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# Exploration of the impact of Inflammatory Bowel Disease fatigue on the Health-Related Quality of life of adults.

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## Abstract

**Background:** Fatigue is a frequently reported symptom of Inflammatory Bowel Disease (IBD), experienced by patients with active disease and when in remission. Fatigue related to chronic conditions plays a significant negative role in health-related quality of life (HRQoL), but patients' experience of this have not been researched in IBD.

**Aim:** To explore patient experience of IBD fatigue and its impact on HRQoL in adults diagnosed with IBD.

**Methods:** A systematic literature was undertaken to explore the impact of IBD fatigue on HRQoL in adults. Search terms were developed and combined encompassing concepts of 'Fatigue', 'IBD and 'HRQoL'. A narrative synthesis was conducted.

To explore patient experiences of the impact of IBD fatigue on HRQoL, qualitative, semi-structured in-depth interviews were conducted with adults with Crohn's Disease in remission, recruited from out-patient clinics in the UK. Eligibility and medical history were confirmed at recruitment. Interviews were audio-recorded and transcribed verbatim. Thematic analysis was employed to analyse data using NVivo 12 software.

**Results:** Eleven publications were deemed eligible for inclusion in the systematic literature review. Studies revealed experience of fatigue was

significantly related to three HRQoL areas; symptom acceptance, psychosocial factors and physical activity.

Interviews of 14 adults with IBD fatigue revealed that there were three key themes that reflect the patient experience:

I. 'The new normal' established through adaptation to, and acceptance of, IBD fatigue impact on daily life.
II. 'Energy as a resource' describes participants attempts to better manage fatigue through planning and prioritising tasks.
III. 'Keeping healthy' encompasses participants beliefs that good nutrition, good general health and keeping active permit them to better manage fatigue.

**Conclusion:** Adults with IBD fatigue try to establish a sense of 'new' normality. However, this is often at the expense leisure activities. The study also indicates that conservation of energy through planning and prioritising tasks and high levels of social support were associated with better self-reported HRQoL. Further research is required to explore physical activity-based intervention in relation to IBD fatigue.

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## Abbreviations

| | |
|---|---|
| **5-ASA** | Aminosalicylic acid. |
| **ADL** | Activities of daily living. |
| **Anti-TNF-α** | Anti-Tumour Necrosing factor-Alpha. |
| **AZA** | Azathioprine. |
| **BRC** | Biomedical Research Centre. |
| **CASP** | Critical Appraisal Skills Programme. |
| **CBT** | Cognitive behavioural therapy. |
| **CD** | Crohn's disease. |
| **CFS** | Chronic Fatigue Syndrome. |
| **CR** | Critical Realism. |
| **CRP** | C-reactive protein. |
| **DA** | Thematic Discourse Analysis. |
| **EuroQoL** | Euro Quality of Life. |
| **FACIT-F** | Functional assessment of chronic illness therapy-Fatigue. |
| **FIS** | Fatigue Impact scale. |
| **FMT** | Faecal microbiota transplantation. |
| **FSS** | Fatigue Severity Scale. |
| **GCP** | Good Clinical Practice. |
| **GI** | Gastrointestinal. |
| **GWAS** | Genome Wide Association Studies. |
| **GT** | Grounded theory. |
| **HBI** | Harvey Bradshaw Index. |
| **HCP(s)** | Health Care Professional(s). |
| **HDI** | Human development index. |
| **HRA** | Health Research Authority |
| **HRQoL** | Health Related Quality of Life. |
| **HV** | Healthy Volunteer(s). |
| **IBD** | Inflammatory bowel disease. |
| **IBD-F** | Inflammatory Bowel Disease Fatigue Scale. |
| **IBDQ** | Inflammatory bowel disease Questionnaire. |
| **IBD-U** | Inflammatory bowel disease Unclassified. |
| **IDA** | Iron Deficiency Anaemia. |
| **IPA** | Interpretive Phenomenological Analysis. |
| **JBI** | Joanna Briggs Institute. |
| **LTC(s)** | Long Term Condition(s). |
| **MeSH** | Medical Subject Headings. |
| **MFI** | Multidimensional fatigue inventory. |
| **MRI** | Magnetic Resonance Imaging. |
| **MRS** | Magnetic Resonance Spectroscopy. |
| **MS** | Multiple sclerosis. |
| **MTX** | Methotrexate. |
| **N-ECCO** | Nurse European Crohn's and colitis organisation. |
| **NICE** | National institute for health and care excellence. |
| **NIHR** | National Institute of health Research. |
| **NHS** | National Health Service. |
| **OEDC** | Organisation for economic co-operation and development. |
| **PEO** | Population/Problem, Exposure, Outcome. |
| **PIS** | Participant Information Sheet. |

| | |
|---|---|
| **PRISMA** | Preferred Reporting Items for Systematic Reviews and Meta-Analyses. |
| **PROSPERO** | International prospective register of systematic reviews. |
| **PSC** | Primary Sclerosing Cholangitis. |
| **PST** | Problem solution therapy. |
| **QoL** | Quality of Life. |
| **RA** | Rheumatoid Arthritis. |
| **RCT** | Randomised controlled Trial. |
| **REC** | Regional Ethics Committee. |
| **RN** | Registered Nurse. |
| **SFT** | Solution focused therapy. |
| **TA** | Thematic Analysis. |
| **TNF-a** | Tumour Necrosing factor-Alpha. |
| **UC** | Ulcerative colitis. |
| **WHO** | World Health Organisation. |

# 1. Introduction and background

People with Inflammatory Bowel Disease (IBD) are affected by numerous symptoms, undergo lifelong clinical interventions and have an increased chance of malignancy.[1,2] Fatigue is one of the most reported symptoms by people with IBD.[3] However, IBD fatigue is only identified in a relatively small proportion of those affected.[4,5]The complex aetiology of IBD fatigue, subjective nature and lack of a standardised fatigue measure add to the challenge of developing suitable and effective management methods.[3,6,7]

IBD typically has an early onset and is a chronic, incurable, condition. It does not characteristically shorten lifespan, therefore addressing how patients cope with their disease is a principal aspect of care.[8] This thesis aims to explore current perspectives of the impact of IBD fatigue on the health related quality of life (HRQoL) of adults with IBD. This chapter will detail the current evidence surrounding IBD fatigue, the contributing factors, measurement and management methods.

## 1.1 Inflammatory bowel Disease

### 1.1.1 Definition

Crohn's Disease (CD) and Ulcerative Colitis (UC) are the two main forms of IBD.[9] Both are immunologically mediated chronic, systemic, inflammatory diseases of the gastrointestinal (GI) tract that are idiopathic and relapsing in nature.[10] UC was first defined in 1909 with CD first described as a condition in 1932.[11,12]

### 1.1.1 Aetiology and Pathogenesis

Exact aetiology of IBD remains uncertain. Research results from animal models and human genetics studies indicate that CD and UC are heterogeneous diseases, characterised by various genetic abnormalities. The inception and relapse of disease is triggered by environmental factors that break the mucosal barrier which in turn stimulates immune responses and alters the balance between beneficial and pathogenic enteric bacteria.[13–15]

The role of genetic factors is indicated by familial cluster cases and higher incidence demonstrated in identical twins.[14,16,17] Large scale 'genome wide association Studies' (GWAS) have so far found 163 genetic loci linked with IBD onset.[18–20]

### 1.1.2 Epidemiology

Incidence and prevalence of IBD is increasing globally.[21–23] Historically IBD incidence has varied according to geographical location, with higher incidence in the western world being linked to industrialisation. However emerging data speculates that there is increasing incidence in eastern countries, theoretically linked to immigration, westernised diets, lifestyles and better healthcare systems.[24,25] In the UK it is estimated that there are 300,000 people affected by IBD. CD and UC affects 5-10 and 10-20 new patients, respectively, per 100,000 people per year.[26]

The incidence of IBD in western culture is estimated to be around 2-15 per 100000 per year for UC and 0.9-11.6 per 100000 per year for CD.[27] The peak onset age for UC is 30 and 20 years for CD. However, there are several studies that demonstrate that a diagnosis of IBD can occur at any age.[28] Most epidemiological data concurs that there is a median peak in the onset of IBD symptoms between the ages of 20-30.[29–31]

Prevalence of IBD correlates with reported incidence rates, suggesting IBD is most prevalent in westernised cultures.[24,32,33] The prevalence of IBD varies widely from 30-200/100000 for UC and 1.2-106/100000 for CD.[34] In areas with a high incidence of UC there also appears to be a trend of high CD incidence, the ratio of UC:CD is approximately 2:1.

### 1.1.3 Symptoms

Diagnosis of IBD is typically based on symptom history alongside a combination of clinical tests and histological findings.[35,36] Patients present with multiple symptoms including abdominal pain, recurring or bloody diarrhoea, weight loss and fatigue.[37] Not all patients present with all of these indicators, and some may have less common symptoms such as joint pain. Symptoms have been described as subjective, unpleasant and distressing.[38] Symptoms can fluctuate, with periods where the symptoms are severe (flare-ups), followed by times when there are few or no symptoms at all (remission).[39] UC is restricted to the Colon however distribution of CD varies. Colonic disease is present in 25% of patients, 25% have ileitis and 50% have ileocolonic disease. A

further 33% present with perianal CD and 5-15% present with oral or gastro-duodenal disease.[37,40]

### 1.1.4 Financial cost

The management of long-term conditions (LTC[s]), such as IBD, is widely acknowledged as one of the principal challenges facing the 21st century National Health Service (NHS). An estimated 70% of total health care expenditure in England is associated with 30% of the population with one or more LTC.[41] IBD treatment has improved, mainly due to prescription medication, however this has brought around a significant increase in healthcare costs.[42] The cost of care for IBD patients is estimated to be in the range of £631 - £762 per patient per year.[43] This suggests an overall annual cost to the NHS of up to £470 million, earlier research estimates the annual average cost of care per patient to be as high as £3,000.[21,44] In a UK study, six-month direct medical costs for patients who required a period of hospitalisation were 20-fold higher than for IBD outpatients who remained in remission.[45] Disease flares responding to outpatient management were associated with a two-three fold augmentation in costs compared to patients in remission.[46]

### 1.1.5 Management and treatment of IBD

#### 1.1.5.1 Medications

There are many medications used in the treatment of IBD with the aim of inducing and maintaining disease remission.

5-aminosalicylic acid (5-ASA) is an anti-inflammatory drug. 5-ASA is known to inhibit the production of cytokines and inflammatory mediators. However, the mechanism underlying the intestinal effects remains unknown.[47,48]

Thiopurines have varied clinical applications. In IBD they are used as immunosuppressive agents, resulting in the inhibition protein synthesis.[49,50]

Anti-Tumour Necrosing factor-Alpha therapies (Anti-TNF-α) have a wealth of research supporting their efficacy in the treatment of IBD, especially when used in combination with corticosteroids.[51,52] TNF-α is a potent pro-inflammatory and pathological cytokine in inflammatory diseases such as IBD.[53–55] CD that has been unresponsive to anti-TNF-α treatment may respond to ustekinumab. Ustekinumab is a human monoclonal antibody treatment that works by binding to interleukin-21 (IL-21) and IL-23, to stop the production of cytokines that trigger the inflammatory response in the body. It is a treatment recommended by the National Institute of Clinical Excellence (NICE) for psoriasis and psoriatic arthritis. Evidence now shows that it can improve symptoms in CD.[56,57]

Methotrexate (MTX) therapy is utilised for many inflammatory conditions such as rheumatoid arthritis (RA). The clinical efficacy of MTX was also established for steroid dependent CD.[58] More recently, MTX has been used in the paediatric CD population, both as a single agent and as a concomitant therapy with anti-TNF-α treatment.[58,59] The mechanisms of action of MTX are complex. Anti-inflammatory and immunomodulatory actions of low doses are likely due to inhibition of folate dependent enzymes.[60,61] MTX is an inexpensive and well-characterised immunosuppressive drug, which has demonstrated proven efficacy for more than 20 years in patients with CD.

#### 1.1.5.2 Surgery

Precise timing and specific procedure planning in IBD is often fraught with controversy.[62] In both UC and CD laparoscopic procedures appear to be associated with increased operative times but also decreased morbidity whilst providing similar functional results to open procedures.[63]

A number of surgical procedures may be contemplated in the treatment of UC, each with benefits and risks. Often surgery will leave the patient with decreased HRQoL due to post-surgical indisposition.[63,64] The pan-enteric nature of CD leads to significantly high reoccurrence rates.[64] Surgical conservatism is the current general rule. Advances in the medical management of CD have decreased the need for surgical

interventions, however it is estimated that between 70-90% of patients will need surgery at some point during their disease.[65]

#### 1.1.5.3 Faecal transplantation

Faecal microbiota transplantation (FMT) is the process of replacing defective gut microbiome of IBD patients with healthy microbiota from healthy donors. FMT has demonstrated variable efficacy in the treatment of active UC in three randomised control trials (RCT) to date.[66–68] Historically FMT has been recognised as a feasible and effective procedure, yet the first RCT assessing the clinical efficacy of FMT by duodenal infusions, achieving sustained clinical remission in over 90% of CD Patients, was not published until 2013.[69]

## 1.2 Fatigue in IBD

IBD fatigue is one of the top 5 research priorities highlighted by the Nurses European Crohn's and Colitis Organisation (N-ECCO).[70,71] Fatigue is an extremely common complaint amongst patients and has been identified as one of the most burdensome symptoms of IBD.[70,72–75] Recently, the symptom of fatigue has received greater attention as part of overall HRQoL assessments in patients with LTCs, including IBD.[76] The subjective nature of fatigue, poor understanding and lack of proven therapies means it is often underestimated by clinicians.[35,77] IBD fatigue has been reported as multidimensional and complex, impacting individual's activities of daily living and reducing their HRQoL.[72]

### 1.2.1 Fatigue in LTCs

Fatigue in LTCs is defined as an 'extreme and persistent sense of tiredness, weakness or exhaustion'[78] which can be physical, mental or both and is not easily resolved by sleep or rest.[79] Fatigue can be attributed to both physical and mental exertion[80,81] or as the outcome of pathological processes.[80,81] The international classification of diseases presents fatigue as an assortment of physical, cognitive and emotional symptoms affecting undertaking of daily tasks.[76,82]

Fatigue it is experienced by most people at some point in life and can usually be related to excessive physical activity, stress or ill health.[83] In LTCs, fatigue can lead to a chronic depletion of energy reserves and result in functional impairment.[84] This type of fatigue is often referred to as chronic fatigue.

LTCs are most commonly linked with psychological fatigue, but are also associated with muscle deconditioning and inflammation.[3,38,85] Psychological fatigue generally correlates poorly with traditional markers of disease and frequently co-exists with abnormalities in mood, such and anxiety and depression.[86–89] The approach to any patient with fatigue is the exclusion of common treatable causes for both psychosocial and physical fatigue.[76] The causal relationship between chronic fatigue and diminished HRQoL is not completely understood.[90,91]

### 1.2.2 Prevalence of IBD Fatigue

Prevalence of IBD fatigue is reported as 41-48% for patients in remission and 71-86% in active disease.[35,38,92–94] Fatigue in UC (in remission) varies from 22-36% , and 27-41% in CD.[84,90,95,96] In a population with mixed disease activity, fatigue prevalence was reported as 44-64%.[97–100] The reported prevalence of IBD fatigue may be confused by severe and complex IBD presentations. There is also the limitation of the use of different fatigue measurement scales and tools, with no clear cut off point to define fatigue that requires an intervention.

Similar levels of fatigue have been reported in other LTCs when compared with IBD, one study suggesting the fatigue in Multiple Sclerosis (MS) shows similar characteristics to that observed in UC.[101] Despite reported similarity of IBD fatigue prevalence to that seen in other LTCs, as a symptom IBD fatigue has only recently begun receiving a similar level of attention.

### 1.2.3 Measuring IBD Fatigue

Currently there are no clinical guidelines on how to measure IBD fatigue in practice and no cut-off point for diagnosing IBD fatigue using measures that have been validated in an IBD cohort.[102] Diagnosis of IBD fatigue is at the discretion of the Health Care Professional (HCP). The IBD Fatigue scale (IBD-F)[103] and the Functional Assessment of Chronic Illness Therapy Scale (FACIT-F)[99] are validated in IBD cohorts

but are not widely implemented and do not have diagnostic cut-off points.

Many different scales measuring types of IBD fatigue have been developed. The Multi-Dimensional Fatigue Inventory scale (MFI) is most widely used.[104] Some of these scales are symptom specific such as the Fatigue Impact Scale (FIS)[105] whilst others focus on HRQoL measurements.[106] The IBD questionnaire (IBDQ) was developed with an IBD cohort, however it is designed to measure HRQoL rather than fatigue and encompasses just one question relating to fatigue and one on energy levels.[107]

### 1.2.4 Contributing factors of IBD fatigue

It is important that we consider fatigue within a biopsychosocial model of care and contemplate how physical and psychological factors interact as possible causes of IBD fatigue.[3,6,75]

There is positive association between disease activity and high levels of fatigue.[4,108–111] Throughout the literature there are also other identifiable factors, both modifiable and not, contributing to IBD fatigue. Below is a brief summary of those identified in the contemporary literature.

#### 1.2.4.1 Malnutrition

Malnutrition is highly prevalent in IBD, especially in CD.[112] Two mechanisms of malnutrition are reported; The first associated to disease severity where patients avoid eating due to disease symptoms (e.g. nausea, abdominal pain). The second is reduced dietary intake, linked to fasting (e.g. prolonged restrictive diets).[113,114]

Malnutrition is described as the predominant cause of loss of lean body mass and muscle strength in IBD.[115,116] IBD subjects are at risk of nutrient deficiencies due to chronic inflammation and malabsorption.[117] Serum concentrations of several nutrients (beta-carotene, vitamin C, vitamin E, selenium, zinc, Magnesium and vitamin D) antioxidant status were all shown to be lower in CD cohorts when compared to healthy controls.[118] Primary therapy using nutrition to treat IBD is moderately well supported in CD, but not in UC.[114,119,120]

As with other LTCs such as chronic fatigue syndrome (CFS) and MS, the gut-brain axis is presumed to play an intrinsic role in the pathogenesis of IBD Fatigue.[91,121] IBD is a disease of the gut, therefore effecting the gut-brain axis making it likely that the arc could be significantly altered in IBD compared with MS or CFS. There is increasing evidence to suggest that gut microbiota functions as mediator in bidirectional communication between the nervous system and the gut.[122]

#### 1.2.4.2 Iron

Iron deficiency anaemia (IDA) is one of the most common disorders in the world, one third of people with IBD experience recurrent IDA.[123,124] Female gender has been shown to be the strongest risk factor for IDA in both CD and UC, followed by elevated CRP. IDA can have multiple aetiologies such as malabsorption, or a combination of factors. [91,100,125] Other causes of IDA, specifically in IBD, include chronic intestinal bleeding, inflammation and certain types of medications used in the management of IBD.[102] Chronic fatigue is commonly caused by IDA and may debilitate patients as much as abdominal pain or diarrhoea.[91,114] The majority of IBD associated IDA can be successfully treated with medications.[91,114,123]

#### 1.2.4.3 Thiamine

The classic syndrome caused primarily by thiamine deficiency is Beriberi.[126,127] In IBD, Beriberi might occur due to thiamine transporter dysfunction or anomalies involved in thiamine metabolism. The administration of high doses of thiamine increases the concentration of thiamine levels in the blood, restoring normal glucose metabolism throughout t the body, reducing fatigue.[128] These observations are based on small study cohorts, therefore findings are only indicative rather than confirmatory.[129]

#### 1.2.4.4 Other Vitamins and Minerals

B12 Vitamin and folate deficiency, driven by inflammation in mucosal layers, can disrupt normal functioning of the nervous system, producing declines in cognitive functioning and symptomatic fatigue. [130–132] A higher prevalence of Vitamin B12 deficiency was observed in a cohort of 257 IBD patients (195 CD, 62 CD) when compared to healthy controls, with 14.9% of IBD and 4.2% of controls found to be B12 deficient.[133] The prevalence of folate deficiency was higher in CD patients than in healthy controls, 13.3% vs. 3.4%. This study showed that vitamin B12 and folate deficiencies were more common in patients with CD than those with UC and controls.

