

Original research

Systematic review: the impact of inflammatory bowel disease-related fatigue on health-related quality of life

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ABSTRACT:

Background Fatigue is frequently reported in inflammatory bowel disease (IBD) and impacts on health-related quality of life (HRQoL). HRQoL has not been systematically reviewed in IBD fatigue.

Aim To investigate what impact IBD fatigue has on HRQoL in adults with IBD.

Methods Systematic searches (CINAHL, EMBASE, PsychINFO, Medline) were conducted on 25 September 2018, restricted to 'human', 'adult', 'primary research' and 'English language'. Search terms encompassed concepts of 'fatigue', 'IBD' and 'HRQoL'. A 5-year time limit (2013–2018) was set to include the most relevant publications. Publications were screened, data extracted and quality appraised by two authors. A narrative synthesis was conducted.

Results Eleven studies were included, presenting data from 2823 participants. Fatigue experiences were significantly related to three HRQoL areas: symptom acceptance, psychosocial well-being and physical activity. Patients reporting high fatigue levels had low symptom acceptance. Psychosocial factors were strongly associated with both fatigue and HRQoL. Higher social support levels were associated with higher HRQoL. Physical activity was impaired by higher fatigue levels, lowering HRQoL, but it was also used as a means of reducing fatigue and improving HRQoL. Quality appraisal revealed methodological shortcomings in a number of studies. Notably, use of multiple measures, comparison without statistical adjustment and fatigue and HRQoL assessment using the same tool were some of the methodological shortcomings.

Conclusion Psychosocial factors, symptom management and acceptance and physical activity levels have significant impact on HRQoL.

Significance of this study

What is already known on this topic

- ▶ Fatigue is frequently reported in inflammatory bowel disease (IBD) and has been identified as one of the most burdensome symptoms.
- ▶ IBD fatigue has been reported as multidimensional and complex, impacting individual's activities of daily living and reducing health-related quality of life (HRQoL).
- ▶ The subjective nature of fatigue and poor understanding means it is often underestimated by clinicians.

What this study adds

- ▶ This work identified the experiences of fatigue were significantly related to three HRQoL linked themes: symptom acceptance and management, psychosocial well-being and management and physical activity.
- ▶ Psychosocial factors were strongly associated with both fatigue and HRQoL.
- ▶ Physical activity was impaired by higher fatigue levels, lowering HRQoL, but it was also used as a means of reducing fatigue and improving HRQoL.

Results support application of psychosocial or exercise interventions for fatigue management. Further exploration of HRQoL factors in IBD fatigue is required, using validated fatigue and HRQoL measures.

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INTRODUCTION

Fatigue related to inflammatory bowel disease (IBD) and other long-term conditions (LTCs) is defined as an 'extreme and

Significance of this study

How might it impact on clinical practice in the foreseeable future

- ▶ Better understanding of the impact of IBD fatigue will help patients and clinicians better manage fatigue, for individuals with IBD this has the potential to improve HRQoL, reduce costs to the National Health Service and allow patients to feel a sense of control over their treatment through effective self-management.
- ▶ This review has identified areas for possible further research with use of validated fatigue and HRQoL measures and clearer characterisation of disease activity to define a diagnostic cut-off for IBD fatigue.

persistent sense of tiredness, weakness or exhaustion,¹ which can be physical, mental or both and is not easily resolved by sleep or rest.² Fatigue can be attributed to both physical and mental exertion^{3,4} or as the outcome of pathological processes.^{3,4} The International Classification of Diseases code presents fatigue as an assortment of physical, cognitive and emotional symptoms affecting undertaking of daily tasks.⁵ It is not known whether fatigue in a given disease is a result of being chronically ill or whether it represents a specific symptom of that disease.⁶

The prevalence of IBD fatigue is reported as 41%–48% for patients in remission and 71%–86% in patients with active disease.^{7,8} The most frequently experienced symptoms of IBD are pain, urgency and fatigue.^{9–15} IBD fatigue is one of the top five research priorities highlighted by the nurses European Crohn's and Colitis Organisation (N-ECCO) due to its pervasiveness and negative impact on health-related quality of life (HRQoL).^{12,16} The symptom of fatigue in LTCs has received greater attention as part of overall HRQoL.⁶ However, to date, there has been no thorough appraisal of the impact of IBD fatigue on an individual's HRQoL.

