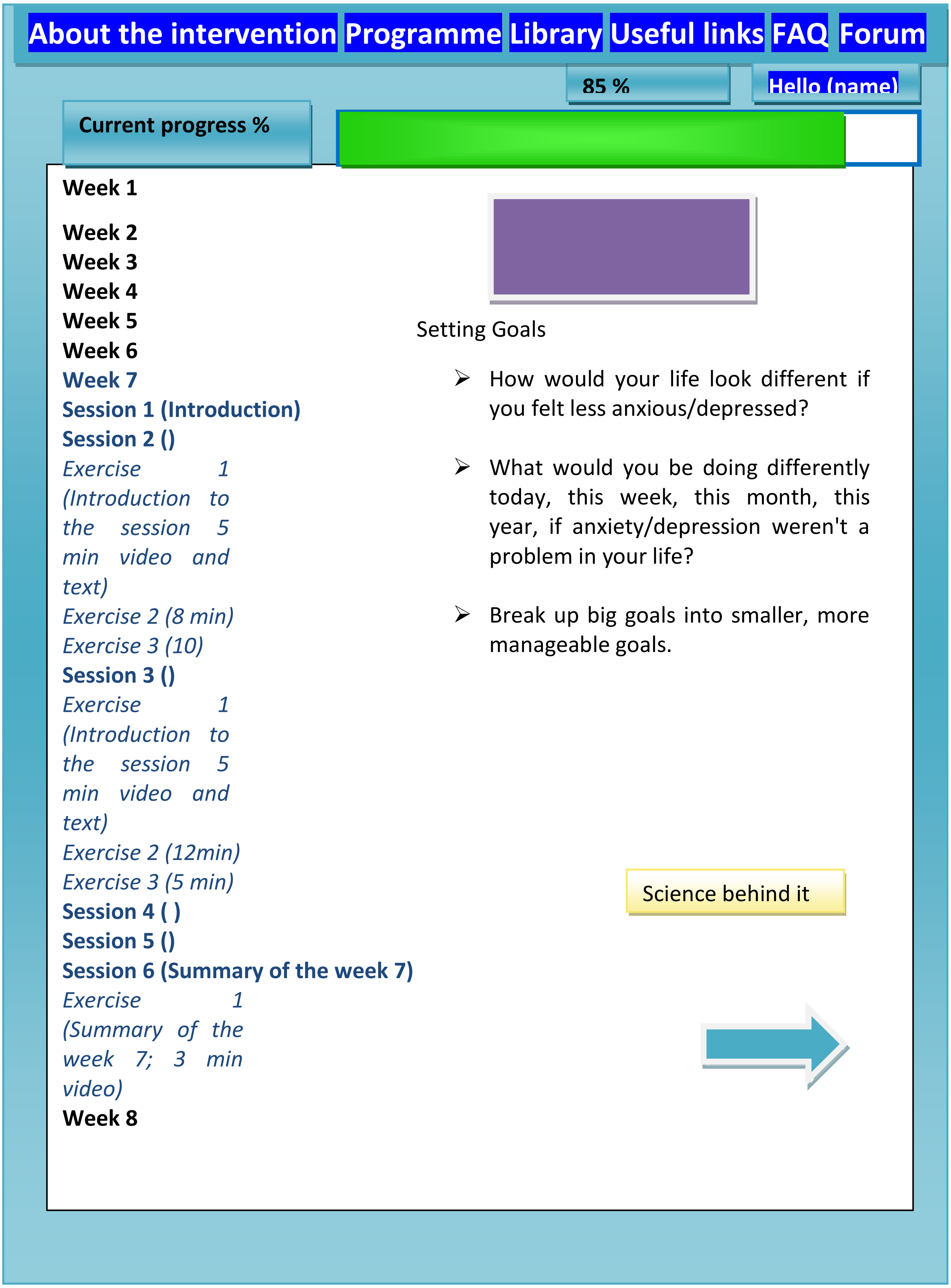
For the best result, download the programme material
Participate in all exercise, review sessions more than once if you need to, you can write down the important points of each session
Read or review the extra materials available in the library or via the links.