A deficiency of vitamin D impairs muscle strength and increases the risk of developing health conditions such as osteopenia and osteoporosis.[134–136] Vitamin D levels are negatively correlated with the disease severity of both UC and CD.[137]

Vitamin D, B12, Selenium, Zinc and magnesium deficiency have each been individually implicated in the development of muscle fatigue.[138,139] There is emerging evidence linking tobacco use to immune function, and fatigue through vitamin D pathways in IBD.[4,140,141]

#### 1.2.4.5 Psychosocial factors

Depression is the more prevalent psychological co-morbidity when compared to anxiety disorders in IBD, potentially influencing both the onset and clinical course of the disease.[142] There is noteworthy

association in IBD between baseline anxiety and depression scores, symptoms flares, and disease relapse at 12 and 18 month follow up.[143,144] People with UC report pointedly more worrying over disease complications when compared to other LTCs.[145,146]

Worse psychological well-being has been independently associated with IBD fatigue. [7,111] Individuals who were able to adapt their behaviour in accordance with their chosen goals have lower levels of fatigue when compared to those people who are not able to adapt.[141,147]

Individuals report that their life was significantly or somewhat affected socially by IBD symptoms, even when in remission.[145] Romantic relationships are often affected by IBD fatigue, with individuals reporting difficulties in starting and maintaining intimate relationships. Relatives play in important role in the process of fatigue acceptance, their support in managing disease related symptoms, such as fatigue, are highly valued by IBD patients.[95,148–150]

#### 1.2.4.6 Sleep

Sleep disturbance is a chronic problem in IBD patients, especially those with stomas.[145,151,152] The importance of sleep in IBD has recently gained attention with published studies demonstrating an association of increased sleep disturbances with increased disease activity and a higher risk of disease relapse.[153]

Sleep is considered an important environmental and behavioural factor of the inflammatory process.[153–155] A multivariate analysis revealed depressive symptoms and disease activity are significant independent predictors of sleep disturbance. A strong correlation between fatigue, sleep disorders and sleep quality appears common in active disease.[102] However, sleep deprivation is not restricted to those patients with active disease.[156] Sleep disturbances have been associated with increased fatigue scores.[90,157,158]

#### 1.2.4.7 Medication

Fatigue is seen as a possible side effect of most registered pharmacological drugs used in IBD.[159,160] Interestingly, the cessation of biologic therapies has been associated with reduction in levels of IBD fatigue.[4] However, this reduction in fatigue could be related to a reduction in disease severity or possibly even induction of remission. Conversely, findings in three small intervention studies reported that infliximab [94,161] and adalimumab [160] significantly improved IBD related fatigue, indicating the ambiguous relationship between biological therapy in IBD and fatigue symptoms.

#### 1.2.4.8 Muscle mass and physical activity

People with IBD have been shown to have reduced muscle strength when compared to healthy controls.[162] The prevalence of sarcopenia is high in young CD patients and strongly related to osteopenia.[163] IBD related fatigue is associated with a reduced physical activity levels and

decreased muscle strength.[164,165] An exercise-based study demonstrated a statistically significant ($P < 0.05$) improvement in HRQoL after participants took part in a low intensity walking programme.[166] This is echoed in other studies that report an inverse relationship between fatigue and physical functioning and fitness levels of people with IBD.[95,164,165]

#### 1.2.4.9 Pain

IBD symptoms, including abdominal pain, are associated with psychological dysfunction.[167,168] severe pain is reported by 58.7%-85.5% of people with IBD.[169,170] Evidence suggests that higher levels of pain contribute to more severe fatigue[93], however this theory is not universally supported.[171,172] This lack of consensus is likely due to the subjective nature of reporting levels of both pain and fatigue, as well as the heterogeneity of the samples studied to date.

### 1.2.5 Non-modifiable factors

Variance in incidence of IBD fatigue across age and geographic locations suggests that environmental factors significantly influence the development of IBD symptoms.[173,174] Individuals who are unemployed and those who have lower educational level report more severe IBD fatigue.[4,84,96,141,172] Multiple studies reported that females experience higher levels of IBD fatigue than males. [84,108,111,159,175] A number of cross-sectional studies[160,175,176], and one longitudinal study[111], found

that younger age was associated with more severe fatigue. However other studies did not confirm this relationship.[4,100,172,177]

Individuals with a shorter disease duration report higher levels of fatigue than those with a longer disease duration.[101,109,149,159] This is arguably related to the aforementioned psychological factor of being able to adapt to disease burden. Number of relapses [4,149], but not the number of IBD related hospital admissions [178], are linked to higher levels of fatigue. Numerous studies have suggested that there is no difference in fatigue severity dependant on disease location.[90,96,99,108,111,179] Yet others have discovered that individuals with CD report higher levels of fatigue when compared to UC. [7,141,172,175] In UC, having a subtotal colectomy and pouch formation was associated with lower fatigue levels compared with those in the highest quartile of disease activity.[109] Some studies have shown a strong association between fatigue and co-existing co-morbidities, having increased fatigue compared to those who did not.[172,177,180]

### 1.2.6 Pharmacological management

Thiamine replacement therapy has shown encouraging results in one study.[129] However the methodological limitations of the study, small sample size and lack of control group, make it difficult to draw firm conclusions.

A pilot study considering physical activity and/or Omega-3 therapy in IBD has shown evidence to suggest that physical activity might have a role in reducing levels of fatigue.[181]

Three studies looking at anti-TNF-α therapy, infliximab [94,161] and adalimumab[160], have shown positive therapeutic effects, with a significant reduction in fatigue in the intervention groups. However the high cost and side effects limit their use as a first line treatments for fatigue in IBD.[182]

### 1.2.7 Non-pharmacological management

Fatigue was assessed as a secondary outcome in a stress management study in CD, reporting that self -directed stress management demonstrated a small reduction in fatigue ($p<0.1$).[147]

Cognitive Behavioural therapy (CBT) has been implemented as an intervention for depression in adolescents with IBD.[183] This manual based CBT approach has been adapted and is currently being explored as a management method in IBD fatigue.[184] Solution focused therapy (SFT) and problem solving therapy (PST) both reduced fatigue and increased HRQoL scores in patients with CD.[185,186] SFT seems most feasible, with lower attrition rate, and is therefore a promising novel tool in the management of fatigue in CD patients. These methods have been tested in both a pilot and RCT settings, adding to the validity of the results. However, there is questionable evidence of effectiveness

due to the short intervention period and the lack of clarity describing the content of the interventions.

### 1.3 Health-Related Quality of Life

Increasing life expectancy has highlighted the need for other measures of health, capturing the quality of the years someone lives. IBD is incurable and, owing to the physical and psychological impact of the disease, significantly reduces patients HRQoL.[187] The concept of quality of life (QoL) is not a new one, in 1995 the World Health Organisation (WHO) recognised the importance of improving peoples QoL.[188] When QoL in considered in the context of health and disease, it is commonly referred to as HRQoL to differentiate from other aspects of QoL.

Health is a multi-dimensional concept, HRQoL is also multidimensional and incorporates areas related to physical, mental and social functioning.[189] HRQoL goes beyond the direct measures of health and focuses on the QoL consequences of health status. HRQoL represents the functional effect of an illness and its consequent therapy upon a patient, as perceived by the patient. It encompasses several dimensions of life, including physical functioning, psychosocial functioning, role functioning, mental health and general health perceptions. HRQoL is determined by socio-demographic, clinical and psychological and treatment-related determinants.[190,191]

Clinicians and public health officials use HRQoL to measure the impact of chronic illness. Additionally National Institutes of Health, e.g. cancer institute, have included evaluation and improvement of HRQoL as a public health priority.[192]

## 1.4 Research focus

### 1.4.1 Aims and Objectives

The aim of this research thesis is to gain an understanding of the impact of IBD fatigue on HRQoL of adults with IBD, with a view to offering guidance for further research.

The following objectives have been identified in order to achieve the research aim;

I. Clarify factors of IBD fatigue that impact on HRQoL of adults with IBD.
II. Critically evaluate the current evidence on IBD fatigue and its relation to HRQoL of adults with IBD.
III. Explore patient experiences of IBD fatigue and its impact on daily life.
IV. Make recommendations for areas of further research.

### 1.4.2 Outline of research methods

An exploratory review of current evidence in IBD fatigue was produced, and published, to provide background for this thesis.[193] A systematic literature review was conducted to inform on the current evidence on

the topic of the relationship between IBD fatigue and HRQoL. Semi-structured interviews were conducted with adults with IBD fatigue. Interview transcripts were analysed to explore individual's experiences and perceptions of IBD related fatigue and its impact on HRQoL. Using results from the literature review and the interview study, the thesis will explore the themes that became evident throughout the analysis, developing a theory relating to the relationship between specific fatigue factors and their impact on an individual's HRQoL.

Appendix 1 presents a Gantt chart developed by the Student to demonstrate timelines of the research project.

### 1.4.3 Role of researcher

Throughout the thesis, where applicable, I will refer to myself as 'the student' to acknowledge my developmental role within the project, the active form of 'I' is employed only where reflective comments will be provided. The role of the student will involve day to day management of the study; screening, recruitment and interviewing of study participants, data collection, transcription, analysis and dissemination of findings.

## 1.5 Value of this research

IBD fatigue is highlighted as top research area by specialist clinicians and fatigue is an extremely common symptom amongst patients with IBD.[70–75] However there is not, to date, any other study which explores the relationship between IBD fatigue and HRQoL. Stratifying themes from the systematic literature review and patient interviews identified

the areas of greatest impact on HRQoL. This highlighted areas that are best targeted for intervention development to improve HRQoL related to IBD fatigue.

### 1.6 Summary

This chapter presents current evidence on IBD and available treatment options in the United Kingdom. Fatigue is consistently associated with depression, anxiety and sleep difficulties in high quality studies, although causal direction of the relationship remains unclear. More recent research has highlighted the relevance of previously unexplored aspects such as cognitive factors. The challenge of developing suitable and effective IBD fatigue management methods lies within its subjective nature and lack of a standardised measure. Interventions for fatigue in IBD are under-researched. The proposed research will identify key HRQoL factors that are most affected by IBD fatigue. This will provide focus for future research into nonpharmacological interventions for IBD fatigue.

## 2. The impact of IBD fatigue on HRQoL: A systematic review.

### 2.1 Introduction

Clinical outcomes are often poorer in IBD than for healthy populations. Impaired HRQoL has been highlighted as significant factor pertaining to fatigue, particularly during disease relapse.[187,194,195] Evidence exists regarding modifiable and non-modifiable factors related to fatigue and multidisciplinary approaches to symptom management in IBD.[196] However there has been little specific evidence gleaned regarding fatigue management or the psychosocial effects of IBD fatigue. The most contemporary literature reviews considering IBD fatigue were conducted in 2013[35] and 2016.[196] No review to date has focused on the impact of IBD fatigue on HRQoL.

The aim of this chapter is to explore the current evidence on IBD fatigue and its impact on HRQoL. This will be achieved by conducting a systematic literature search, critical appraisal and synthesis of the existing data.

The following review question was developed using the format: Population, Exposure, Outcome (PEO) The Study Question was: *"What is the impact of IBD fatigue on the HRQoL of adults with IBD?"*

## 2.2 Types of review

A successful literature review is one that creates a solid underpinning for advancing knowledge and does not duplicate previous work.[197] Choosing the correct type of review is paramount for successful execution.[198,199] The choice of synthesis method is driven by the aims of the review. A surplus of review designs and terminology, with little consensus on the ideal method to synthesise data, can make choosing the type and process of review difficult to decide on.[200,201]

Narrative reviews often appear as a chapter in a thesis or dissertation, summarising the related research which has already been conducted and how the thesis fits into the research in the field. Alternatively, a critical review requires a more detailed examination of the literature in order to compare and evaluate a number of perspectives relating to the topic. Scoping reviews are most often used at the beginning of articles, dissertations or research proposals.[202] This type of review is conducted before research begins, and sets the stage for this research by highlighting gaps in the literature, and explaining the need for the research about to be conducted. Conceptual reviews groups articles according to topics.  It provides a snapshot of the current 'understanding' of the topic, discusses how this was reached, and attempts to determine whether a greater understanding can be suggested. Finally, there are ‘state of the art’ reviews, which are conducted periodically with a focus in the most recent research. It

describes what is currently known regarding the research topic and highlights remaining disagreements.

After considering examples of reviews, the aim and academic requirement of this chapter, a narrative review was considered the most appropriate. Narrative reviews allow inclusion of different study types. This systematic literature review will be used to inform the thesis and provide a sense of how the research undertaken will fit into the existing evidence on the topic of IBD fatigue.

## 2.3 Search strategy and selection of papers

Inclusions and exclusion are based on pre-set criteria for specific systematic searches of the literature and provide boundaries for the review. [203,204] The inclusion and exclusion criteria are stated before starting the literature search in order to minimize possible bias. Inclusion criteria help to identify studies of interest, if the criteria are too broad or too narrow, it can lead to an ineffective screening process.[203,204]

Searching the literature on IBD fatigue was approached in a broad manner to allow for differences within the phenomenon to be captured. This was achieved by searching multiple databases and utilising a wide variety of search terms. The search was also designed to be narrow

enough, though the use of appropriate search limitations to set boundaries and the direction for literature retrieval.[205,206]

The systematic search was performed on 25/09/2018. Databases searched were EMBASE, CINAHL, PsychINFO and MEDLINE. These databases were selected to provide a combination of medical and healthcare related databases likely to afford a broad field of search across disciplines without diluting the retrieved articles with unrelated articles.[207] Each database was individually searched to ensure inclusion of all relevant publications.[208] Prospective searches of the database medical subject headings (MeSH) and free text searching demonstrated that the same publications were available on MEDLINE and PubMed Databases, so the decision was made to not search PubMed. Grey literature searching was used to maximise the number of publications retrieved.[209,210] This was conducted by searching google scholar, reference lists of included publications and registered controlled trial registers.

Search terms were determined through consideration of previously reviewed literature and scoping searches of Google Scholar. These are displayed in Table 2.1. The most frequently used term was fatigue, other terms such as ‘energy level’ [73], ‘tiredness’[147], ‘decline of vitality and vigour’[149] and ‘energy and vitaility’[211] were also present, therefore these terms were included. Searches were performed with the ‘suggested search terms’ and ‘explode’ selection to enable databases to use synonyms and suggest the closest corresponding subjects to the

original search terms. The Boolean operator 'OR' is used within each facet to maximise the searches, with the operator 'AND' utilised between facets to combine terms.

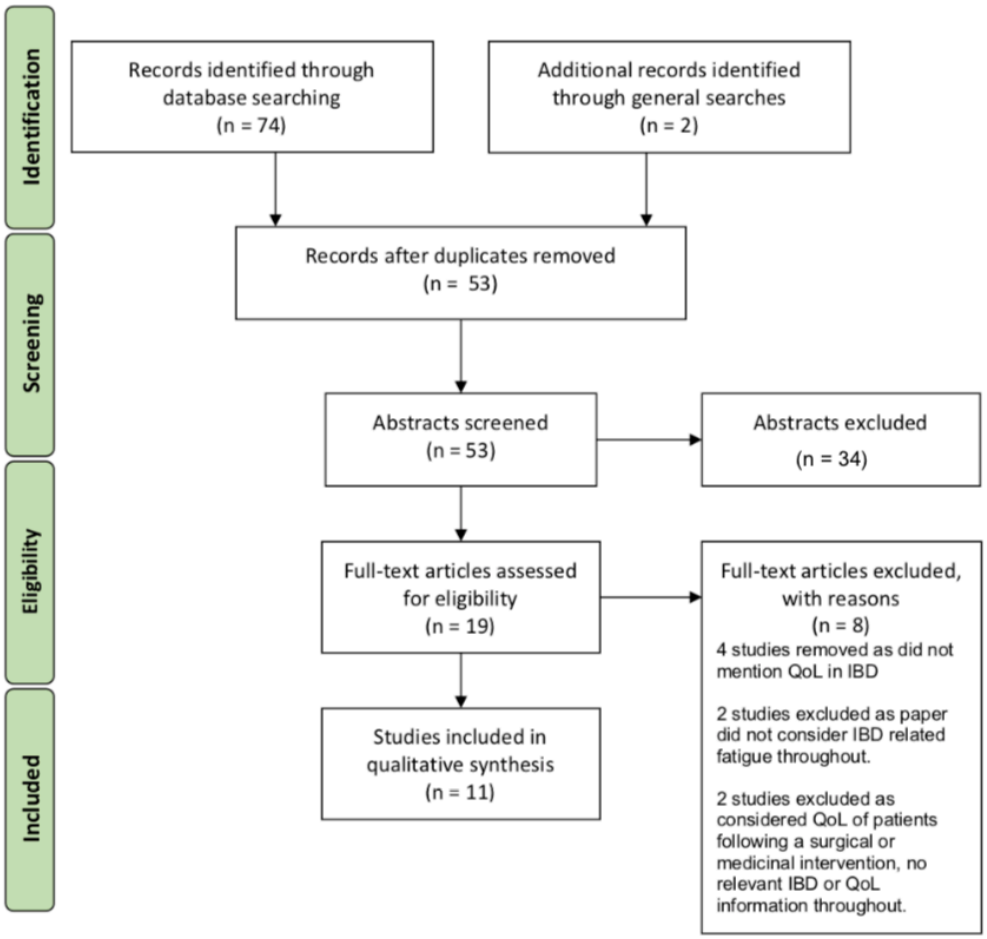
**Table 2.1:** Search Terms

| Fatigue | IBD | Quality of life |
|---|---|---|
| Fatigue (MeSH) | Inflammatory Bowel Disease * | Quality of Life |
| Fatigue* | IBD | Health related quality of life* |
| Lethargy (MeSH) | Ulcerative Colitis* | Life Quality |
| Lethargy | UC | HRQoL |
| Low energy* | Crohn's Disease* | |
| Vigour* | CD | |
| Vitality* | | |
| Exhaustion* | | |
| Key=* free search term for truncation | | |

Searches were restricted to 'human', 'adult', 'primary research' and 'English language' publications. Studies of any kind (qualitative, quantitative or mixed methods) published in English were considered if IBD fatigue was mentioned in the abstract. Commentary papers and literature reviews were excluded. A time limit of 5 years (2013-2018) was set to ensure inclusion of the most up to date information. Due to limited number of publications related to IBD fatigue, no studies were omitted from the review based on quality, however quality was considered when reviewing study findings. Studies that did not meet the inclusion criteria were retained, if relevant, for background information.

Searches yielded 76 publications, with 11 studies being included in the review. Information is displayed in Figure 2.1 according to PRISMA guidelines.[212] A list of the included papers is shown in Table 2.2

*Figure 2.1: PRISMA diagram for Systematic literature search and selection*



| Table 2.2: Included full text articles. | | | |
|---|---|---|---|
| **Author(s) in full.** | **Year published** | **Title of study** | **Type of study** |
| Castillo-Cejas, M. D. Robles, V. Borruel, N. Torrejón, A Navarro, E. Peláez, A. Casellas, F. | 2013 | *Questionnaires for measuring fatigue and its impact on health perception in inflammatory bowel disease* | Cross sectional. |
| Czuber-Dochan, W. Dibley, L.B. Terry, H. Ream, E. Norton, C. | 2013 | *The experience of fatigue in people with inflammatory bowel disease: An exploratory study* | Qualitative. |
| Viazis, N. Mantzaris, G. Karmiris, K. Polymeros, D. Kouklakis, G. Maris, T. Maris, T. Karagiannis, J. Karamanolis, D.G. | 2013 | *Inflammatory bowel disease: Greek patients' perspective on quality of life, information on the disease, work productivity and family support.* | Qualitative. |
| Cohen, B. L. Zollga, H. Shah, S. A. Leleiko, N. Lidofsky, S. Bright, R. Flowers, N. Law, M. Moniz, H. Merrick, M. Sands, B. E | 2014 | *Fatigue is highly associated with poor health-related quality of life, disability and depression in newly-diagnosed patients with inflammatory bowel disease, independent of disease activity* | Prevalence |
| Devlen, J. Beusterien, K. Yen, L. Ahmed, A. Cheifetz, A.S. Moss, A.C. | 2014 | *The burden of inflammatory bowel disease: A patient-reported qualitative analysis and development of a conceptual model* | Qualitative |
| Opheim, R. Fagermoen, M.S. Bernklev, T. Jelsness-Jorgensen, L.P.Moum, B. | 2014 | *Fatigue interference with daily living among patients with inflammatory bowel disease.* | Cross Sectional. |
| Van Langenberg, D.R. and Gibson, P.R. | 2014 | *Factors associated with physical and cognitive fatigue in patients with Crohn's disease: A cross-sectional and longitudinal study* | Cross sectional. |
| Artom, M. Czuber-Dochan, W. Sturt, J. Murrells, T. Norton, C. | 2017 | *The contribution of clinical and psychosocial factors to fatigue in 182 patients with inflammatory bowel disease: a cross-sectional study.* | Cross sectional. |
| Habibi, F. Habibi, M.E.Gharavinia, A. Mahdavi, S. Akbarpour, M. Baghaei, A. Emami, M. | 2017 | *Quality of life in inflammatory bowel disease patients: A cross-sectional study* | Cross sectional. |
| Skrautvol, K. and Naden, D. | 2017 | *Tolerance limits, self-understanding, and stress resilience in integrative recovery of inflammatory bowel disease* | Qualitative |
| Villoria, A. García, V.Dosal, A. Moreno, L. Montserrat, A. Figuerola, A. Horta, DianaCalvet, X. and Ramírez-Lázaro, M.J. | 2017 | *Fatigue in out-patients with inflammatory bowel disease: Prevalence and predictive factors* | Prevalence |

## 2.4 Quality appraisal and data extraction

It is a fundamental skill for any healthcare researcher to be able to identify and appraise the evidence in order to integrate it, where possible, with clinical context.[213] Critical appraisal is the course of action for systematically examining research to assess its reliability, value and relevance to the research question.[214]

Quality of studies was assessed using forms specific to study design from the Joanna Briggs Institute (JBI) to allow for comparison of quality across study types.[215] An adapted form from critical appraisal skills programme (CASP) guidelines[216] was considered, however JBI forms have been shown to be the most coherent when considering validity of qualitative studies.[217] The JBI tools are more widely used within the University of Nottingham, the base for the review. Standardised tools promoted extraction of similar data across all included studies. Data was extracted using a JBI data extraction tool by two independent reviewers. A table displaying the summary of quality appraisal is available in Appendix 3.

The data extracted included specific details about the populations, context, culture, geographical location, study methods and the phenomena of IBD fatigue relevant to the review question. Due to the limits of time and feasibility all papers were read in full but only data reflecting the aims of the review were extracted, a selective approach that proves useful where there is a large volume of data.[206] Information

and analysis regarding HRQoL was limited for some studies, but present and therefore deemed important to include given the comprehensive and systematic nature of the review. A table displaying the summary of extracted data is available in Appendix 4.

## 2.5 Results

### 2.5.1 Sample Characteristics

Eleven studies are included in the review, four qualitative [35,218–220], five cross sectional studies[4,172,179,221,222] and two prevalence.[108,223] Geographical locations of the research studies included the UK (2), USA (2), Norway (2) and Spain (2), with one study each from Australia, Iran and Greece. All are considered to be developed countries with good quality healthcare.

The review presents data from a total of 2823 adults. Study sample sizes ranged from n=13 to n=1181. Females represented 54% of the sample. Most settings were outpatient departments, however studies also used online participation and interview/focus group data collection. A total of 1550 participants studied had CD (54.9%), 1182 had UC (41.9%), 85 healthy volunteers (HV) (3%) and 6 with IBD-unclassified (IBD-U) (0.2%). Reported fatigue prevalence ranged between 26.4% and 54%. All studies reported data from mixed disease states (active, quiescent).

### 2.5.2 Measurement tools

Throughout the review 26 different questionnaires were utilised, the majority of studies used unvalidated questionnaires. Two studies used unvalidated questionnaires of the authors' own design.[35,218] Questionnaires measured fatigue, HRQoL, disease activity, anxiety and depression, sleep quality and work productivity. Studies described the questionnaires used but did not provide a rationale for specific tool selection. Of note is the observation that some studies used two or more scales to measure HRQoL and/or fatigue. This implies that there is no consistent, reliable measurement tool for either. Study findings should be considered in a way that reflects the subjective nature, and reporting, of IBD fatigue. The extensive variety of questionnaires used throughout the review points to the multifactorial nature of IBD fatigue.

### 2.5.3 Fatigue measurement

The MFI[104] was used by two studies.[179,221] The MFI has been examined and validated in IBD[175] However its responsiveness to changes in fatigue level has not been assessed.

The Fatigue Severity Scale (FSS-5) was used by two studies.[172,179] The questionnaire focuses on perceptions of fatigue interference with physical, cognitive and social functioning. The FSS is designed to differentiate fatigue from depression. The limitations of this measure are its subjectivity and lack of validation in IBD cohorts.

The FIS[105] was utilised in two studies.[179,224] This scale is widely used in clinical research but has not been validated in IBD. Throughout the reviewed literature the FIS demonstrated the most consistent statistical correlation results between fatigue and HRQoL.

The only dimensional tool for fatigue that considers HRQoL, validated in an IBD population, IBD-F scale.[103] This was used in only one study.[221]

### 2.5.4 HRQoL measurement

The Short-form 36 (SF-36)[106], a generic QoL measure, was used in one study[108], however the more frequently used measures of HRQoL throughout the review were the IBDQ[225] and the EuroQoL-5D.[226–228] The disease-specific IBDQ-36 and a shortened version, the IBDQ-9, is translated and validated for its use in multiple languages.[225] The IBDQ-36 was used by 4 studies[179,221,222,229], and the IBDQ-9 in 3.[179,223,229]

The EuroQol-5D is a short generic utility measure that provides both a descriptive profile and an overall index for HRQoL. Validation of the EuroQoL-5D is well established and has been tested in IBD cohorts.[226–228] The EuroQoL-5D was used in two studies.[108,179]

## 2.6 Data analysis

A form of thematic analysis (TA) was considered most appropriate for this literature review. This approach is recommended when the phenomenon is not well understood or when the studies reviewed are heterogeneous.[230] TA is used to synthesise and identify dominant findings from published research and make generalisations.[230,231] The limitation of TA is the possibility of being overly reductive and emphasising less important themes. However, using this analysis method enables replication and drawing of valid conclusions from data relating to their context. There are no systematic guidelines to follow for TA, however there are some general principles. The lack of formal guidelines could perceivably limit the findings of the analysis through its lack of standardisation. However, this also creates opportunity for intuitive analysis outside of rigid guidelines. The aim is to discover smaller categories from a large amount of text, these smaller data pieces are then combined to form overarching themes.[230,232]

Following the principles highlighted by Elo and Knygas[230], analysis included three phases: open coding, creating categories and abstraction. The open coding phase relies upon the research question driving the coding process so that only valid data is highlighted and further examined.[205,231,232] Open coding involved highlighting the text when reading, later the highlighted sections were grouped and categorised. During categorisation each category was named and combined into larger themes.

The abstraction phase involved conveying a general description of the topic being researched to the themes identified. Through continually comparing and contrasting the similarities and differences of the studies, themes became more understandable and relatable to the research question. Through the processes of data extraction and TA, three themes developed; Symptom acceptance, Psycho-Social well-being and Physical activity.

Table 2.3 displays the distribution and frequency of the main themes throughout the reviewed studies.

**Table 2.3: Main themes from the reviewed literature.**

| Reviewed studies. | Main Themes | | |
|---|---|---|---|
| | Symptom acceptance and management | Psycho-social well-being | Physical Activity |
| Castillo-Cejas, M. D. Robles and V. Borruel, N. *et al* | | | x |
| Czuber-Dochan, W. Dibley, L.B. and Terry, H. *et al* | x | x | x |
| Viazis, N. Mantzaris, G. and Karmiris, K. *et al* | x | x | |
| Cohen, B. L. Zollga, H. and Shah, S. A. *et al* | x | x | x |
| Devlen, J. Beusterien, K. and Yen, L. *et al* | x | x | x |
| Opheim, R. Fagermoen, M.S.and Bernklev, T. *et al* | x | x | x |
| Van Langenberg, D.R. and Gibson, P.R. | | | x |
| Artom, M. Czuber-Dochan, W. and Sturt, J. *et al* | x | x | x |
| Habibi, F. Habibi, M.E. and Gharavinia, A. *et al* | x | | x |
| Skrautvol, K. and Naden, D. | x | x | x |
| Villoria, A. García, and V.Dosal *et al* | | x | |

## 2.7 Themes from the literature.

### 2.7.1 Symptom acceptance and management

Ability to accept diagnoses and IBD symptoms can depend on care received from health care professionals (HCPs). One study reports 31% of participants were informed about disease advances, however only 30% of those obtained information from HCPs.[218] The same study reports 26% of participants do not discuss treatment with HCPs, with 40% feeling HCPs are unsupportive.[218] When seeking support from HCPs participants reported they were often made to feel like fatigue is an inevitable part of IBD that must be accepted.[35]

Participants who report feelings of a lack of control over IBD symptoms experience higher fatigue levels.[221,222] Altered self-image and fears about stigma caused participants to hold back sharing their diagnosis with friends, family, colleagues and employers.[35,218–221] Negative fatigue perceptions were associated with greater negative impact of fatigue on daily activites.[221]

One study presented an entire theme concerning management of fatigue with participants stating that '*with time and experience, you learn to be able to detect those feelings of tiredness and overdoing things'*.[35] 'Normalising behaviours' were described in terms of the participant incorporating their management techniques into daily life in order to reduce the impact of fatigue on daily activities. Those patients who utilise self-help techniques were more likely to report higher levels

of fatigue.[172] Improvements were seen in levels of fatigue over time as patients made adjustments to lifestyle.[4] Participants deemed by the authors to be using poor methods of fatigue management experienced higher level of fatigue.[221,222]

Understanding tolerance limits and being able to adjust lifestyle to manage symptoms were highlighted as important steps for some participants.[220] Higher levels of IBD-related distress, e.g. lack of symptom acceptance, have been shown to be associated with reduced HRQoL.[221]

### 2.7.2 Psycho-social well-being.

Anxiety and depression are explored in the majority of the reviewed studies. [4,35,108,179,218,220–223] Fatigue can cause psychological distress to the extent that intervention would be merited.[223] A substantial number of patients feel depressed (60%) or even angry (25%) because of IBD.[218] Both UC and CD patients with fatigue reported having problems with anxiety and depression, this corresponded to lower HRQoL in these populations.[108,222] Emotional, cognitive and behavioural factors were associated with fatigue and HRQoL, above and beyond the influence of sociodemographic and clinical factors.[221]

Fatigue burden is frequently reported by study participants as a reason for limited or missed social interaction oppourtinties.[35,218,219] Family and friends are often described as being supportive, however some

participants reported family and friends were often lacking in understanding of IBD symptoms, particularly fatigue.[220] Participants reported that they were mindful about depending heavily on family support. Participants said they would feel more supported if the people around them were better informed about IBD fatigue.[35]

Social support included support from HCPs, however this was often reported as lacking.[35,218] Support from family and friends may compensate for the gaps in support from HCPs that participants describe.[218]

Interestingly, none of the studies considered the impact of fatigue on intimate relationships. Only one study touched on the subject when reporting participants feel unable to disclose IBD to a new partner for fear of the stigma of 'unseen' symptoms, such as fatigue.[219] Two studies contained participants views regarding children, and how their levels of fatigue have negatively impacted their decisions to start, or add more children to, a family.[35,219]

More than half took time off work for IBD related reasons, with 40% reporting IBD symptoms interfered with working capability.[218] IBD symptoms have influenced participant decisions regarding work life and career plans.[35,219] Patients report not progressing in careers, choosing not to take on more responsibility or reducing their working hours due to IBD fatigue.[35,108,219,220] Some reported that employers are not always

supportive in relation to their IBD, for example by not allowing extra breaks or taking the time to understand the symptoms of IBD.[35,218]

### 2.7.3 Physical activity

Avoidance and 'all or nothing' behaviours associated with high levels of fatigue were linked to reduced HRQoL.[221] Low physical energy impacted participants ability to have a fulfilling life.[35] Both CD and UC patients with fatigue reported having problems undertaking usual daily activities, such as cooking and cleaning, when compared to those without fatigue.[108] However very few participants reported issues with self-care regardless of fatigue level.[108] Patients who commenced a regular exercise program had greater improvement in the fatigue scores than those who did not.[4] Establishing a regular routine between activity and rest helped some participants ascertain physical fatigue tolerance limits.[220] Balance between being able to understand when to rest, but also maintaining a healthy average amount of daily activity was important to participants.[220]

## 2.8 Methodological considerations

Descriptive analysis was used once to analyse qualitative data[218], and TA three times.[35,219,220] One study adopted seemingly appropriate statistical testing however did not reach its required sample size to meet a 95% confidence interval, the sample described was predominantly in disease remission however it is hard to discern whether they have pooled mixed disease activity to some extent.

Statistical programmes were used to perform multiple analysis in all of the review cross-sectional studies.[4,172,179,221,222]

Using questionnaires designed by the authors makes it difficult to ensure validity of the results as the studies did not use a validated fatigue or HRQoL index.[35,218] Two studies reported findings based on incomplete data sets; the reliability of the authors' conclusions could be questionable.[108,221] The cross-sectional nature of the majority of included studies precludes inference of causality and cannot determine the stability of measured variables, offering only a partial view at one time point.[4,172,179,221,222] Three studies improved validity by controlling for disease activity and demographic variables.[108,172,221]

Skrautvol[220] presents a possibly biased sample by providing results from a sample of 13 with only 3 male participants. Positives of the study are that data saturation was reached and the study presentation was supported with participant quotations from qualitative interviews.

Particular strengths of the study from Viazis *et al* [218] include the large participant cohort, amongst the largest in IBD literature. The high response rate to the questionnaire (94.48%) indicates very low none-response bias. 25% of the study population have disease longevity of over 10 years, meaning authors are better able to assess patient ability to adapt the lifestyle to manage their IBD. Opheim [172] did not control for depression or sleep activity, meaning type 2 statistical errors are unable

to be ruled out, particularly for subgroup analysis. Devlen *et al*[219] conducted both qualitative and focus groups Interviews. This minimises the limitations of each type of data collection, however the sample size was small. Van langenberg[4] tested separate data sets for physical and cognitive fatigue scores. Accounting for similarities and differences in the sample demographic thus making it less likely that results be confounded by external factors.

No studies explicitly explored the relationship between medications and IBD fatigue. Only one study presented data from participants being monitored clinically for their biological or immunosuppressive therapies.[223] The scope of background information collected, disease activity levels, depth of data relating to types and magnitude of fatigue and its effects appears to vary vastly between studies.

## 2.9 Discussion

Knowledge gained from this literature review has been compared and contrasted against the wider literature on fatigue in IBD and other LTCs. The definition of fatigue across LTCs, including IBD, shares characteristics; subjective, excessive, persistent and abnormal nature, reduced energy and muscle strength which is disproportionate to the level of activity, impacting daily physical and cognitive functioning and leading to impaired HRQoL.[6,78,101,233–237] Fatigue in LTCs has a predominantly negative impact on every aspect of an individual's life.[238,239]

The primary contributing factor of fatigue across LTCs is widely reported to be the condition itself.[240] However disease activity cannot independently explain the presence or severity of fatigue as patients in remission also report fatigue.[38,84,95] The link between increased disease activity and increased levels of fatigue is presented in many of the included studies.[4,35,108,179,218,220–223] However, links between IBD activity, fatigue and HRQoL is contemplated only in one study.[179]

### 2.9.1 Symptom acceptance and management

Changes of self-image and self-esteem caused by IBD are distressing.[241] These negative emotional experiences affect HRQoL and should be recognised by HCPs. Low self-esteem may lead to feelings of guilt.[242] Potential positive experiences of IBD had not been considered at all throughout the review. A LTC can, after time, build an individual's resilience and raise awareness of life's limitations.[220] A diagnosis of IBD can sometimes be a relief, eventually getting an answer to questions regarding symptoms.[243,244]

Patients with IBD often feel it is important to remain 'in control' of their health.[241,245] Unpredictability and uncertainty concerning IBD relapses, treatment options and possible side effects are also reasons for distress.[241] Symptoms are reported more frequently when the patient has difficulty in coping with the demands of the disease.[149,246]

Acceptance of IBD and using effective coping strategies seem to have positive impact on symptom activity, whereas negative attitude and ineffective strategies worsens HRQoL.[149,242,246] The reviewed literature raises the importance of patients being able to recognise their own limits.[220] Maladaptive strategies, such as all or nothing behaviours, lead to lower HRQoL.[245] Being overwhelmed and having a lack of energy is a source of distress which strongly affects HRQoL.[220,241,247] HCPs should assess coping styles of the patient, as the effects of poor coping styles are shown to negatively impact HRQoL.[248]

Different management methods have been reported by participants; Most are ineffective or only have short-term effect on relieving, but not eliminating, IBD fatigue. Fatigue management methods used in other LTC included rest, psychological adjustments, task prioritisation and seeking support. [234,240,249–251] Interventions have been tested in a relatively small number of studies, often in uncontrolled or pilot studies. The diversity of interventions, study design and use of varied measurement tools do not readily allow for comparison of outcomes. There is a lack of good quality intervention studies in IBD fatigue. This is likely due to the lack of data concerning delineating fatigue factors, meaning targeting interventions are almost impossible.

### 2.9.2 Psycho-social well-being

The articles contain few references to stigma [35,218–220] however it seems to affect IBD patients life in multiple ways. Stigma is found to be independent of level of disease activity.[252] Stigma reported by

participants was connected with the perceived views of employers, co-workers and friends. This is supported in the wider IBD literature.[241,252,253] In the case of IBD fatigue, stigma results from perceived physical weakness, cognitive limitations, reduced social activity and the inability to fulfil certain roles within and individuals personal and professional life.[254] Stigma is associated with many LTCs where the individuals characteristics are perceived to be flawed by the disease.[255–258] Lack of support from colleagues, related to stigma, worsens HRQoL.[241,247] Often the steps taken to adjust the work environment to accommodate IBD symptoms, such as incorporating more rest periods, can lead to feelings of isolation. The effect of IBD fatigue on work life and career are reported in several of the reviewed articles.[35,108,218] Patients in full time work experience significantly higher QoL than those in part time work, unemployed or absent due to sickness.[242,259]

A range of negative emotions are associated with IBD fatigue and mentioned briefly in the review publications, these are echoed in other IBD studies.[241,242] Depression and anxiety have a recognised link with IBD. These can be measured with ease, using several well validated and standardised questionnaires.

A study in MS showed a cycle of depression leading to social isolation, which in turn leads to a reduction in social support, contributing to increased depression.[150] This cycle also presents in IBD fatigue.[95,149]

Social support has also been found to be a reserve of energy.[149] Disengagement from social activity greatly affects a patient's HRQoL, causing emotional distress.[241,248] [242] IBD fatigue impacts on social activity and undertaking leisure activites.[241,242,247,248] Patients worry that their illness restricts their own and their families social activites.[241] Social support groups, networks and counselling are evidenced to positively impact on HRQoL.[245,248]

Close relationships with friends are positively meaningful and important in coping with the disease.[220,241] IBD fatigue has been reported to be a daily concern of 66% of patients, however only 44% of family and friends and 36% of HCPs demonstrated agreement with the patients perceived fatigue levels.[97] This kind of discrepancy may result in patients feeling misunderstood and isolated, leading to under reporting of symptoms. Some HCPs still consider IBD symptoms as purely psychological in nature causing emotional distress.[242]

### 2.9.3 Physical activity

Benefits of physical activity on an individual's level of fatigue was implied in a recent RCT.[181] The pilot study compared exercise advice, dietary advice, dietary supplementation of Omega-3 fatty acids and placebo. It found that fatigue was pointedly reduced in the exercise group.[181] Evidence from the review demonstrates that those who commenced a regular exercise program generally had greater improvement in fatigue scores.[4] This is supported in the wider literature

were introducing higher levels of exercise is associated with feeling and functioning better for patients with LTCs.[260–262] There is very little evidence regarding exercise or physical activity in IBD fatigue.

## 2.10 Strengths and limitations

The reliability of a study measures the possibility of repeating the research findings results that are similar.[263–265] The literature search process has been explained in detail to enable repetition of the research. The methodology is transparent enough to allow a near exact replication of data extraction and conclusions.[263–265] However, through the use of TA, there is a possibility that the study themes could emerge differently. To increase reliability of this thesis, the categories and subcategories were reached through discussion with academic supervisors. The research question was formulated to be as unambiguous as possible. Continuous conversations with academic supervisors occurred throughout to ensure a unanimous decision regarding article searches and quality appraisal criteria, reducing the risk of bias. Multiple databases were searched, and only relevant publications considered. Each publication was discussed by at least two researchers, with a third being consulted if there were any discrepancies, there were no discrepancies during the search, data collection or analysis. The outcomes represent an accurate response to the research question.

## 2.11 Summary and future directions for research in IBD

This systematic literature review has been accepted for publication. Eleven studies were deemed eligible for inclusion presenting data from a total of 2823 adults with IBD. Studies revealed experiences of fatigue were significantly related to three HRQoL areas; Symptom acceptance, psychosocial factors and physical activity. This literature review implicates the need to further explore and raise awareness about IBD fatigue and fatigue related experiences of IBD patients.