Science behind it

to keep interest bullet points are appearing in coherence with video

Each bullet point links to more detail text materials

Appendix 20 Example of consistency of appearance of the screen and presentation of text in bullet points



Week 1

Week 2
Week 3
Week 4
Week 5
Week 6
Week 7
Session 1 (Introduction)
Session 2 ()
Exercise 1 (Introduction to the session 5 min video and text)
Exercise 2 (8 min)
Exercise 3 (10)
Session 3 ()
Exercise 1 (Introduction to the session 5 min video and text)
Exercise 2 (12min)
Exercise 3 (5 min)
Session 4 ( )
Session 5 ()
Session 6 (Summary of the week 7)
Exercise 1 (Summary of the week 7; 3 min video)
Week 8

Setting Goals

- How would your life look different if you felt less anxious/depressed?
- What would you be doing differently today, this week, this month, this year, if anxiety/depression weren't a problem in your life?
- Break up big goals into smaller, more manageable goals.

Appendix 21 Patients' and health professionals' views about online psychological interventions (PI) for inflammatory bowel disease (IBD) codebook

Themes	Primary codes	Secondary codes	Tertiary codes	Files	References
Experience of living with IBD and comorbid anxiety and/or depression					
Bidirectional relationship				20	46
	anxiety and depression impacts on IBD			4	6
		ability to engage		7	10
		adherence to medication, intervention		7	10
		anxiety, depression drive symptoms		7	16
		frequent flyers		1	1
		IBD symptoms could be over or underestimating		2	2
		QOL		5	5
	IBD impacts on mental health			5	7
		always at the back of your mind		4	7
		angry, exasperated, hopeless		2	2
		anxiety		16	40
		be out of control		4	7

Themes	Primary codes	Secondary codes	Tertiary codes	Files	References
		been lucky		4	5
		depression		18	44
		fear, worry		10	17
		impact depends on emotional resilience of individual		9	14
		medication for IBD influence mental health		2	3
		medications for mental health are not absorbing		1	1
		stress		7	13
		symptoms embarrassment, body image leads to depression and anxiety		5	10
		what's the point, lack of motivation		6	10
		younger more affected		2	2
	IBD impacts on QOL			8	11
		embarrassing subject		7	11

Themes	Primary codes	Secondary codes	Tertiary codes	Files	References
		housebound		6	13
		influence on social life, work, family		9	18
		no difference in remission		4	7
		pain and fatigues difficult to manage		5	14
		response to diagnose		0	0
			acceptance of the disease	4	9
			denial	3	4
			hope for cure	2	2
			should have been diagnosed earlier	1	1
			trauma of diagnosis	3	3
			why me, anger, resentfulness, self-pity	2	3
		takes all your life		10	13
Health care integration					
	both patient			10	18

Themes	Primary codes	Secondary codes	Tertiary codes	Files	References
needed	and health professionals should be involved in management	be expert in yourself		5	8
		people with depression and anxiety less likely to manage their own		5	6
	Cinderella services			18	40
	holistic care	different patients need different care		2	2
		fear of hospitals, doctors		5	7
		rejection of outside interference, treatment		2	2
		false economy		2	4
		IBD more difficult to manage if you have anxiety and depression		6	7
		involvement in patients' support from diagnose to complications		5	6

Themes	Primary codes	Secondary codes	Tertiary codes	Files	References
		different patients need different care		12	19
		NHS let me down			
			alone with disease, don't have a voice	7	14
			coping strategy	14	21
			cost of treatment	2	2
			family, friends are supportive, rely on family support	9	26
			fragmented care, no continuity of care	7	12
			I know more than GP	2	2
			no support, trust	5	9
			not receiving psychological help	11	21
		personal judgment		9	16

Themes	Primary codes	Secondary codes	Tertiary codes	Files	References
		referral to GP, psychologist, IBD nurse		10	21
			cooperation between departments, services	8	13
			handling referral to psychologist sensitively	3	3
			haven't not done referral to psychologist	1	2
			long-term effect unknown	1	2
			outcomes of psychological help depends on the level of patients' acceptance	1	1
			patients' reaction on referral	10	13
			positive outcomes of referral to psychologist	11	14

Themes	Primary codes	Secondary codes	Tertiary codes	Files	References
			psychological approach not always beneficial for depression	1	1
		support from health professionals		1	1
			been offered psychological help	3	7
			gastro team to recognise psychological problem and refer to the specialist	6	16
			IBD nurse is supportive	6	11
			nurse has more time than doctor to support	2	2
			psychological support from GP	2	2
			rely on health professionals	2	3
			women doctors	1	1