The literature review revealed common themes however there was no explicit link between IBD fatigue and HRQoL. There is scope for further exploration of how IBD fatigue affects people's day to day lives, impacting on HRQoL. A qualitative interview study would be of benefit in this area. The impact of the identified themes such as physical activity need to be explored and delineated; Does exercise help improve fatigue levels and HRQoL or is it the social interaction that it brings that helps more?

The impact and long-term course and consequences of IBD fatigue have not been studied. There would be benefit in prospective long-term cohort studies with serial measures of IBD fatigue alongside other measures, such as HRQoL, anxiety and depression, physical activity, disease activity and measures of disease burden. Exploring this information would allow a better understanding of IBD fatigue and would provide a foundation for development and testing of interventions

for better symptom management. Further research with use of validated fatigue and HRQoL measures; and clearer characterisation of disease activity would help define a diagnostic cut off for IBD fatigue that requires an intervention. Expert opinions regarding the style and use of interventions would be valuable. This could be obtained through the use of a Delphi survey encompassing views from experts in psychology, sociology, exercise and IBD.

## 3. Interview study

### 3.1 Introduction

Qualitative research in IBD, to date, has explored participants' lived experiences of IBD[266–268] Formal investigation regarding people's experiences of IBD related fatigue and its impact on HRQoL is currently lacking. Undertaking this work has the potential to highlight areas for future research focus, by emphasising areas of daily life that are most impacted by IBD fatigue.

In order to achieve objective 3 as set out in the thesis aims and objectives, the student undertook semi structured interviews with adults with IBD who report experiencing IBD fatigue.

### 3.2 Position of the researcher

The student assumed a critical realist position[269],recognising herself as an active part of the research process, aware of the importance of considering the influence of her own experiences in the shaping of the study and interpretation of the results.

#### 3.2.1 Critical Realism

Critical Realism (CR) is gaining attention as an alternative to both positivism/empiricism and constructivism as a philosophical stance for research and evaluation. CR evolved from the writings of the philosopher Roy Bhaskar[270] and is a branch of philosophy that distinguishes between 'real' and 'observable' worlds.[271,272] CR is the

belief that the 'real' is not observable and exists independent from human perceptions. The world as we understand it, is constructed from perspectives and experiences, through what is 'observable'. Therefore, according to CR, unobservable constructs cause observable impact.[273] This was chosen by the student as the epistemological stance as it best fit the exploration of participant beliefs and experiences in constructing the understanding of the impact of IBD fatigue on HRQoL. The distinctive feature of this form of realism is the denial that there is objective or certain knowledge of the world, and the researcher should accept the possibility of alternative valid accounts of any phenomenon.

CR has achieved widespread acceptance as an alternative both to naïve realism and to radical constructivism, views that deny existence of any reality apart from our constructions.[274] This was not deemed an appropriate stance when exploring the HRQoL experiences of participants, as they do not take into account the exploratory nature or possible alternative valid accounts of phenomena presented by participants.

### 3.3 Study approvals.

The interview study was conducted as a sub-study to the study shown below:

| | |
|---|---|
| Study Title (Main study) | Non-invasive approaches to identify the cause of fatigue in inflammatory bowel disease patients. |
| REC reference | 17/EM/0431 |
| Protocol number | 17083 |
| IRAS project ID | 233733 |
| ClinicalTrails.gov | NCT03670693 |

The study was reviewed by the East Midlands - Nottingham 1 Research Ethics Committee (REC) and received approval through the Health Research Authority (HRA). HRA and REC approval is available in the appendices (Appendix 8.5).

The main study hypothesizes that the aetiology of IBD fatigue lies collectively with peripheral muscle deconditioning and brain central fatigue. To address this hypothesis, the investigators aim to recruit a cohort of fatigued and non-fatigued CD patients in remission and age, gender, muscle mass, and physical activity matched HV.

Fatigue was defined through questionnaires at screening. Peripheral and central roles in fatigue aetiology will be investigated. Peripheral muscle deconditioning will be investigated whilst the potential of central

fatigue will be examined through various measures using magnetic resonance imaging.

## 3.4 Sample size

An initial approximation of sample size is needed for planning, the adequacy of the final sample size must be evaluated continuously during data collection.[275] Using guidance from literature regarding qualitative sampling and previous research considering similar cohorts and research area, an initial sample size of 20 participants was chosen.[276,277] The adequacy of the final sample size was continually assessed during the data collection process, when a point of 'data saturation' was established this was discussed with the principal investigator and recruitment to the interview study was closed.

### 3.4.1 Data saturation

Data saturation has realised acceptance as a methodological principle in qualitative research. However, there is uncertainty as to how saturation should be measured.[278] Saturation is defined within the literature in varying ways, at times it is not defined at all.[279] Saturation is most frequently defined as: 'the point in coding when you find that no new codes occur in the data'. This can further be explained as where there are mounting instances of the same codes.[280–282]

The concept of data saturation originates in grounded theory (GT) [283], but is now used across a range of approaches in qualitative

research.[284] Saturation is the most commonly billed measure of qualitative rigour offered by authors.[263,285,286] In this study the interview transcripts were coded at the same rate as recruitment, therefore the student was able to assess signs of data saturation during the transcription and coding processes. When the student believed that there were no new codes being generated from the interviews the principal investigator was informed. The study went on to recruit two further participants. This was to ensure that there were no new codes being generated from the interviews. When the student was confident that data saturation had been achieved, the principal investigator was informed and the recruitment to the interview sub-study was closed.

### 3.5 Recruitment strategy

Access to participants was facilitated through an existing working relationship with National Institute of Health Research Nottingham Biomedical Research Centre (NIHR Nottingham BRC).

Purposive sampling was used, seeking to maximise the depth and richness of the data to address the research question.[287] There are three main sampling techniques presented in qualitative literature; convenience, purposive and theorectical.[288] While many authors appear to share concurrent definitions of theoretical sampling,[289–292] employing and describing the theoretical sampling process can present a particular challenge to novice researchers. As such purposive sampling was selected as the next best option as a technique that has a more

coherent theory to follow and was better suited to the study resources and timeframe.

Participants from the main study were given a participant information sheet (PIS) (appendix 8.10) for the sub study when screening processes for the main study was completed. Only those participants with IBD and were considered fatigued were approached. Those participants who were willing to take part in the interview study expressed their interest and the interview was scheduled for a time that was most convenient for them. There were also participants that were approached from the NIHR Nottingham BRC expression of interest database. This is a database of people who have previously taken part in research who are happy to be contacted again to take part in future research. Only those who have a confirmed diagnosis of IBD were approached, and those who expressed an interest were screened and then those who scored as fatigued (>14) on the MFI questionnaire[148] were invited to take part.

### 3.6 Eligibility criteria

Participants were recruited from the 'IBD Fatigue' study (IRAS: 233733). Inclusion and exclusion criteria for the fatigued participants for both the main and sub study are detailed in table 3.1 below.

**Table 3.1: inclusion and exclusion criteria.**

| Inclusion criteria | Exclusion Criteria |
|---|---|
| • Aged 16-75 years of age<br>• BMI <30kg/$m^2$<br>• Diagnosed with CD<br>*in remission, as displayed by:*<br>• HBI score <4 [293]<br>• CRP <5 mg/L<br>• Faecal calprotectin <50 ug/g [294,295]<br>*Fatigued as defined by:*<br>• MFI-20 score >14 in any domain [148] | • HADS >8<br>• Haematological or biochemical abnormalities (E.g. Iron Anaemia)<br>• Renal failure<br>• Hypokalaemia<br>• Pregnancy of childbearing in the last 6 months<br>• Vitamin B complex deficiencies<br>• Active or previous prescriptions of corticosteroids in the last 12 weeks<br>• Overt muscle wasting (defined as 2 standard deviations outside the age-related norm as measured by DEXA)<br>• Fatigue starting after the onset of Thiopurine therapy<br>• Present arthritis or arthralgia<br>• Surgical intervention in the last 12 weeks |

It was decided that for the purposes of the main study, the patient sample would solely consist of patients with CD. This was decided because firstly, from an experimental perspective the study was underpowered to deconstruct the effect of the intervention by disease type. Moreover, the prevalence of fatigue is higher in CD than in UC which made recruitment more feasible.[40,296,297]

## 3.7 Methodology

A qualitative semi-structured interview study utilising thematic analysis (TA)[298] was chosen to explore participants experiences of IBD related fatigue and its impact on HRQoL.

### 3.7.1 Data collection

Semi-structured interviews allow for detailed accounts to be shared by participants, with scope for the student to follow up on potential areas for further discussion. Individual interviews are the most appropriate choice to discuss possibly sensitive health issues and associated experiences, compared to other types of qualitative data collection such as focus group work. Interviews are best suited to collecting information regarding peoples understanding, perceptions and eperiences.[299,300] There are broadly three types of interviews used in qualitative research; structured, semi-structured and unstructured interviews.[301]

In structured interviews, a list of pre-determined questions are asked to the respondent. The questions are not altered during the interview and no follow-up questions are asked to get an explanation on a given answer.[302] The strengths of this interview strategy are rapid data collection and analysis process due to the fact that there is little chance of either the interviewer or respondent to get deviated from the topic. This technique was not chosen for this study due to the lack of freedom to explore the topic through follow up questions and deviations from the interview schedule.

Un-structured interviews are conducted with little or no preparation. Interviews begin with an opening question, with the interview progressing by asking questions on the basis of the response of the first question. These interviews require the interviewer to form questions in such a way so that they will get the maximum detailed responses.[303] Unstructured interviews are very time consuming and they usually last for a number of hours, and are difficult to participate in and manage due to the lack of pre-determined questions.[304] This type of interview technique was considered for this research study; however, it was deemed too time consuming, with not enough structure for the student and it was felt it would not provide such different data from that acquired from undertaking a semi-structured interview technique.

Semi structured, in-depth interviews are the most widely used interview format, most commonly they are only conducted once for an individual and take between 30 minutes and several hours to complete.[300] Interviews are organised around a set of pre-determined, open ended, questions, with other questions emerging from the dialogue of the interview. Interviews are conducted in this manner to gain greater clarification through exploration of detailed descriptions of the studies topic from participants.[287]

The iterative nature of the qualitative research process in which preliminary data analysis coincides with data collection can often result in alterations to the interview questions as the researchers are able to better focus the interviews questions according to the topics emerging

as data collection progresses. Furthermore the interviewer should be prepared to deviate from the prepared questions during the interview as digressions can be productive as they follow the interviewees' interests, knowledge and experiences.[305,306] This often takes shape using a process called reflective questioning.[307] Reflective questioning creates opportunities for individuals to reflect aloud, be heard by one or more colleagues, and be prompted to expand and extend thinking through follow-up questions.[308]

### 3.7.2 Data analysis

Given the lack of previous research exploring fatigue in IBD and its impact on HRQoL, TA was considered a suitable method to gain an overall exploratory understanding of the pattern of experience in this population.

Traditionally TA has been seen as a process performed within major analytic traditions such as GT[309,310], however more recent work, particularly in the field of psychology, have framed TA as a method in its own right.[298] In contrast to other exploratory methods such as interpretive phenomenology, which follows an in-depth, idiographic approach, TA allows greater flexibility to include participants from a somewhat heterogenous background.[311] This was considered important for the present research, seeking to gain an overall insight into the experience within the IBD population rather than a particular sub-group.

TA is a method for identifying, analysing and reporting patterns within data.[309] There is general agreement that TA, much like GT, should include interleaving between data gathering and analysis and that theory should be formed from data through a process of perpetual comparative analysis.[292,312–314] [315]There are no set rules to conduct a study or way to gather and analyse data, nor is there a set way to achieve validation of the research.[316] Rather, there are methods of data collection and analysis that are more or less suited to meet the research question.

TA differs from other analytic methods that seek to describe patterns across qualitative data, such as framework analysis, content analysis, interpretive phenomenological analysis (IPA) and GT. Both GT and IPA seek patterns in the data, but are theoretically bounded.[317,318]

The Framework Method is becoming a more frequently used approach for management and analysis of qualitative data in health research due to its use in multi-disciplinary and mixed methods studies which are becoming increasingly commonplace in applied health research.[319] Framework method was developed by researchers for use in large-scale policy research.[320] Framework analysis does not allow for creation of themes based on the data, instead it facilitates constant comparative techniques across a matrix of *a priori* themes.[319] This method was not appropriate as the aim in this study was to explore

patient perspectives, without the use of *a priori* knowledge or themes which might influence the findings of the study.

Content analysis looks directly at communication through analysis of texts, and allows for translation between qualitative and quantitative operations, this can be useful when considering statistical tests for analysis. However, Content analysis is extremely time consuming and is prone to being lacking in theoretical base.[321] It can be difficult for researchers to draw meaningful inferences about the relationships and impacts implied in a study as Content analysis is inherently reductive and relies heavily on word counts.[322] Therefore neither framework method nor content analysis were appropriate for use in an exploratory research question.[323]

An inductive, semantic TA was designed, in accordance with the research question and the researcher's epistemological position. An inductive approach means the themes identified will be strongly linked to the data, without trying to fit into pre-existing coding frame.[324]

### 3.8 Research process

After completion of the TA, leading to the development of a thematic map, results from the TA were compared to the findings of the systematic review. Although presented as though chronological, the systematic review and interview study occurred concurrently, so as one could not influence nor bias the other.

### 3.8.1 Data Collection

#### 3.8.1.1 Interview preparation

Interview preparation is important, in particular the preparation of an 'interview schedule' (Appendix 8.6). The focus is on identifying topics to be covered rather than particular questions. This follows positivist methodology, rather than the constructivist view that knowledge is created and negotiated through the conversation between the interviewer and the interviewee.[277] The main difference between constructivism and positivism is that positivism argues that knowledge is generated in a scientific method, whilst constructivism maintains that knowledge is 'constructed' by experts and it opposes the idea that there is a single methodology to generate knowledge.[325,326] Qualitative positivism employs nonquantitative methods of data collection, such as interviews, and observation within conventional positivist assumptions about the nature of social reality and the production of knowledge.[72] Reality is assumed to be definite, detached from the researcher, and understanding is sought through the use of "objective" methods of data collection.[327–329]

During in depth interviews it is necessary for the interviewer to develop rapport with the interviewee.[330,331] Rapport involves trust and respect for the interviewee and the information they share. It is a means of establishing a safe and comfortable environment for sharing experiences.[287,301,332,333] Establishing this rapport can be difficult, particularly if the participant is nervous or feels uncomfortable. The

challenges that face the researcher in establishing rapport with the participant are ensuring the correct environment, introduction and interview process.

There were numerous challenges faced by the student. It was sometimes a struggle to book an interview space in the research unit as it is a busy outpatient department. This added to the difficulty in establishing times and dates that were appropriate for both the participants and the student. This was overcome by the student providing as many times and dates for participants to choose from, and prompt booking of interview rooms to avoid having to alter appointments or change plans with participants. This encouraged participants to keep their appointments and prevented any drop out or withdrawal of participants.

An unforeseen issue was the student's familiarity with some participants; the student had worked with some of the participants in the professional role of research nurse. This familiarity might have led to some participants feeling uncomfortable sharing personal and potentially intimate details. This was overcome, to the best of the student's ability, by reminding the participants that their contributions to the study would remain anonymous outside of the interview room, all participation is voluntary and establishing a rapport consistent with conducting an interview.[334]

#### 3.8.1.2 Interview process

The interview process comprises of 6 stages; arrival, introduction, starting the interview, during the interview, ending the interview and after the interview.[335] The arrival and meeting of the interviewer has a crucial effect on the success of the interview. Participants must be put at ease as mentioned above. Participants received the PIS for the interview study during their screening for the main study. Early introduction of the study information ensured that the participant was aware of the purpose and level of their involvement. Verbal consent was obtained in order to book the time and place for the interviews. Valid informed consent was received by the student on the day, prior to undertaking the interview.

When beginning the interview, it was important to establish background information to contextualise the interview.[315] This enables the researcher to access a deeper understanding of the data, and also guide the interview and interview questions in order to obtain richer data.[315] During this phase, broad open-ended questions were used to help the participant establish confidence. This helps the participant 'settle into' the interview, reducing feelings of anxiety and increasing their willingness to share detailed responses.[336]

The themes of interest shaped the interview, the direction and content of the interview was dictated by topics that arose and were deemed interesting and relevant by the interviewer.[320] This enables the

interviewee to provide detailed, in depth responses to questions that are also sensitive to the nature of the topic.[337] Continuity of theme is important as participants are likely to be thinking in a focused way about topics they don't naturally consider in as much depth. During the core phase of interviewing a technique used to help with recall, the critical incident technique[338], was used to extract details of specific incident or examples. This involved asking people to focus on the details of specific incidents rather than generalisations and allowed the collection of much more detailed responses than might have been given with open ended questioning.

In the lead up to the end of the interview it was clearly signalled to the participant by stating "we are coming to the end of the interview now" during the conversation. Participants were always asked 'do you have anything else to add?'. This allowed participants to wrap up conversation, making any final statements. After the close of the interview the participants were thanked for their time and contributions.

Interviews were digitally recorded, and later transcribed by the student. Careful consideration was given to the placement of the recorder and the environment that the interview was conducted in order to reduce such issues as poor recording quality and background noise.[339]

#### 3.8.1.3 Transcription and field notes

Following the interview, the student transcribed the digital recording, destroying it afterwards. Through the student completing her own transcription it offers an additional opportunity to familiarise with the data.[340] Transcribers often have difficulty in converting the spoken word into text form because of sentences structure, the use of quotations, omissions and mistaking words or phrases for others.[340] This raises the issues of editing transcription text. There are general transcriptions conventions that the student followed, the use of punctuation and capital letters, and devices used to communicate how the transcriber heard the spoken word, such as using a series of dots to indicate a pause.[341] The transcripts represented the recordings with as little editing as possible in order to best mirror the spoken word. The student has taken into consideration the balance between editing and readability of the transcription, as well as confidentiality and ethical practice. To enhance readability, some researchers choose to remove idioms such as the 'ums' and 'ers' and 'you know', as well as the repetition of words that occur naturally during conversations. One argument for doing this was that reading such words would be tedious, there are pragmatic reasons such as reducing word counts. However the student chose to use the 'light tidying-up' technique, leaving in the verbal hesitations as they add context to the discourse and are important for the TA.[342] To maintain confidentiality, with no loss of contextual data, only those quotes that represent specific places, names or other recognisable items were edited, replaced with general

or explanatory terms in square brackets.[343] Consideration was given to spoken words that might seem very different in comparison, for example words from regional dialects, speech patterns and impairments.[342] There were no incidences of these throughout the transcription process, however the student had previously decided that in such circumstance the students would have transcribed the spoken words phonetically, as it was believed that altering the language may have changed some of the context in the information presented.[342,344,345]

### 3.9 Data Analysis

The six phases of TA were followed and revisited several times in a recursive process to develop final themes.[298] These phases are presented in the next section. Given the substantive dataset generated from the study, coding and organisation of the data was conducted within NVivo 12 software. Computer assisted qualitative data management software is a recent development.[346,347] Software programs do not analyse the data but are aids in the management and analysis process. Use of data management programmes can save time, make procedures more systematic, reinforce completeness and permit flexibility with revision of analysis procedures.[348]

### 3.9.1 Familiarising with the data

To aid the familiarity with the data and for consideration of additional contextual information such as emotion and other non-verbal cues, reflective journal entries pertaining to each interview were revisited and transcripts were checked for accuracy against audio recordings.

### 3.9.2 Coding the data

The coding process involves theme identification through reading and re-reading of data. Emerging themes become the categories for analysis.[349] The method of coding chosen for this study was the data-driven inductive approach.[309] This complements the research question by allowing themes to emerge directly from the data. Deductive *a priori* template of codes approach was not used.[350] This involves a template of codes from a codebook to be applied as a means of arranging text for interpretation. When using a template, the codebook is defined before commencing in-depth analysis of the data. As this was an exploratory research question, a framework was not used as this did not allow for emergent themes to be produced.

The coding process involved identifying an important element within the text and encoding it prior to the process of interpretation.[309] An important element within the text is a 'good code' if it captures the qualitative richness of the phenomenon being discussed.[309]

Transcripts were coded line-by-line, assigning sections of data to a code which summarised the material according to what each extract

revealed. However, it is unavoidable that the student held the research questions in mind throughout the process, introducing an element of bias. Encoding the information organises the data to identify and develop themes from them. Examples of coding are available in appendix 8.7

### 3.9.3 Searching for themes

Fifty-three codes were generated from the data. Many were found to have significant overlap and were merged. After complete coding of the dataset had been conducted, some codes were considered less prominent to the research question (e.g. relating to medications) and were removed from analysis. Codes were restructured and grouped within the NVivo programme. Code names were printed to enable more visual freedom in moving codes to create a dynamic thematic map.[309] Themes emerged as codes were repeated, becoming prominent, other codes were not repeated and became less prominent. All codes were used in the generation of themes. Various stages of this process are shown in Appendix 8.8.

### 3.9.4 Reviewing themes

Through generation of a thematic map, the analysis process returned to the NVivo programme to group codes into prospective themes. These were altered as analysis progressed. This afforded the opportunity to review the thematic map in terms of how each data item contributed to each theme. As a whole, the majority of participants contributed to each

theme. Themes were provisionally named, and extracts collected for each from the data. Particular attention was paid to internal homogeneity and external heterogeneity of themes to ensure that each contributed something meaningful with minimal overlap.[298,324]

### 3.9.5 Defining and naming themes

During this process the student engaged with research supervisors to support reflexivity and gain clarity over derived themes. Reflexivity is commonly viewed as the process of a continual internal dialogue and critical self-evaluation of a researcher's position as well as active acknowledgement that this position may affect the research process and outcome.[351,352] The role of reflexivity is further discussed in chapter 6.

### 3.9.6 Producing the report

The report aims to provide a convincing narrative of the researcher's interpretation of the data. To accurately reflect the voices of the participants, the student followed the established practice of using quotations in qualitative research.[353] the use of verbatim quotations is discussed further later in this thesis.

### 3.10 Production of a thematic map

Thematic maps are utilised to display extraction of basic themes, organising/sub themes and main themes.[314] This is a widely used procedure in qualitative analysis. Thematic maps do not aim to uncover rationalisations for findings, instead providing a technique to visualise themes and find explicit connections and their significance to the analysis.[354] The three classes of themes can be described as follows: Basic themes are the most basic or lowest-order theme that is derived from the textual data and individually say very little about the text or group of texts as a whole. Sub themes are middle-order themes that organise the basic themes into groups of similar matters. Sub-themes are more revealing of context within the texts. Main themes represent sections of the texts as a whole. A set of texts may well yield more than one main theme, depending on complexity of the data and analytic aims.

A thematic map was developed starting from basic themes and working inwards toward a main theme. Thematic maps are presented graphically as web-like nets to remove any notion of hierarchy, giving fluidity to the themes and emphasizing the interconnectivity throughout the analysis. Importantly, however, the maps are only a tool in analysis, not the analysis itself.[205,355] The thematic map will be presented in the results chapter.

### 3.11 Ethical considerations.

The study was conducted in accordance with ethical principles that have their origin in the declaration of Helsinki, the principles of good clinical practice (GCP) and the framework for Health and Social Care.[356,357]

The student identified and responded appropriately to ethical principles of research with human participants throughout the study: respect for participants, valid informed consent procedures, specific permission required for audio recording, voluntary participation and no coercion, full disclosure of funding sources, the presumption and preservation of anonymity, data protection, provision of grievance pathways and appropriate and full reporting of methods.

There are four main ethical issues related specifically to an interview study; Reducing risk of harm, protecting participants information, fully informing participants about the nature of the study and reducing risk of exploitation.

Participants were fully informed that their interview would be digitally audio recorded. The process was altogether described in the PIS, informed consent form and was reiterated verbally directly prior to the interview. Digital recordings of interviews were destroyed following transcription. Informed consent, the avoidance of deception, the right to withdraw, debriefing and confidentiality are primary considerations in

ethically conducting research.[316] Having participants sign an informed consent helps to maintain professional boundaries.[358] Maintaining confidentiality of participants study contributions was of paramount importance. Some authors argue that the nature of data obtained from in depth interviews can limit confidentiality as utilising pseudonyms or changing key characteristics is not always sufficient to guarantee anonymity.[359] Therefore particular attention was paid to redacting or replacing key information such as place names, employment details and locations.

There are also pragmatic safety issues that were considered when undertaking this interview study, such as the positioning of the researcher in the room when interviewing.[360] For safety, the researcher should always be positioned closest to the exit with a barrier (often a desk) in between the interviewer and the interviewee. These attentions were already in place as standard procedure in a healthcare setting.

### 3.12 Summary

A CR position was assumed to undertake qualitative semi structured interviews of adults with IBD fatigue. The study had approvals from REC and HRA. Sample size estimated to be 20 based on previous work and literature. Final sample size was realised through the concept of data saturation, resulting in 14 participants being in recruited. Purposive sampling was used to recruit participants from the 'IBD fatigue' main study and the expression of interest database at the

Nottingham NIHR BRC. Participants were screened and presence of IBD fatigue confirmed using questionnaires. TA was used to generate themes from interview transcripts. The student undertook interviews, transcription, TA and generation of a thematic map. Results are presented in the next chapter.

## 4. Interview study results

### 4.1 Interview characteristics

Interviews took place between 14-09-2018 and 12-07-2019. Interview duration averaged 53 minutes and 46 seconds, with a range of 37:18 - 62:24 minutes. Interviews were conducted in an interview room within the Nottingham NIHR BRC.

### 4.2 Sample characteristics

Interviews were conducted with fourteen participants. There were nine females (64%). All participants identified themselves as of a 'White British' ethic origin. Respondents were an average of 37.3 years of age, with a range of 21-64 years. Symptoms of IBD fatigue were experienced for an average of 10.9 years. Eleven (79%) participants reported that fatigue was constant and three (21%) reported Intermittent fatigue.  Further sample demographics are shown in table 4.1.

**Table 4.1:** Sample characteristics

| ***Sample characteristics*** | | ***sd*** |
|---|---|---|
| Age in years, mean *(sd)* | 37.3 | *13.5* |
| Female gender (%) | 64 | |
| ***Disease status*** | | |
| Mean HBI score *(sd)* | 2 | *1.5* |
| Average disease duration (mean time since diagnosis of IBD in years) | 9.2 | *7.4* |
| ***Fatigue status*** | | |
| Mean length of time fatigue has been present in years *(sd)* | 10.9 | *4.6* |
| Reported constant fatigue symptoms (%) | 79% | |
| Reported intermittent fatigue symptoms (%) | 21% | |
| Mean MFI-20 score *(sd)* | 12.5 | *2.6* |
| Mean IBD fatigue scale score *(sd)* | | |
| Section 1 | 9 | *5.4* |
| Section 2 | 47 | *15* |
| ***Medications*** | | |
| Immunosuppressants (%) | 36 | |
| Biologicals (%) | 21 | |
| Aminosalysate (%) | 7 | |
| Antidepressants (%) | 14 | |
| ***Employment status*** | | |
| full time Working/Student (%) | 86 | |
| Part time (%) | 14 | |
| unemployment (%) | 0 | |
| ***level of education*** | | |
| A level or equivalent (%) | 50 | |
| Degree level (%) | 21.5 | |
| Postgraduate level (%) | 21.5 | |
| Doctoral level (%) | 7 | |
| ***Surgical intervention*** | | |
| Ileostomy (%) | 7 | |
| Ileal resection (%) | 29 | |
| Hemicolectomy (%) | 7 | |
| ***Relationship status*** | | |
| Married (%) | 36 | |
| Relationship/Co-habiting (%) | 28 | |
| Single (%) | 36 | |
| ***Smoking*** | | |
| Never (%) | 79 | |
| Past (%) | 14 | |
| Current (%) | 7 | |

**Key: (%)**=percentage of total sample (N=14); ***(sd)****= standard deviation;* ***HBI****= Harvey Bradshaw Index Score;* ***MFI-20****= Multiple Fatigue Inventory- 20 questionnaire;*

### 4.3 Use of verbatim quotations

It is suggested that using quotations enhances the validity of the conclusions made. Showing how the findings emerged establishes an 'audit trail' and could contribute to strengthening reliability of the findings.[344] One limitation of relying on direct quotations to provide evidence is the length of the selected quotations could be constrained by space available for publication. There are contrary beliefs regarding this use of quotations to evidence a specific point of view. It could be argued that in most series of interview transcripts, a researcher would be able to find at least one quotation to support any point they might wish to make.[332]

Verbatim quotations offer readers greater depth of understanding and help illustrate why a person has particular views or perspectives.[342] Individuals' spoken words can display strength of views or depth of feelings or, on the other hand, passivity and lack of engagement in ways that the researcher's own narrative could not.[361] While the researcher might describe findings using terms such as ''fatigue' or 'lethargy' when describing findings, the actual words spoken were often a better representation of the depth of feeling.

Commitment to giving research participants a voice was a priority for the student. Enabling individuals to put across their own definitions and understanding of the impact of health on their day-to-day life was important. Presenting verbatim quotations in this context provides the

opportunity for people to express their feelings or beliefs in the way that they themselves perceive them.[342] Giving people a voice by using their spoken words is also a way of demonstrating the value in what they say, and their contribution to the study and its findings.[343] Some believe that participants' spoken words have more impact than researchers narrative in conveying life experiences to readers.[277,362]

There is structural benefit in using quotations, breaking up a large passage of text by inserting spoken words may keep the readers focus.[340,361] The use of TA leads to the expected breakdown of transcripts into smaller quotes and sentences. This may, however, take way some of the continuity of flow which may be a disadvantage in explaining interpretation of meaning. The student had to make decisions about how far to break up the interview transcripts into verbatim quotations, and how to weave these into the text in a way that best represented the findings from the thematic analysis.

### 4.4 Themes

Data analysis resulted in identifying three main themes and eight sub-themes (figure 4.1). The process of theme generation is displayed in appendix 8.9.

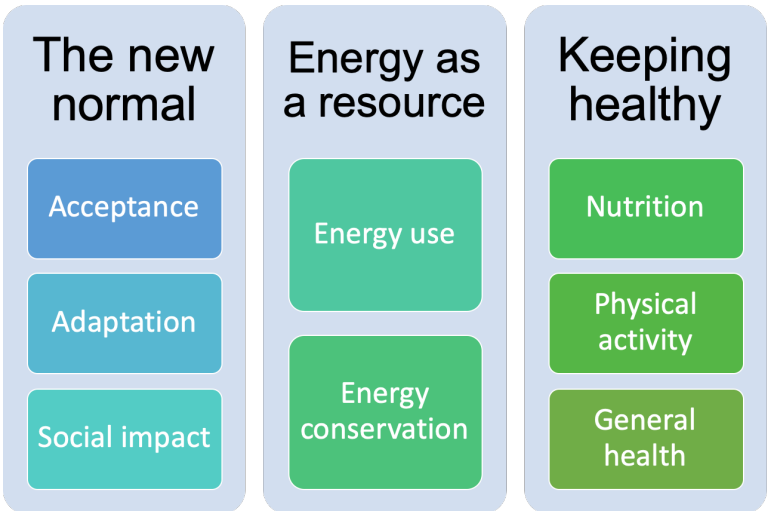



Figure 4.1: Main themes and sub-themes.

#### 4.4.1 Theme 1- The new normal

Participants described how living with IBD fatigue had become 'normal' for them. A sense of a 'new normal' has been established through acceptance of IBD fatigue and adaptation in everyday life, most obviously affecting social interactions. One participant reported that through undertaking the interview study it *"made me realise how much [IBD fatigue] does affect me, and how normal it has become*" (IT06).

##### 4.4.1.1 Acceptance of fatigue symptoms

Participants described and defined IBD fatigue in their own words Descriptions related to how fatigue made them feel and the impact on day-to-day activities. Definitions used language to describe the physical

feelings of fatigue; *"Like I am wearing a heavy coat all of the time"* (IT14) and *"I feel like my bones are heavy and I am tired all over"* (IT08). In attempts to understand how IBD fatigue impacts cognitive function and mental ability, respondents were able to describe the impact fatigue has on daily activities such as "*fatigue is a blanket that covers every kind of thing I try and do*" (IT04). Participants described differences between tiredness and fatigue; *"fatigue is much worse, like a whole-body lack of energy, tiredness can pass but fatigue sticks around no matter what I do"* (IT08).

Participants were keen to distinguish the differences between 'physical' and 'mental' fatigue, putting into their own words how the different kinds of fatigue impact on their day-to-day life:, "*I think I am just much better at managing my physical symptoms and maybe just get on with my mental fatigue*" (IT03). Some described how physical and mental fatigue are equally debilitating "*Fatigue leaves me completely drained, I can't focus just as much as I can't really do much physically*" (IT07), and were able to describe how this impacted on their day-to-day life, "*I struggle quite equally with the two different kinds of fatigue, it's just as difficult for me to get out of bed some mornings as it is for me to focus on something at work".*

IBD fatigue was accepted and its impact on their ability to undertake daily tasks at home, *"I have just come to accept it, it is a way of life now"* (IT13), and at work *'there's no question, I definitely can't do as*

*much as I used to do"* (IT02). However, there was a sense of resilience and persistence with participants reporting *"I don't let my symptoms stop me from doing what I want"* (IT02). Motivation to keep up with the same daily activities as before IBD fatigue and in comparison, to those without fatigue, was important to participants, *"I just don't let it get on top of me. It's the motivation thing, so long as I keep going, embrace the fact that things will take a bit more effort for me to do the same things as other people do"* (IT03).

#### 4.4.1.2 Adaptation

The most predominant adaptation discussed was making plans; "*if I plan and use my day wisely it means I have enough energy left at the end of the day for more fun things*" (IT11). Making plans allowed participants to take control of their day-to-day life; "*I can take control of my workday, manage my day better*" (IT11) and "*I make plans so that I don't let my Crohn's dictate my life*" (IT13).

Adaptation comes about from previous maladaptive techniques such as all or nothing behaviours "*I used to think about what I wanted or needed to do the most and then I would do that and hope that I had enough energy left to do the rest, if I didn't I would cancel plans or call in sick to work, I did my best to stop doing that as that's unhealthy behaviour*" (IT13). Some participants acknowledged that utilising adaptive behaviours requires greater effort " *[fatigue] makes things harder to do, it takes more effort, both in the actually doing the thing, like going out or*

*making dinner, but it takes times to plan it too. I have to put in a lot of effort planning*" (IT03).

Adaptation involved establishing new limits *"I plan to do enough with my day so that I am tired, but not exhausted, I know my limits"* (IT09) and constructing new behaviours utilising management techniques with planning, "*pacing [myself]"* (IT01) and building in opportunities for rest being the most utilised techniques, "*I take my time, plan and make sure I can have a rest*" (IT02).

Adapting encompassed activity at home, at work and during leisure time. Participants reported establishing a "*Crohn's routine*" (IT02) at home. During work activity participants reported they were better able to adapt if they had established relationships with their colleagues and managers "*good working relationship with by boss that I can do the things that I can do"* (IT02). Participants reported that leisure time was dictated by the availability to "*rest and take time off work, and try and plan things as far in advance*" (IT03).

#### 4.4.1.3 Social impact

IBD fatigue appears to have a significant impact on social interactions. "*It has the biggest impact on my social life*" (IT04). Planning and engaging with social events, intimate relationships, level of understanding of IBD fatigue of family friends and colleagues and feelings regarding guilt were all affected. One respondent reported that

they felt that interacting socially actually alleviated feelings of fatigue "*laughing and joking and seeing my friends helps me feel better*" (IT08).

Intimate relationships appear to be particularly impacted by IBD fatigue; participants reported that high levels of fatigue can lead to extended periods of little to no intimate relations with partners- "*when I'm really worn out it can be weeks where we don't do anything*" (IT06),adding to the feelings of isolation due to IBD fatigue. Weekly routines designed to prioritise work can de-prioritise intimacy: "*we don't really spend any time together in the bedroom, except for weekends*" (IT05).

The understanding of IBD fatigue by family, friends and colleagues was reported as important to participants throughout the interviews. Most reported that they felt that they had good social support, often the understanding of the disease was still lacking; "*I think that they understand that I have an illness that can mean I can't always do things with them, but I don't think that they actually understand the disease*." (IT10), "*It took a long time for me to make people understand how unwell I felt*" (IT11). This could add to feelings of isolation. Not all participants reported a lack of understanding, one participant reported that their partners understanding and appreciation of the impact of IBD fatigue "*has contributed to us being close*" (IT07). Support of colleagues has been discussed in the adaptations sub-theme, but it was also reported as a way of alleviating fears of social stigma in the workplace, '*I felt I was able to say I don't feel like I can do that, and I didn't get*

*judged or laughed at*" (IT09). This might contribute to a sense of normality that is so often reported as the aim for patients with IBD.

Respondents stated that they were often left feeling guilty over missing or cancelling social engagement due to IBD fatigue, "*I feel like I am letting my friends down, and they don't deserve to have their evenings ruined by my health, or lack of it*." (IT14). Guilt could relate to either having IBD fatigue or how the IBD fatigue impacts on individuals, or both, but it was clear that participants are very affected by feelings of guilt.

Some participants discussed worries related to how they would be perceived by others, "*I worry about looking like I am always ill, like the flaky friend who is constantly cancelling plans*" (IT08). Participants often based this feeling on comparison to others, "*I feel like I get much more tired, more quickly, than those around me, and it can be annoying and sometimes embarrassing*" (IT05). Very often this was related to the workplace *"I don't want people to think any less of me, like I can't do my job, like it is something that stops me from being able to do things like other people can*" (IT11). This could lead to feelings of lessened self-worth, lowered self-esteem and reduced motivation to maintain social relationships and interactions, even though participants acknowledged that these are important to them.

### 4.4.2 Theme 2 - Energy as a resource

Throughout the interviews participants referred to 'levels of energy' and how these are utilised by prioritising activities and conserved through planning tasks. Most of the participants referred to energy as a commodity, this belief might be a way of contextualising and understanding fatigue, and may also be way of better communicating fatigue to others. A prominent feature of most interviews was that participants believed that they were perpetually at a 'deficit' in terms of levels of energy; "*I feel like I start off with a negative balance anyway, like I wake up in the morning and I already don't have enough energy to make it through the day before I have even done anything*" (IT05).

#### 4.4.2.1 Energy use

Energy use was discussed in terms of allocating certain amounts of energy to each task, then prioritising each task. "*every task I do has to be weighed up in terms of how much time and energy it will take to complete it*" (IT11). This is based in the reports that participants reported that they felt they could "*run out of energy quickly*" (IT13).

Often employment or studying was prioritised over other tasks and activities; "*I give all I have got at work which leaves me really tired and with no energy left for outside of work things*" (IT06). Only one participant reported "*I try and strike a balance between my work life and home life"* (IT11). If individuals are not able to enjoy an active social or personal life outside of work this could contribute to low mood, lack of social interaction and lowered self-esteem. Without frequent social

interaction participants could start to lose a sense of self and become trapped in an unhealthy, maladaptive pattern of attempting to manage their IBD fatigue.

Prioritising tasks often is dependent on current perceived levels of energy, this suggests that participants are very self-aware in terms of their health and the impact of IBD fatigue on daily life "*the way it affects me the most is my motivation. I feel worn out, so I don't do things that at the time don't seem essential*" (IT10). Even after prioritising tasks, average daily tasks often required extra effort; "*I really heave to push through it and just get on with what I need to do, it takes extra concentration and effort, but I can do it so long as I give myself plenty of time to look after myself*" (IT12).

All or nothing behaviours were prevalent throughout the interviews, particularly regarding daily tasks at home such as housework. "*By the time I get home I don't have any energy left to do anything around the house*" (IT05). This type of behaviour was often weighed against the need for energy for ongoing daily tasks, or activity over subsequent days; "I *start out at a deficit, if I then go and blow all of the energy I have on doing all of the washing and hoovering and cleaning in one go then I won't be much good for the rest of the day, or even the day after*" (IT13). The abundance of all or nothing behaviours suggests that there is a lack of awareness of fatigue management techniques, such as poor task prioritisation or lack of motivation.

#### 4.4.2.2 Energy conservation

Participants reported that 'making plans' was integral to maintaining a sense of 'normal' and achieve all daily activities. "*I plan what I need to do each day and make sure I have enough energy to be able to do all the things I want to do*" (IT08). Again, encouraging and maintaining motivation to undertake tasks was important to participants "*it's important for me to plan ahead, set small goals and work towards the next one, it keeps my motivation up to keep going*" (IT13). Preparing to undertake daily activities was important for individuals; "*I plan around what jobs I have to do on that day, or that week, try and space out the big jobs, make sure there's time for me to build up the energy to do them, or have time after a big job to recuperate*" (IT07).

One of the main management techniques employed was to introduce more rest into their daily routine; "*I just have to make sure that I have to rest, sleep, to make sure I have time to catch up on my sleep and have the energy to go to work the next and the next days jobs*" (IT12). As aforementioned, participants often felt like they started at a deficit in terms of amounts of energy, and felt that extra rest would help them to recoup expended energy, "*I focus on getting my energy back so I can start the next day a fresh*" (IT07). Some participants reported that they were unable to incorporate rest into their daily routine which impacted their ability to undertake daily tasks; "*I feel like I don't have the time to rest during the day*" (IT05), "*I don't get time to build in rest times*" (IT06). Although some participants discussed extra rest being a means of

recuperating and restoring energy levels, most participants agreed that even after building in rest periods they were unable to feel well rested; "*incapable of catching up on the energy I am using up*" (IT03).