Themes	Primary codes	Secondary codes	Tertiary codes	Files	References
			understand more		
	research is good		been offered psychological help	2	3
	team of people should care for IBD with comorbid anxiety and depression			12	14
Lack of awareness about the disease				1	1
	lack of awareness about mental health issue among consultants			3	3
	look well outside and be rotten inside			4	6
	patients unaware of psychological problem			5	7

Themes	Primary codes	Secondary codes	Tertiary codes	Files	References
Online psychological intervention is good, but not for everyone					
	barriers				
		busy lifestyle, head in the sand		3	4
		computer illiterate, learning difficulties, not well educated		8	15
		do not need now		3	4
		embarrassment, stigma attached to mental health		3	3
		enjoy the sick role		1	1
		feed loneliness		1	3
		if doesn't work for me		2	2
		lack of motivation		4	5
		negative attitude to the Internet and mobile apps		3	11
		no access to the Internet		1	1
		not tailored to the individual		2	4

Themes	Primary codes	Secondary codes	Tertiary codes	Files	References
		older population would not use		5	7
		personal interaction is important		8	8
	clinician-assisted online programme				
		personal level is important		22	70
		should be an option		11	14
	expectation				
		accepting the condition		1	1
		have information, reassurance		4	7
		have positive outlook, QOL		5	7
		help flares through management of stress		1	1
		manage anxiety and stress		6	10
	experience of psychological intervention			8	22

Themes	Primary codes	Secondary codes	Tertiary codes	Files	References
	facilitators				
		accessibility and flexibility, confidentiality		14	26
		computer illiterate, but use with the spouse help		1	1
		encouragement		0	0
			been tailored	2	3
			do not need encouragement	1	1
			endorsement from health professionals	17	32
			family support	2	2
			keep interest	2	3
			knowing expected outcomes	4	4
			motivation	6	10
			other patient's improvement	8	19
			repeated reminders	5	7

Themes	Primary codes	Secondary codes	Tertiary codes	Files	References
			transformation, getting health benefits	14	28
		gender differences		2	2
		importance of other patients experience		2	5
		positive attitude towards the Internet and mobile apps and or participation in the online intervention		11	26
			have a go	5	6
			would complete the online programme	11	19
		social anxiety		1	1
		there is nothing else		4	5
		to find information		1	1
		younger, more savvy		3	3

Themes	**Primary codes**	**Secondary codes**	**Tertiary codes**	**Files**	**References**
	limited role of computerised therapies			4	6
		involvement in self-directed programme - a mixed bag		10	13
		uncertainty about completion of the programme, it's individual		11	15
	previous experience of using apps and Internet			21	40
	understanding of talk therapy			23	36
	wish to take control of their own treatment			9	15
To facilitate, existing online PI programme required changes to the visual					
	colour			19	22
	format and user-friendliness			0	0
		negative feedback		1	1
		positive feedback		20	50

Themes	Primary codes	Secondary codes	Tertiary codes	Files	References
and contextual presentation	number and duration of session			24	69
	pictures			6	10
	Suggestion what to include				
		activities, information to download		2	2
		anger, anxiety, stress management, relaxation techniques, goal setting, coping strategy		9	20
		chat, support, focus group, forum		5	17
		clinician-assisted option recommendations		3	3
		consistency in layout		1	2
		glossary		1	1
		information about disease		7	15

Themes	Primary codes	Secondary codes	Tertiary codes	Files	References
		itself and anxiety and depression			
		mobile friendly version		2	2
		music		1	1
		Not sure		5	6
		other patients experience, testimonials		6	14
		tailored intervention		7	18
	text, language				
		avoid are you anxious or depressed, yes or no questions		2	3
		bullet points		15	21
		clear plan, less text		5	12
		plain language		15	17
		scientific language		2	5
	video				
		better visual presentation		1	2
		interview with		10	13

Themes	Primary codes	Secondary codes	Tertiary codes	Files	References
		patients			
		introduction videos		7	14
		mobile friendly		1	1
		number and length of videos		24	53
		videos more useful then text or audio, are personalised		9	14
		videos with health professionals		5	6
		when cannot listen be able to read		11	15

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