Energy conservation techniques reported included tendency to 'sacrifice' the undertaking of an activity, either by not doing it, "*I do just write things off as too much effort*" (IT06), or cutting it short. Participants reported this was most frequently leisure or social activities; "*[don't get the chance to do] fun things I guess*" (IT10), "*I don't stay out for long*" (IT12). This type of behaviour could contribute to reduced self-esteem and low mood.

### 4.4.3 Theme 3 - Keeping healthy

#### 4.4.3.1 General health

Participants reported that having a good general health was beneficial for them as it helped them to overcome the feelings of fatigue; *"I think maybe I have a good level of general fitness, so I have a better ability to be able to compensate for fatigue*" (IT09). For one participant this was her top priority during her daily activities, "*it doesn't matter about much else so long as you make sure you're looking after yourself and keeping yourself well*" (IT14).

Most participants reported that they were able to maintain a good level of personal care even when experiencing high levels of IBD fatigue.

However, two participants reported that high levels of IBD fatigue would impact on their choices regarding personal care. One participant reported that they would postpone the task until they had rested, "*"ll skip having a shower and go straight to bed and shower the next day if it's really bad*" (IT10). The other reported that they de-prioritised and sacrificed this personal care due to fatigue, "*sometimes "ll sacrifice having a shower if I don't need one, or shaving and go with a slightly more rugged look if it means I can have more time in bed'* (IT08).

#### 4.4.3.2 Nutrition

Maintaining good nutrition was important for many of the participants interviewed. Respondents reported that the ability to eat and cook nutritional food was impaired by high levels of IBD fatigue; "*I don't want to use the last of my energy on cooking us something to then not be able to eat it and enjoy it -If it takes longer than 30 minutes to cook then I'm not going to make it*" (IT03). There is the potential that nutrition is overlooked in favour of maintaining a functional ability; "*I struggle to concentrate, and heavy meals make it worse*" (IT05). These reports suggest that nutrition is of lesser importance to some participants. Conversely, the majority of participants reported that they ensured they maintained a healthy diet as they believed this would help them reduce levels of IBD fatigue and/or improve the ability to manage IBD fatigue; "*I can plan my day around making sure that I eat properly*" (IT11). Interestingly the task of cooking was often prioritised by participants suggesting this was seen as more important to participants than social

or leisure activities, "*I will always put in the effort to cook something from scratch, get as much healthy food as I can*" (IT14).

#### 4.4.3.3 Physical activity

Many participants reported that physical activity was important in order to be better overcome the feelings of IBD fatigue; " *I think by keeping up regular exercise it keeps me healthy, making it easier to get through that heavy fatigue feeling*" (IT13). Also it was seen as important to have a good level of physical health to be able to manage IBD fatigue as participants felt they would be in a better 'starting' position, "*I find that it's important for me to keep up a level of fitness so that I'm starting off from a good point. If I let my physical fitness decline, I think it would be harder for me to get over physical fatigue*" (IT11).

Respondents reported that physical activity reduced levels of IBD fatigue; "*I can sometimes feel like I have a little more energy, like I have managed to access some reserves in my body, sometimes that helps*" (IT05). One participant reported that undertaking physical activity gave them a sense of achievement; "*When I go to the gym, I do feel better in myself, like I have achieved something"* (IT04). This sense of achievement could encourage feelings of accomplishment and bolster motivation. Participants reported that keeping up a level of physical activity/exercise was something that they included in their planning and that it was just as important as other factors, such as rest, that have an impact on levels of IBD fatigue; "*I like to go to the gym, I try and go at*

*least three times a week. I find keeping active helps me stay at a healthy active level, if I stopped or slowed down, I think I would stop altogether. For me it is just as important to stay active as it is to get lots of rest. It is a momentum thing*" (IT03).

### 4.5 Thematic map

Through analysis and the grouping of themes as described above a thematic map was developed, as shown in figure 4.2.

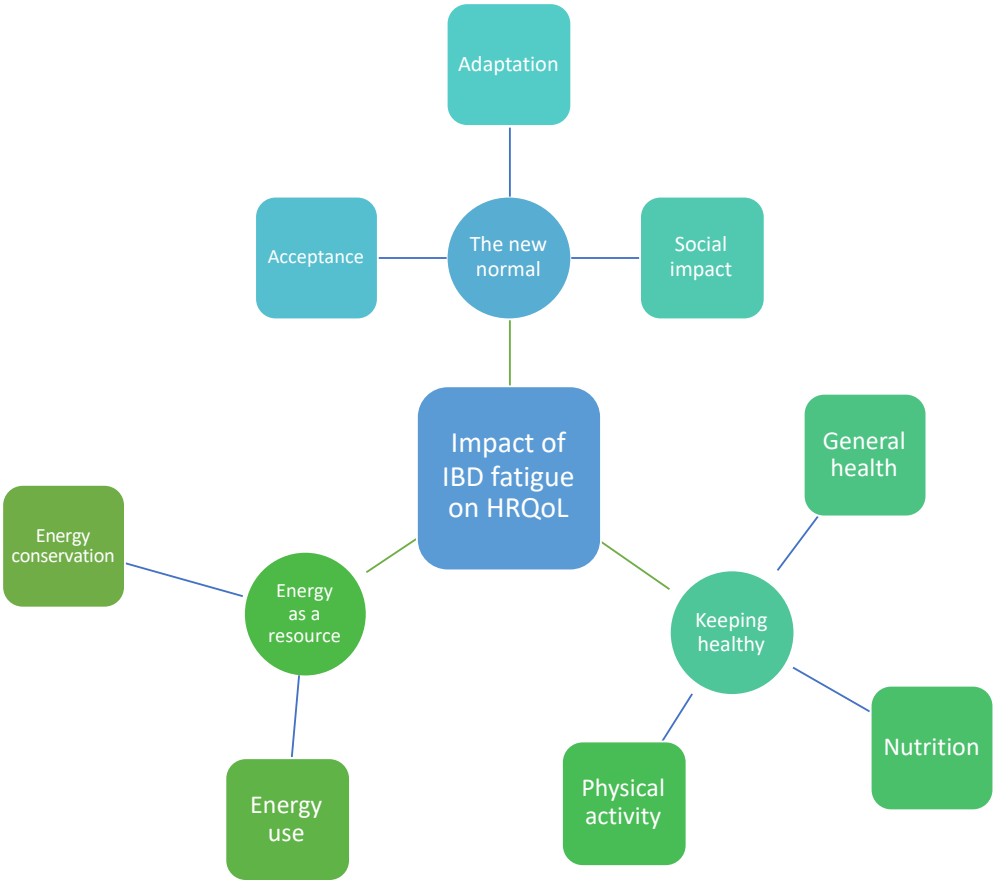



Figure 4.2 Thematic map.

## 4.6 Summary

Thematic analysis of 14 semi structured interviews resulted 53 basic codes, which further developed into three main themes named ‘The new normal’, ‘keeping healthy’ and ‘energy as a resource’. The main impact on participants appeared to be lack of social interaction, lack of motivation and negative impact on self-esteem.

The factors of HRQoL most impacted on by IBD fatigue were alterations made to daily activities through incorporation of management techniques into daily routine and the negative impact on social activities and relationships. Amalgamation of factors contribute to an individual’s sense of lack of control regarding their health. Individuals undertake self-management techniques to try and take back control of their health and symptoms, though techniques can be ineffective, potentially worsening HRQoL.

In the next chapter these results will be discussed in the context of the wider IBD and other LTCs literature.

## 5. Discussion

This chapter will discuss and summarize the findings of this research work in relation to the wider literature in IBD and other, relevant, LTCs.

### 5.1 Themes derived from the systematic literature review and interview study

Themes from the systematic review were “symptom acceptance and management”, “psychosocial well-being” and “physical activity”. These are comparable to the major findings from the interview study where data analysis lead to development of three main themes: “The new normal”, “Energy as a resource” and “Keeping healthy”.

This suggests that the main factors that impact on HRQoL, are developing a sense of ‘*a new normal’* through *symptom acceptance,* managing limited *energy resources* through *symptom management*, and efforts to improve *general health*, through *physical activity* and *psychosocial well-being*, These factors will now be discussed in relation to the wider literature in both IBD and other LTCs.

### 5.2 Interpretation of findings in relation to wider literature

IBD fatigue affects every aspect of an individual’s life and has a detrimental effect on HRQoL.[73,75,171] Impact of IBD fatigue on HRQoL extends beyond the impact upon the individual as a feeling/experience, but instead penetrates the composition of their day-to-day lives and every action and decision they undertake.[363] Since many of those

diagnosed with IBD are young, the impact of fatigue on an individual's education, personal and professional life maybe even greater in IBD than in other LTCs.[97,364]

Predictors of low HRQoL are strong beliefs about the illness impact on daily life, perceived emotional impact of IBD and the coping strategy of 'decreasing physical activity'.[365,366]

### 5.2.1 A 'new normal'

The individual's ability to deal with stress, and cope with IBD fatigue has been shown to have an impact on HRQoL; those with high levels of acceptance, 'good' ways of coping and adapting to life with IBD have better HRQoL.[90,101,149,367] Throughout the interview study, experiences of fatigue varied from one participant to another in terms of how they defined and described fatigue. Some 'had' fatigue, some were 'fatigued'. Most participants described fatigue as an entity that impacted on day to day life through the barriers it presented, as well as how fatigue impacted upon them, making them unable to complete daily tasks.

A variety of different words were used to described fatigue such as 'tiredness' 'worn out' and 'run out of energy'. Participants appeared to have little issue in being able to describe and put into their own words, feelings about and experiences of fatigue. This is in contrast to other studies considering patient experiences in IBD fatigue where it was reported that individuals struggled to describe fatigue. Authors

pertained this to individuals having a lack of understanding regarding their fatigue.[35] This interview study found that participants were able to discuss the physical and mental aspects of fatigue and describe how factors of fatigue impact on daily life. The acceptance of illness is one of significant factor affecting the level of HRQoL in patients with chronic diseases. It is suggested that the higher the levels of symptom acceptance, the higher the levels of HRQoL. This relationship is also evidenced in other LTCs, such as cancer[368], RA[369], respiratory[370] and heart disease.[371]

There are self-motivated  acceptance processes patients use to gain control of their symptoms in LTCs.[372,373] These relate to perceptions of independence and dependence, as well as their feelings of helplessness, their ability to psychologically tolerate their condition, and their perceptions of their efficacy in coping with chronic symptoms.[238] If individuals self-manage their chronic illness successfully, it is likely that their quality of life will be enhanced.[374] it is well reported that individuals with IBD have higher HRQoL when they feel they have some control over their symptoms.[220,241,245]

Self-management techniques instil a sense of responsibility upon the individual to take ownership over their own health.[375] Self-management education can promote positive perceptions of self, and has the potential to greatly enhance HRQoL.[376,377]

Peer support appears to be an important factor for individuals.[378,379] Individuals who display more acceptance by improving their coping behaviours through psychotherapy, such as CBT, have been shown to have better HRQoL. This is also seen in RA, cancer and CFS.[184,233,236,240,380]

An individual's perceived life satisfaction provides a reflection of accomplishments, desires, and unfulfilled needs all at once in relation to the individuals expectations[381,382] Feelings of fulfilment are determined by levels of satisfaction in specific areas of an individual's life.[382] Levels of education, relationship status and living arrangements have not been shown to have an impact on levels of IBD fatigue or associated HRQoL.[7,110] This suggests that a sense of 'fulfilment' is subjective to the individual. How individuals with LTCs cope with perceived societal demands, can lead to feelings of stigmatisation by those without LTCs. Stigma can negatively impact an individuals' personal identity, social life and economic opportunities, in turn contributing to sense of unfulfillment.[383,384]

General demographic influences on HRQoL in IBD fatigue have been noted as including situational factors such as unemployment or financial difficutles.[7,73,110] Patients with IBD have been shown to feel like IBD fatigue stops them from achieving what they perceive as their full potential.[73,385]

### 5.2.2 Adaptations made to daily life

Study participants reported strategies used to better manage daily life with fatigue. Strategies often incorporated planning and prioritising tasks in order to coordinate utilisation of energy and regulate energy levels. Through task prioritisation, regularly favouring work and education, participants reported that they would often miss out on social interactions, reducing or removing leisure activities from daily life. This has a negative impact on HRQoL. Findings from the systematic literature review presented that acceptance of IBD and using effective coping strategies improve levels of HRQoL, whereas negative attitude and ineffective strategies, such as all or nothing behaviours, worsens HRQoL.[149,242,245,246]

Literature relating to management of fatigue in LTCs include counselling and psychological interventions focused on energy management techniques.[386] Successful lifestyle modification has a positive effect on patients' HRQoL in LTCs.[365,387] Individuals with LTCs, such as IBD, RA and MS, often have to adjust their aspirations, lifestyle, and employment arrangements due to chronic symptoms, e.g. fatigue. One third of people with LTCs encounter basic (e.g. financial, housing, employment) or social (e.g. partner, children, sexual or leisure) problems in their daily life. Experiencing basic problems is related to less effective coping behaviours and worse symptom management.[388,389] Self-management of symptoms requires people with LTCs to monitor their health and manage the impact of the illness

on physical, psychological and social functioning in daily life.[390] Individuals with LTCs experience tension between managing and controlling their symptoms whilst being able to do what they would like to do with their lives.[391,392] Contrary to the findings of the interview study and the majority of literature on the topic, Townsend *et al*.[391] indicated that people with LTCs frequently gave priority to maintaining a 'normal' life at the expense of controlling symptoms. 'Normalising behaviours' were described during the interview study in terms of the participants incorporating fatigue management techniques into their daily lives in order to reduce the negative impact that fatigue has on daily functioning. Participants using poor methods of fatigue management, such as task avoidance and all or nothing behaviours, experience higher level of fatigue and worse HRQoL than those who did not.[221,222]

'Self-management' is often used interchangeably with terms such as self-care and patient education. Self-care is interpreted by many authors as consisting of those tasks performed at home by 'healthy' people to prevent illness, rather than merely managing existing illness.[393,394]

Several management techniques for IBD fatigue were discussed in chapter 1. Adaptation training, such as multidisciplinary information about IBD, peer support and encouragement for adequate physical exercise appears to have a positive impact on the psychological well-being of IBD patients, improving HRQoL.[378] There is support for self-

management of LTCs to improve HRQoL.[372,395] However barriers exists; many individuals with LTCs are highly symptomatic, face frequent healthcare interventions and do not have strong financial or social support, thus making self-management regimens difficult to maintain.[390,396,397] Group education for fatigue management in MS has been shown to offer improvements in fatigue and HRQoL when compared to no intervention. Participant education included elements from CBT, focus on energy effectiveness, self-management and self-efficacy theories.[398,399]

#### 5.2.2.1 Attenuated social interaction

Multiple studies report that disengagement from social activity due to high levels of IBD fatigue has a negative effect on HRQoL.[149,241,242,248] The interview study revealed that the most common adaptation in the day-to-day lives of participants was reduction, or complete loss, of social interaction. Evidence suggest that 68% of IBD patients with fatigue have experienced social restriction in some way, such as an inability to undertake hobbies or leisure activities.[241,242,247,248] Patients worry that their fatigue restricts not only their own, but also their families social activites.[241] Close relationships with friends, social support groups, networks and counselling are evidenced to positively impact on ability to better manage IBD fatigue, improving HRQoL.[245,248] A perceived lack of social support has been shown to be related to increased levels of IBD fatigue [149]

Individuals living with LTCs are at high risk of social isolation.[400] Social relationships are frequently disrupted and frequently disintegrate under the stress and management of LTCs.[375] Tension displayed by participants shifting between hiding their illness at times and at others wanting to talk about it, can be understood through previous work on the 'shifting perspectives' model of chronic illness.[401] Focus on the LTC and associated symptoms shifts from 'in focus' to 'background' depending on circumstances, particularly, situational and environmental factors such as employment and social activities. HCPs, friends, family and colleagues commonly refer to the terms acceptance and denial when describing an individual's response to a LTC.[402] This can contribute feelings of isolation and negatively impact on HRQoL.

Social support, the sharing of concerns and experiences with family, friends and HCPs helps to maintain daily activities and higher HRQoL.[97,378]

### 5.2.3 General health

Participants reported they made extra efforts to maintain a level of 'good general health', such as sustaining good nutritional intake and keeping physically active, in order to better overcome feelings of fatigue. This was a particular element of 'self-management' reported by participants.

Nutrition in IBD was discussed in chapter 1. Insufficiencies of dietary vitamins and minerals can contribute to higher levels of fatigue regardless of any pre-existing LTCs. IBD subjects are at risk of nutrient deficiencies due to chronic inflammation, malabsorption and a change in eating behaviour.[117] Elimination diets, dietary restriction and the addition of nutritional supplements to habitual diet are commonly reported to be used by people with fatigue in LTCs.[403–408] There is much evidence relating to how 'healthy diets' can reduce the risk of developing a LTC, however there is scarce information regarding maintaining good nutrition in LTCs in terms of managing symptoms.[409] In some LTCs , such as COPD and MS, there is patient focused information available relating to the importance of making time to prepare and eat a healthy diet when managing a LTC, even when fatigued.[114,410,411] Managing dietary intake offers the individual a sense of control when living with a LTC which is often unpredictable.

Results from both and the systematic literature review and the interview study revealed that physical activity was important to individuals with IBD fatigue. Reportedly both reducing levels of IBD fatigue and improving HRQoL. In a broad range of LTCs, graded exercise has been suggested as way of managing fatigue.[386] There is no evidence of negative side effects of moderate physical activity in people with stable IBD.[412,413] Adults who are physically inactive are at much higher risk of feeling fatigue than those who are physically active.[414]

Exercise has been shown to reduce fatigue and improve HRQoL in MS[415,416] RA[406] and CFS.[417,418] Most exercise interventions described utilise aerobic exercise, some use a combination of both aerobic and resistance exercise. Modes of exercise typically included cycling, walking, and swimming; however, climbing, yoga, dancing and aerobics were also featured.[386,406,415–418] There is little data regarding the impact of exercise on HRQoL in IBD, that which does exist is either of poor quality or is contradictory, as presented in a systematic literature review undertaken by the student during this studentship[419]

In one study patients with moderately active IBD reported that HRQoL improved by 19% in the physical activity intervention group and 8% in the control group (who did not do the exercise programme). The effect of a three-month low-intensity walking program (30 min of walking, three times a week) was investigated in CD patients with moderate disease, and although improvements in HRQoL were observed, there were no significant differences between intervention and control groups.[166] This study did not solely focus on the impact of physical activity on IBD and HRQoL.

In these studies, it is unclear what lead to improvements in HRQoL. There is the possibility that taking part in the study allowed increased social interaction, both through engagement with the researchers and also other study participants. There is the prospect that taking part in the research study provided individuals a platform for acceptance

and/or better understanding of the symptom of IBD fatigue allowing for better adaptation and management.

Exercise is a form of self-management that an individual can use to take back a sense of control over their LTCs. Although not yet described in IBD this has been discussed in various other LTCs.[420]

## 5.2 Summary

Through exploration of findings in light of the wider literature it has been made evidence that the main factors that impact on HRQoL, are developing a sense of '*a new normal'* through *symptom acceptance,* manage limited *energy resources* through *symptom management* of IBD fatigue, and efforts to improve *general health*, through *physical activity* and *psychosocial well-being*,

Symptom acceptance, management and lifestyle adaptation and the beneficial impact on HRQoL is well reported in the wider IBD literature and in other LTCs. Physical activity is widely acknowledged as beneficial for individuals with IBD and other LTCs, however the literature considering the impact of physical activity on HRQoL is lacking and therefore no clear conclusions can be drawn on this topic.

# 6 Conclusion

During this chapter research objectives will be summarised, and conclusions given. Recommendations for future research will be discussed. Importantly the contribution of this research to the understanding of patient experiences in IBD will be clarified. Additionally, a section reflecting on the research process that has been undertaken and the role of the student is included to discuss quality, validity and reliability alongside the academic progress and learning experiences of the student.

## 6.1 Recommendations for areas of further research.

Conclusions have revealed that there are three main themes derived from both the interview study and the systematic literature review. Two of these themes, developing a sense of '*a new normal'* through *symptom acceptance* and management of limited *energy resources* through *symptom management*, have a significant evidence base in the literature. However, the third theme encompassing management techniques focused on maintaining 'good health' lacked in supporting literature in both IBD and other LTCs.

Therefore, the recommendation is to explore the role that patient beliefs about 'good health' impact on IBD fatigue and HRQoL. In particular there is scope for development of a physical activity-based intervention to treat IBD fatigue and measure improvement in HRQoL. Development of a self-management intervention for individuals with IBD, such as an exercise or physical activity intervention, has the potential to reduce

IBD fatigue, improve HRQoL, reduce costs to the NHS and allow patients to feel a sense of control over their treatment through its self-management element.

### 6.2 Contribution to knowledge

The present study extends the findings of previous research on IBD fatigue by considering the impact of IBD fatigue on HRQoL of adults with IBD. This is important because no other research to date has explored how HRQoL is impacted by IBD fatigue.

As acknowledged in the recently published IBD guidelines, IBD fatigue continues to be recognised as an important factor in the treatment of IBD.[421] More importantly IBD fatigue continues to be one of the most burdensome symptoms for people with IBD and requires better understanding in order to improve the care of patients.

Further to progressing the knowledge on the topic of IBD fatigue, using TA methodology has allowed the student to further advance the use of TA as a method in its own right.

### 6.3 Assessing and ensuring quality.

There remains some disparity in what constitutes quality in qualitative research.[422] Researchers often adopt a particular stance, such as interpretive or positivist, and criticise research that does not conform to their expected paradigm. There is consensus regarding four characteristics of good qualitative research; ‘Sensitivity to context’,

'commitment and rigour', 'transparency and coherence' and 'impact and importance'.[314,423,424] Each was addressed during the interview study; Sensitivity to context was considered by taking into account previous relevant research whilst 'keeping an open mind' in order to consider the participants perspectives and being sensitive to ethical considerations. Rigour was established through engagement with the topic and the participants, completing thorough data collection and analysis. Transparency and coherence were achieved through making it clear how data were analysed and how conclusions were drawn. Utilising a close link between the data and conclusions drawn enables a clear course that is open to interpretation of the layers of analyisis.[424] Impact and importance of the research affects the dissemination and the significance of the study findings, encompassing the transferability and generalisability of the results in this thesis and any subsequent academic publications.

### 6.3.1 Limitations

Although adequate for TA, the sample size of n=14 was smaller than the desired sample of 20. However, data saturation was met and has been shown to be achievable in TA with a sample size of 12 interviews.[286] Participants were self-selected, with many coming from the same established research patient group. It is possible that self-selected participants were inherently more open to talking about their experiences and are less representative of the wider IBD population. Further to this, it is also possible that those patients who are most symptomatic are the ones most willing to discuss symptoms and

impact, also making this sample less representative of the wider IBD population.

The data were coded, and themes identified by one person, the student, and the analysis then discussed with academic supervisors. This process allowed for consistency in the method but failed to provide multiple perspectives from a variety of people with differing expertise. For future research using this method, the coding of data could involve several individuals.[425]

### 6.3.2 Reflexivity and rigour

Reflexivity in qualitative research incorporates efforts to consider a researcher's own thoughts, actions and potential bias in light of different contexts.[426] Measures to support this included reflections following each interview, offering valuable detail about the interview not captured in the audio recording. Regular meetings with research supervisors and engagement with qualitative research groups provided support to develop ideas and concepts throughout the research process.

The concept of trustworthiness or rigour is essential in any kind of research, helping to ensure the methodological and ethical soundness of the research and its quality.[323] In qualitative research, rigour refers not to rigid adherence to rules and procedures, but to the methodology and methods chosen for conducting the study. The researcher needs to clearly and visibly demonstrate the process and the rationale behind

the decision making and how the study results were derived to make the process auditable to the reader.[427,428]

The student was aware of her previous professional experience of working with patients with IBD, recognising the importance of acknowledging the way these previous experiences may impact upon the approach and interpretation of information gathered during the course of the study. Although presented as a linear procedure, the research analysis was an iterative and reflexive process. The data collection and analysis stages in this study were undertaken concurrently, actively revisiting the previous stages of the process before undertaking further analysis to ensure that the developing themes were grounded in the original data.

In the process of reflexivity, the student was constantly adjusting behaviour, such as the type of questioning utilised, to benefit the research process.[352] Recording thoughts after interviews and reflecting on these at the time of data analysis as a way of controlling for bias and consequently to improve the study rigour.[428,429]

### 6.4 Resources and Constraints

Resource consideration when undertaking research should encompass time, funding, equipment for data collection and analysis, environments, participants and expertise.[430]

When contemplating participant recruitment, motivations for participation should be considered.[431] There was no inconvenience allowance for participants taking part in this study, therefore it was not considered likely that participants would be taking part for financial or personal gain. Historically, the NIHR Nottingham BRC has provided a research active population of individuals with IBD. There were no perceived or experienced difficulties in recruitment to the study.

There are several rooms available in research areas in which the interviews were undertaken. At times it was difficult to reserve rooms due to a high level of activity in research areas, therefore it was important to manage time and book efficiently, as well as manage participants expectations of availability of appointment times and dates. By offering a wide choice of dates and times the student actively facilitated recruitment, however the quantity of available appointments had to be balanced against the availability of space on the research unit. There were no withdrawals of consent or participation from this study. Whilst it was possible to book other outpatient areas, such as a bed space, the student chose to book only interview rooms. This was considered important in order to maintain privacy. Undertaking interviews in an undisturbed environment was considered important when discussing personal experiences, creating a safe space for participants to talk honestly and openly. Being able to conduct the interviews in the most appropriate rooms improved the quality of the data collected by ensuring high quality audio recording, allowing for

better transcription. Recording equipment was provided by the research centre, the equipment had been used recently by other researchers and research students. This ensured that it was good quality equipment that was fit for purpose.

The student undertook specific training provided by the University of Nottingham for researching sensitive or distressing topics in order to be better prepared to work within a topic that some participants might find difficult to discuss. Other support offered to participants included referral to specialist clinicians and IBD nurses if clinically required, signposting to counselling services and other support networks such as official Crohn's and Colitis UK social media groups.

Having clinical experience in the care of patients with IBD enabled the student to better understand some of the clinical details discussed. At times being a novice researcher can be an asset, asking important questions that could be overlooked by someone with more experience, such as asking the participant to explain something they said as it might not be familiar, could in fact offer a better understanding of the participants meaning of the terms or words they used. In preparing to conduct a study it is important to consider the effects of expertise and to determine whether or not specific training is required. The student has undertaken appropriate training within the University of Nottingham in order to take an active role in data collection. There was readily available academic and specialist clinical support from both

supervisors. This allowed the student to discuss ideas, with the opportunity to challenge the student's way of thinking and produce learning opportunities.

There was no specific funding for this project, however the main study was funded by a competitive research grant from the Crohn's and Colitis UK charity. All interview data was collected, transcribed, analysed and interpreted by the student. Access to analysis software (NVivo 12) was available through the University of Nottingham.

### 6.5 Role Conflict

The position of the student throughout the research process presented an interesting point surrounding possible role conflict; novice researcher versus experienced Registered Nurse (RN).

There is evidence to suggest that it is common for boundaries between professional and research roles for RNs to become blurred.[432] This problem has been well documented in the nursing literature on qualitative research.[433]

When a researcher is identified as a RN, with the potential to influence the researcher-participant interaction. Nurse researchers may experience role conflict when deciding how to introduce themselves to participants. Interviewers are aware that the initial introduction will influence the participants perception of them.[434,435] If researchers identify themselves as 'nurse-researchers', then participants with positive experiences with nurses may feel comfortable sharing intimate

information which they might not have otherwise.[433] Conversely, if participants' healthcare experiences have been negative then they may purposefully omit information, especially if they are aware that the nurse has a professional responsibility to act on any disclosed information.

If participants are unfamiliar with the process of research, then they may view the interviewer in the more familiar role of 'nurse' and attempt to focus the interaction towards their clinical concerns.[436] To minimize role conflict, researchers need to be able to clearly define and articulate their roles to participants.[435] For this reason the student identified herself as a nurse researcher to participants throughout the study. An extra complication exists if the researcher conducts research interviews with his/her own patients.[437] Some authors believe that clinicians should not interview their own patients because they may feel compelled to participate.[438] For this reason the student was explicit in detailing that participation was voluntary, had no implication on routine clinical care, participants were not under the clinical care of the student at the time of their participation and that withdrawal at any time was possible.

### 6.6 Self-reflection

This research project started amid difficulties with the original focus of the research aiming to explore the relationship between questionnaire data and physiological data from a parallel mechanistic study. However, after several faltering starts, due to equipment failures, the main study

was behind schedule, therefore the research focus of this master's thesis was realigned to exploring the impact of IBD fatigue on HRQoL through a qualitative interview study.

The research topic and objectives were discussed, readjusted and agreed in discussion between the student and both academic supervisors. This was highlighted in the student's first year review as an area of focus. The process of preparing for a first-year review was a good learning experience, as it helped the student focus the research topic but also see the progress and work that had been accomplished thus far. The input of the internal assessor at this point was invaluable, by offering support and guidance at that stage it meant the student was able to produce a higher quality thesis by the end of the period of study.

The student felt comfortable in the topic due to experience in clinical IBD nursing practice. Similarly, the day to day management of the research project was straightforwardly undertaken due to experience as a research nurse. The student felt well supported by academic supervision and had everyday access to resources, such as software and recording devices, through both the Nottingham BRC and the University of Nottingham.

The student was challenged by never having conducted semi-structured interviews before. Neither had she used NVivo software, which led to some difficulties when beginning data analysis, however,

undertaking graduate school courses from the University of Nottingham helped gain knowledge and experience in both of these. Although the student found the courses useful it was often difficult to book and attend these whilst working full time in a clinical role.

Successful journal publications during the studentship enhanced learning and gave the student a sense of satisfaction having undertaken purposeful research with meaningful results. The student attended multiple regional, national and international conferences during the studentship and presented research findings in both poster and oral format. The student grew in confidence in delivering presentations, discussing and answering questions from peers. The learning achieved through exploring epistemology, methodologies and modes of data analysis has allowed the student to go on and work on other research projects and commence writing a PhD proposal.

Advice for future students would be to ensure the research focus and objectives are well defined and are clear to both the student and supervisors to avoid the need for major revisions to work already undertaken. Embracing training opportunities improved experiences for the student and offered learning for unfamiliar concepts and techniques.

## 6.7 Summary

This is the first study to explicitly examine the experience of IBD fatigue and its impact on HRQoL. Through the undertaking of a systematic literature review and a semi-structured interview study, novel insights have been gathered into participants' experiences of IBD fatigue and its effect on their daily lives.

The key factors that impact on HRQoL, are developing a sense of '*a new normal'* through *symptom acceptance,* managing limited *energy resources* through *symptom management* of IBD fatigue, and efforts to improve *general health*, through *physical activity* and *psychosocial well-being*, Amalgamation of factors contribute to an individual's sense of lack of control regarding their health. Individuals undertake self-management techniques to try and take back control of their health and symptoms, though techniques can be ineffective, potentially worsening HRQoL.

The recommendation for future research is to explore the role that patient beliefs about 'good health', in particular physical activity, impact on IBD fatigue and HRQoL. This work would complement ongoing NIHR programme work into psychological and patient education management interventions for IBD fatigue. [439] Development of a self-management intervention focused on physical activity would be novel, and have real potential to improve HRQoL, reduce costs to the NHS and allow patients to feel a sense of control over their treatment through effective self-management.

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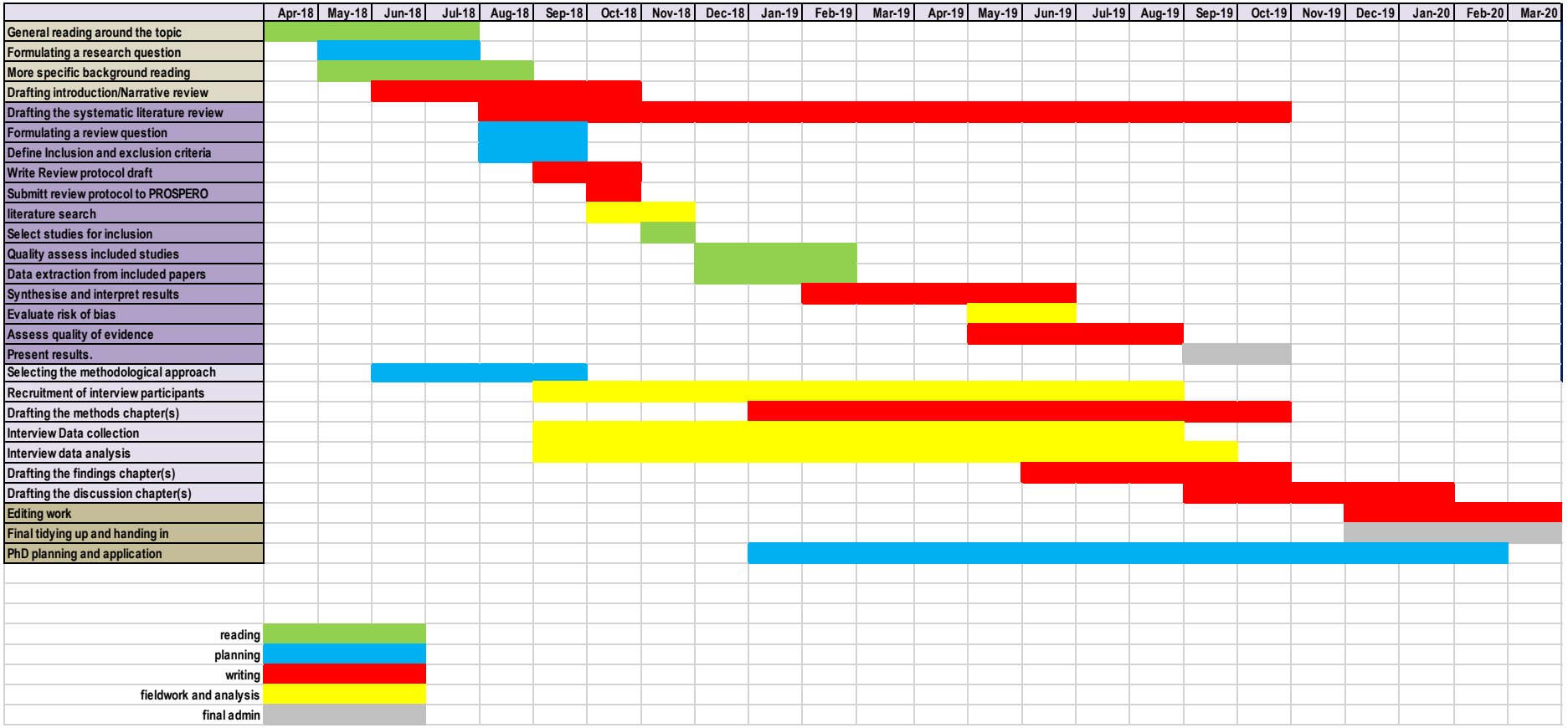
# 8. Appendices

## 8.1 GANTT chart



## 8.2 Systematic Literature review - Protocol

| | |
|---|---|
| **Review Title** | Systematic review: The Impact of Inflammatory Bowel Disease (IBD) related fatigue on quality of life of adults with IBD. |
| **Anticipated Start Date** | 01/10/2018 |
| **Anticipated completion date** | 01/10/2019 |
| **Conflicts of interest** | None to declare. |
| **Review question** | What are the areas of impact of IBD related fatigue on QoL of adults diagnosed with IBD? |
| **Searches** | The Databases searched will be MEDLINE, EMBASE, CINAHL, PsychINFO, and PubMed. Medical subject headings and free text searching will be used to maximise the number of papers retrieved (Hart, 2001; Atkinson et al., 2015). Each database will be individually searched (Booth *et al*, 2012).<br>Searches will be restricted to 'human', 'adult', 'primary research' and 'English language' publications. Due to the recent uptake of research in the area, a comprehensive review in 2013 completed by WCD and the fact that historical studies have been built upon more recently, a time limit of 5 years will be set, in order to include only the most relevant and up to date information. |
| **Conditions or domain being studied** | IBD related fatigue. |
| **Participants/population** | Adults with IBD who experience IBD related fatigue as identified by use of any fatigue scoring tool. |
| **Intervention(s), exposure(s).** | The focus of the review is to synthesise the experience and objective impact on quality of life (QoL) as reported by adults with IBD who are identified as having IBD related fatigue. The causal relationship between chronic fatigue and diminished QoL is not completely understood, though an intricate interaction of several factors, such as pain, malnutrition, physiological distress, sleep difficulties and ongoing inflammation is reportedly involved. Despite the reported similarity of fatigue in IBD prevalence to that seen in other health conditions, as a symptom IBD fatigue has only recently begun to receive a similar level of attention in research and clinical practice. A consensus on the standard care for IBD-related fatigue, particularly regarding screening and management, is non-existent.<br>Through the review we aim to delineate the impact the IBD fatigue has on an individual's QoL. Additionally, the review aims to identify and analyse the factors attributed to the impact of IBD fatigue on QoL |
| **Types of study to be included.** | Studies of any kind (qualitative, quantitative or mixed methods) published in English will be considered for the review if IBD fatigue was mentioned. Abstracts, case studies, commentary papers and reviews papers will be excluded. |
| **Context.** | Study populations can come from any healthcare setting, only studies that originate and/or consider a study population based in a country that is part of the 'organisation for |

## 8.3 Systematic literature review – Quality appraisal of literature

Qualitative study appraisal;

| Author(s) | Year | Is there congruity between the stated philosophical perspective and the research methodology | is there congruity between the research methodology and the research question or objectives? | is there congruity between the research methodology and the methods used to | Is there congruity between the research methodology and the representation and analysis of data | Is there congruity between the research methodology and the interpretation of results? | Is there congruity between the research culturally or theoretically? | Is the influence of the researcher on the research, and vice- |
|---|---|---|---|---|---|---|---|---|
| **Czuber-Dochan, *et al.*** | 2013 | 1 | 1 | 1 | 1 | 1 | 1 | 0 |
| **Viazis, *et al.*** | 2013 | 0 | 0 | 0 | 0 | 1 | 0 | 0 |
| **Devlen, *et al.*** | 2014 | 1 | 1 | 1 | 1 | 1 | 0 | 0 |
| **Skrautvol, *et al.*** | 2017 | 1 | 1 | 1 | 1 | 1 | 0 | 0 |

Cross-sectional study appraisal;

| Author(s) | Year | Were the criteria for inclusion in the sample clearly defined? | were the study subjects and the setting described in detail? | was the exposure measured in a valid and reliable way? | were objective, standard criteria used for measurement of the condition? | were confounding factors identified? | were strategies to deal with confounding factors stated? |
|---|---|---|---|---|---|---|---|
| **Castillo-Cejas, *et al.*** | 2013 | 1 | 1 | 1 | 1 | 1 | 1 |
| **Opheim, *et al.*** | 2014 | 1 | 1 | 1 | 1 | 1 | 0 |
| **Van Langenberg, *et al.*** | 2014 | 1 | 1 | 1 | 1 | 1 | 1 |
| **Artom, *et al.*** | 2017 | 1 | 1 | 1 | 1 | 1 | 1 |
| **Habibi, *et al.*** | 2017 | 1 | 1 | 0 | 1 | 1 | 0 |

Prevalence study appraisal;

| Author(s) | Year | Was the sample frame appropriate to address the target population? | Were study participants sampled appropriately? | was the sample adequate? | were the study subjects and the setting described in detail? | was the data analysis conducted with sufficient coverage of the identified sample? | Were valid methods used for the identification of the condition? | Was the condition measured in a standard, reliable way for all participants? |
|---|---|---|---|---|---|---|---|---|
| **Cohen, *et al.*** | 2014 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| **Villoria, *et al.*** | 2017 | 0 | 0 | 0 | 1 | 1 | 1 | 1 |

## 8.4 Systematic literature review - summary of extracted data

| **Summary of Data extracted from the reviewed literature** *(in ascending chronological order)* | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| **Author(s)** | **Year** | **Geographic location** | **study design** | **Sample size and characteristics,** | **Disease activity** | **Fatigue questionnaires and measurements** | **HRQoL questionnaires and measurements** | **Study findings** |
| **Castillo-Cejas, M. D. Robles and V. Borruel, N. *et al*** | 2013 | Spain | Cross Sectional | Two-part study; Part 1/ 99 (55 CD, 44 UC) Part 2/ 137 (70 CD, 67 UC) | Active CD; 49%. Active UC; 46% | DFIS, FSS, MFI. | EQ-5D-5L, IBDQ-9 | High levels of disease activity related to high levels of fatigue. High IBD fatigue related to low HRQoL. |
| **Czuber-Dochan, W. Dibley, L.B. and Terry, H. *et al*** | 2013 | UK | Qualitative | 46 (28 CD, 18 UC) selected from online database | Not disclosed | No questionnaires used, focus group study | | Five themes identified: Experience, causes, management, consequences and seeking support. High levels of fatigue affected physical and cognitive abilities, impacting on everyday life. |
| **Viazis, N. Mantzaris, G. and Karmiris, K. *et al*** | 2013 | Greece | Qualitative | 1181 (827 online questionnaire, 354 outpatient clinic questionnaires) (642 CD, 539 UC) | Not disclosed | Survey of authors own design (unvalidated) | | 60% of patients felt depressed, 25% felt angry because of IBD fatigue. IBD fatigue interfered with social life in more than half of cases also affecting working capability. Respondents report good social support from family and friends. |
| **Cohen, B. L. Zollga, H. and Shah, S. A. *et al*** | 2014 | USA | Prevalence | 220 (125 CD, 95 UC) from Disease registry. | Active CD; fatigued 44%, non-fatigued 18%. Active UC; fatigued 38%, non-fatigued 22%. | FACIT-F scale | SF-36, EuroQoL EQ-5D-5L, IBDQ-32 | Patients with fatigue reported having problems with their usual daily activities, except for self-care. The association of fatigue and impairment were strongest for usual activities. Patients with fatigue had worse valuations of current health status. |
| **Devlen, J. Beusterien, K. and Yen, L. *et al*** | 2014 | USA | Qualitative | 27 participants (4 focus groups), 10 1:1 interviews) (21 UC, 6 CD). | Active disease;22% (CD/UC not specified) | No questionnaires used, focus group study | | Patient reported key burdens of IBD fatigue were impact on lifestyle, on daily activities, ion relationships and psychological health |
| **Opheim, R. Fagermoen, M.S.and Bernklev, T. *et al*** | 2014 | Norway | Cross Sectional | 428 (238 CD, 190 UC) Adult IBD outpatients | Active CD; fatigued 73% non-fatigued 45%. Active UC; fatigued 85%, non-fatigued 58%. | FSS | Nil | 43% CD and 33% UC reported severe fatigue, 39% reported fatigue severely interfered with daily life. Those with higher education status, higher income were less likely to report high fatigue interference. |
| **Van Langenberg, D.R. and Gibson, P.R.** | 2014 | Australia | Cross sectional | 379 (181 CD, 113 UC, 85 Controls) | Active disease: CD 51%, CD follow up group 47%, UC 67%. | FIS | Nil | Patients with IBD reported higher fatigue compared with controls. Improved physical fatigue was associated with establishing a regular exercise routine. Improvement was seen in cognitive fatigue when immunomodulator therapy ceased. |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| **Artom, M. Czuber-Dochan, W. and Sturt, J. *et al*** | 2017 | UK | Cross Sectional | 182 (116 CD, 60 UC) from tertiary care | Those without stoma - Active disease 26%, remission 74% (CD/UC not specified). | MFI, IBD-F | IBDQ-32 | Negative fatigue perceptions, 'all-or-nothing' and avoidance behaviours were associated with worse HRQoL. Impacts on fatigue and HRQoL included employment, education, relationship and smoking status. |
| **Habibi, F. Habibi, M.E. and Gharavinia, A. *et al*** | 2017 | Iran | Cross sectional | 71 (46 UC, 25 CD) | Those with severe disease omitted. Further disease activity data not given. | Nil | IBDQ-32 | 44% of sample reported poor sleep quality, linked to daytime sleepiness and fatigue which decreases HRQoL. Higher fatigue level correlated with poorer HRQoL. |
| **Skrautvol, K. and Naden, D.** | 2017 | Norway | Qualitative | 13 (7 CD, 6 UC) | Not disclosed | No questionnaires used, face to face interview study | | Participants reported the importance of balancing regular physical activity with regular rest, reporting that tolerance limits could be reflected in lack of energy. |
| **Villoria, A. García, and V.Dosal *et al*** | 2017 | Spain | Prevalence. | 177 (127 CD, 50 UC) | Not disclosed | FACIT-F scale | IBDQ-9 | Patients with fatigue had higher scores for depression, sleep disturbance and anxiety, and worse QoL than those without fatigue. A strong negative correlation was seen between HRQoL and fatigue. |

## 8.5 Study approvals

NHS
Health Research Authority

Dr Gordon Moran
Clinical Associate Professor and Honorary Consultant Gastroenterologist,
University of Nottingham
Queen's Medical Centre, West Block D1406
NG7 2UH

Email: hra.approval@nhs.net

10 January 2018

Dear Dr Moran

**Letter of HRA Approval**

| | |
|---|---|
| **Study title:** | **Non-invasive approaches to identify the cause of fatigue in inflammatory bowel disease patients** |
| **IRAS project ID:** | **233733** |
| **Protocol number:** | **17083** |
| **REC reference:** | **17/EM/0431** |
| **Sponsor** | **University of Nottingham** |

I am pleased to confirm that HRA Approval has been given for the above referenced study, on the basis described in the application form, protocol, supporting documentation and any clarifications noted in this letter.

**Participation of NHS Organisations in England**

The sponsor should now provide a copy of this letter to all participating NHS organisations in England.

*Appendix B* provides important information for sponsors and participating NHS organisations in England for arranging and confirming capacity and capability. **Please read *Appendix B* carefully**, in particular the following sections:

- *Participating NHS organisations in England* – this clarifies the types of participating organisations in the study and whether or not all organisations will be undertaking the same activities
- *Confirmation of capacity and capability* - this confirms whether or not each type of participating NHS organisation in England is expected to give formal confirmation of capacity and capability. Where formal confirmation is not expected, the section also provides details on the time limit given to participating organisations to opt out of the study, or request additional time, before their participation is assumed.
- *Allocation of responsibilities and rights are agreed and documented (4.1 of HRA assessment criteria)* - this provides detail on the form of agreement to be used in the study to confirm capacity and capability, where applicable.

Further information on funding, HR processes, and compliance with HRA criteria and standards is also provided.



NHS
Health Research Authority
East Midlands - Nottingham 1 Research Ethics Committee
The Old Chapel
Royal Standard Place
Nottingham
NG1 6FS

**Please note: This is the favourable opinion of the REC only and does not allow you to start your study at NHS sites in England until you receive HRA Approval**

22 December 2017

Dr Gordon Moran
Clinical Associate Professor and Honorary Consultant Gastroenterologist, Academic Program Director for Gastroenterology
University of Nottingham
NIHR Biomedical Research Unit in Gastrointestinal and Liver Diseases
Nottingham University Hospitals NHS Trust
The University of Nottingham, Queen's Medical Centre, West Block D1406
NG7 2UH

Dear Dr Moran,

| | |
|---|---|
| Study title: | Non-invasive approaches to identify the cause of fatigue in inflammatory bowel disease patients |
| REC reference: | 17/EM/0431 |
| Protocol number: | 17083 |
| IRAS project ID: | 233733 |

Thank you for your letter of 20 December 2017, responding to the Committee's request for further information on the above research and submitting revised documentation.

The further information has been considered on behalf of the Committee by the Chair.

We plan to publish your research summary wording for the above study on the HRA website, together with your contact details. Publication will be no earlier than three months from the date of this opinion letter. Should you wish to provide a substitute contact point, require further information, or wish to make a request to postpone publication, please contact hra.studyregistration@nhs.net outlining the reasons for your request.

## 8.6 Interview schedule

Nottingham Biomedical Research Centre

NHS National Institute for Health Research

**Semi structured Interview Schedule**

(Version 2.0 Date: 30/11/2018)

IRAS Project ID: **233733**

**Title of Study:** Non-invasive approaches to identify the causes of fatigue in Inflammatory Bowel Disease patients.

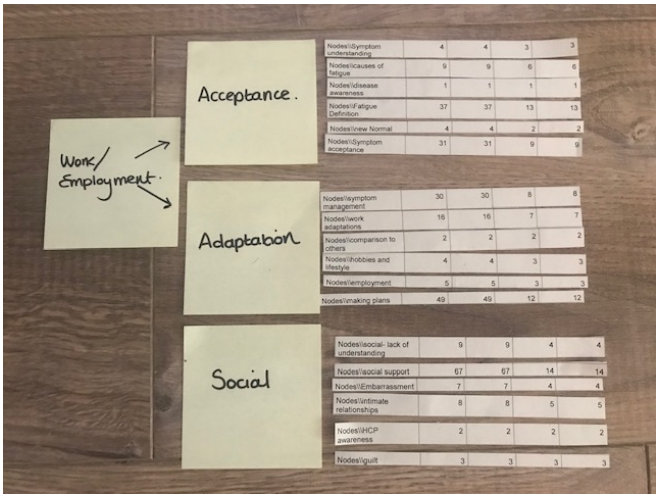
**Title of Sub-study: Patients perceptions and experiences of fatigue in Inflammatory Bowel Disease- a qualitative study.**

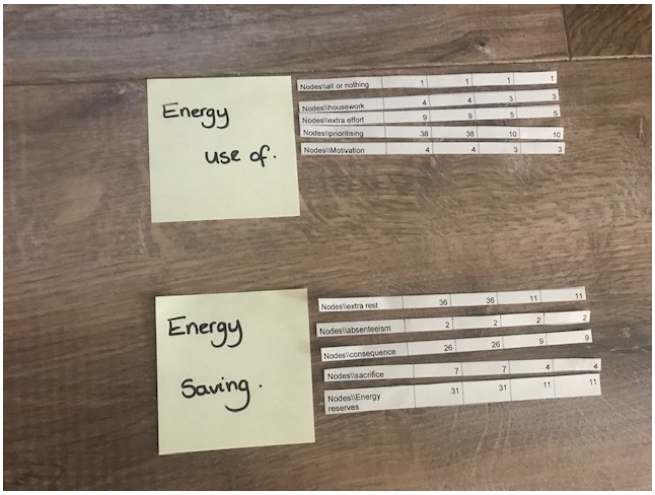
1. Can you tell me about your experiences of fatigue?
   - Experiences of being diagnosed with IBD, what symptoms did you have at the time, was fatigue one of the symptoms, when did you start feeling fatigued in relation to your diagnosis?
   - Have you noticed any specific factors impacting your fatigue? E.g. Treatment, stress.

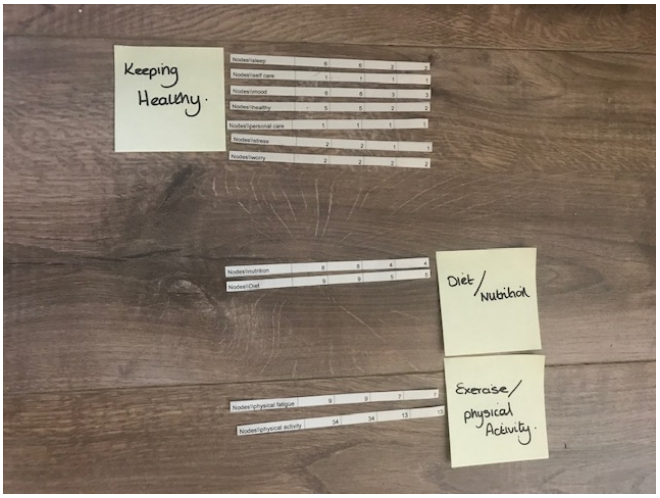
2. Can you tell me how your IBD related fatigue impacts on your day to day life?
   - Experiences at home- impact on day to day activities like cooking, cleaning, pets, Activities of daily living such as washing and dressing.
   - Experiences at work/education.
   - Social Life experiences- travel and choice of places to go, people you speak to and interact with.
   - Leisure time/Hobbies

3. Can you tell me about what sort of things you do to manage your IBD related fatigue that have a major positive effect on your life?
   - Any specific management techniques (if not mentioned before)?
   - Anything that improves or worsens your fatigue?
   - Any positive or Negative experiences associated with fatigue impact on daily life?

## 8.7 Interview study analysis – example of coding organisation



## 8.8 Interview study analysis – example of searching for themes

## 8.9 Interview study – Theme generation

| Theme | Explanation of theme | Sub Themes | Codes |
|---|---|---|---|
| **The new normal** | Adapting to burden of IBD fatigue, adapting daily life and routine. | **Acceptance** | Disease awareness |
| | | | Symptom acceptance |
| | | | symptom understanding |
| | | | new normal- acceptance |
| | | | Fatigue definition |
| | | **Adaptation** | symptom management |
| | | | Employment |
| | | | Making Plans |
| | | | Embarrassment |
| | | | comparison to others |
| | | **Social Impact** | Intimate relationships |
| | | | social Support |
| | | | Social- lack of understanding |
| **Energy as a resource** | The belief that 'Energy' is a commodity that can be used up, built up in reserves and portioned out. | **Energy use** | Extra effort |
| | | | Housework |
| | | | Prioritising |
| | | | Routine |
| | | | All or nothing' behaviours |
| | | | Motivation |
| | | **Energy conservation** | Extra Rest |
| | | | Energy Reserves |
| | | | Sacrifice |
| | | | Consequences |
| **Keeping Healthy** | The belief that having good general health makes people better able to manage IBD fatigue. | **General Health** | Healthy |
| | | | Sleep |
| | | | Personal Care |
| | | | Self-care |
| | | **Nutrition** | Nutrition |
| | | | Diet |
| | | **Physical activity** | Physical Activity |

## 8.10 Participant information sheet.

Nottingham Biomedical Research Centre

NHS National Institute for Health Research

**Participant Information Sheet**
(Version 1.0: 22 June 2018)

IRAS Project ID: **233733**

**Title of Study:** Non-invasive approaches to identify the cause of fatigue in inflammatory bowel disease patients

**Sub Study Title: Interview study into Patients perceptions and experiences of Fatigue in Inflammatory Bowel Disease.**

**Name of Researcher**(s): Dr Gordon Moran, Dr Wladyslawa Czuber-Dochan, Miss Shellie Radford.

We would like to invite you to take part in the above research study. Before you decide we would like you to understand why the research is being done and what it would involve for you. One of our team will go through the information sheet with you and answer any questions you have. Talk to others about the study if you wish. Ask us if there is anything that is not clear.

**What is the purpose of the study?**

We want to investigate how we can best understand the fatigue symptoms reported by IBD Patients. We want to understand your experiences of fatigue and which aspects of fatigue most affect you and why so that we can identify better ways to understand and diagnose IBD related fatigue. With your input, we want to consider how we can re-design and create a fatigue score tailored to meet your specific needs and preferences for fatigue management.

**Why have I been invited?**

You are being invited to take part because you are:

a) A participant in the IBD Fatigue research study

And / or

b) Are known to have fatigue related to IBD.

We are inviting participants to take part in a one-to-one interview to understand your experiences and perspectives of having IBD related fatigue.

**Do I have to take part?**

It is up to you to decide whether or not to take part. If you do decide to take part you will be asked to sign a consent form. If you decide to take part you are still free to withdraw at any time and without giving a reason. This would not affect your legal rights or clinical care.

**What will happen if I take part?**

You will be invited to attend the Sir Peter Mansfield Imaging Centre, University Park, University of Nottingham. Appointments will be made for a time and date convenient for you. A single visit interview, lasting approximately one hour, will be conducted in a consultation room in the unit and will be attended by yourself and the interviewer.

The interview will be audio recorded and conducted in a relaxed and informal manner. Conversation will be led by yourself as you will be asked to describe your personal experiences and perceptions of IBD Fatigue.

The interviews will be converted into a written, anonymised transcript, so you can't be identified from it and the original recording will be destroyed to ensure confidentiality is maintained.

**Expenses and inconvenience allowance**

Participants will not be paid to participate in the study. Travel expenses will be offered for any costs incurred as a result of participation.

**What are the possible disadvantages and risks of taking part?**

Generally, interviews do not pose a physical risk to individuals however it is acknowledged that sharing sensitive information and experiences can in some instances be distressing. You are not asked to share any information that you do not wish to discuss.

**What are the possible benefits of taking part?**

The information we get from your participation in this study will help us to understand what works well with our current systems of care and what we may need to address in order to develop a clinical tool for use in the future.

**What if there is a problem?**

If you have a concern about any aspect of this study, you should ask to speak to the researchers who will do their best to answer your questions. The researchers contact details are given at the end of this information sheet. If you remain unhappy and wish to



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complain formally, the normal National Health Service complaints procedure or NHS Patient Advice & Liaison Service (PALS) office is available to you and can be contacted on Free phone: *0800 183 0204 or via the helpdesk, Main entrance Queens Medical Centre.*

**Will my taking part in the study be kept confidential?**

We will follow ethical and legal practice and all information about you will be handled in confidence. If you join the study, some parts of the data collected for the study will be looked at by authorised persons from the University of Nottingham who are organising the research. They may also be looked at by authorised people to check that the study is being carried out correctly. All will have a duty of confidentiality to you as a research participant and we will do our best to meet this duty.

All information which is collected about you during the course of the research will be kept **strictly confidential**, stored in a secure and locked office, and on a password protected database. Any information about you which leaves the institution will have your name and address removed (anonymised) and a unique code will be used so that you cannot be recognised from it.

Under UK Data Protection laws the University is the Data Controller (legally responsible for the data security) and the Chief Investigator of this study (named above) is the Data Custodian (manages access to the data). This means we are responsible for looking after your information and using it properly. Your rights to access, change or move your information are limited as we need to manage your information in specific ways to comply with certain laws and for the research to be reliable and accurate. To safeguard your rights we will use the minimum personally – identifiable information possible.

You can find out more about how we use your information and to read our privacy notice at:

https://www.nottingham.ac.uk/utilities/privacy.aspx.

Your personal data (address, telephone number) will be kept for 3 years after the end of the study so that we are able to contact you about the findings of the study and possible follow-up studies (unless you advise us that you do not wish to be contacted). All other data (research data) will be kept securely for 7 years. After this time, your data will be disposed of securely. During this time, all precautions will be taken by all those involved to maintain your confidentiality, only members of the research team will have access to your personal data.

Where possible information about you which leaves the site will have your name and address removed and a unique code will be used so that you cannot be recognised from it, however sometimes we need to ensure that we can recognise you to link the research data with your medical records so in these instances we will need to know your name and date of birth.



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**What will happen if I don't want to carry on with the study?**
Your participation is voluntary and you are free to withdraw at any time, without giving any reason.

**Involvement of the General Practitioner/Family doctor (GP)**
There will be no requirement to notify your GP of your participation in this study.

**What will happen to the results of the research study?**

The information that you provide during the interview will be used to identify the IBD Fatigue scale cut off and will be included in the content of the researcher's dissertation for Master of Science (by research) from the University of Nottingham. Should publication of your data occur, it will remain anonymised and you will be notified and informed of where to obtain a copy of the published paper.

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

This research is being organised by the University of Nottingham and is being funded by The Nottingham Digestive Diseases Centre and a Research Grant from Cohn's and Colitis UK.

**Who has reviewed the study?**

All research in the University of Nottingham is reviewed by an independent group of people, called a Research Ethics Committee, to protect your interests. This study has been reviewed and given favourable opinion by [Nottingham Research Ethics Committee 1].

**Further information and contact details**

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## 8.11 Informed consent form

Nottingham
Biomedical Research Centre

NHS
National Institute for
Health Research

**CONSENT FORM**
**Final version 1.0: date 22 June 2018**

IRAS Project ID: **233733**

**Title of Study:** Non-invasive approaches to identify the cause of fatigue in inflammatory bowel disease patients

**Sub Study Title: Interview study Into Perceptions and experiences of Fatigue in Inflammatory Bowel Disease.**

**Name of Researcher**(s): Dr Gordon Moran, Dr Wladyslawa Czuber-Dochan, Miss Shellie Radford.

**Name of Participant:** **Please initial box**

1. I confirm that I have read and understand the information sheet version number **1.0** dated **22/06/2018** for the above study and have had the opportunity to ask questions. ☐
2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason. ☐
3. I understand that relevant sections of my data collected in the study may be looked at by the research group and regulatory authorities where it is relevant to my taking part in this study. I give permission for these individuals to have access to these records and to collect, store, analyse and publish information obtained from my participation in this study. I understand that my personal details will be kept confidential. ☐
4. I agree to be interviewed and understand that the interview will be audio recorded and that anonymous direct quotes from the interview may be used in the study reports. ☐
5. I understand that the information held and maintained by the Health and Social Care Information Centre and other central UK NHS bodies may be used to help contact me or provide information about my health status. ☐
6. I understand that information about me recorded during the study will be kept in a secure database. If the data is transferred it will be made anonymous. Data will be kept for 7 years after the study has ended. ☐
7. I agree to take part in the above study. ☐

| _____ | _____ | _____ |
|---|---|---|
| Name of Participant | Date | Signature |
| _____ | _____ | _____ |
| Name of Person taking consent | Date | Signature |