Increasing life expectancy has highlighted the need for other measures of health, capturing the quality of the years someone lives. Traditional markers for population health, such as life expectancy and causes of death, do not offer information regarding the quality of the physical, mental and social domains of life. The concept of QoL is not a new one, in 1995 WHO recognised the importance of improving peoples' QoL.¹⁷ When QoL is 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 multidimensional concept, HRQoL is also multidimensional and incorporates areas related to physical, mental and social functioning.¹⁸ 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 on 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 sociodemographic, clinical and psychological and treatment-related determinants.^{19,20}

Studies to date have rarely measured IBD fatigue as a primary outcome and there has been limited literature focused on the impact of IBD fatigue on HRQoL. The aim of this review is to synthesise the existing body of knowledge on IBD fatigue and its impact on HRQoL. This work is essential in order to better define the research streams needed to improve HRQoL in people with IBD fatigue.

METHODS

The review question 'What is the impact of IBD fatigue on the HRQoL of adults with IBD?' was developed using the format: population, exposure, outcome.

The final search of literature was performed on 25 September 2018. Databases searched were EMBASE, CINAHL, PsychINFO and Medline. These databases were selected as they were likely to provide a broad combination of medical and healthcare allied papers related to the topic of interest.²¹ To increase the reference retrieval, the medical subject headings (MeSH) and free-text searching were employed, and each database was individually searched.²² Grey literature searching was used to maximise the number of publications retrieved.^{23,24} 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 (table 1).^{9,25–27}

Searches were performed with the 'suggested search terms' and 'explode' selection. The Boolean operator 'OR' was used within each facet to maximise the searches, with the operator 'AND' used between facets to combine terms. Searches were restricted to 'human', 'adult', 'primary research' and 'English language' publications. Studies of any design published in English were considered for the review if IBD

Table 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*		

*free search term for truncation.

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 only the most up-to-date information. Due to limited number of publications related to IBD fatigue, no studies were excluded from the review based on study quality, however quality was considered when reviewing study findings. Studies that did not meet the inclusion criteria were retained, if relevant, for background information.

Quality appraisal and data extraction

Quality of studies was assessed and data were extracted by two independent reviewers (SJR and JMcG), using forms specific to study design from the Joanna Briggs Institute to allow for comparison of quality across study types.²⁸ The data extracted includes specific details about populations, context, culture, geographical location, study methods and the phenomena of IBD fatigue relevant to the review question. Due to the time constraints, all papers were read in full, but only data reflecting the aims of the review were extracted. For several of the studies, information and analysis regrading HRQoL was limited, but present, therefore deemed important to include given the comprehensive and systematic nature of the review.

Data analysis

Thematic analysis was used to analyse data. The analysis included three phases: open coding, creating categories and abstraction. The open coding phase relies on the research question driving the coding process so that only valid data are highlighted and further examined.^{29–31} 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 larger themes were analysed for subthemes through analysis of the coding.

The abstraction phase involved conveying a general description of the topic being researched to the themes identified.

RESULTS

Searches yielded 76 publications overall, with 11 studies meeting inclusion criteria (figure 1). A summary of the included papers and data extracted is shown in table 2.

Sample characteristics

Eleven studies have been included in the review, four qualitative,^{7 32–34} two prevalence^{35 36} and five cross-sectional studies.^{37–41} Geographical locations of the research studies included the UK,^{7 40} the USA,^{33 42} Norway^{34 38} and Spain,^{36 39} with one study each from Australia,³⁷ Iran⁴¹ and Greece.³² All are considered to be high-income countries with good quality healthcare.

The current review presents data from a total of 2823 adults. Study sample sizes ranged from $n=13$ to 1181, and 54% of the sample were female. Most settings were outpatient departments, however there was also use of online participation and interview/focus group data collection. One study combined results from inpatient and outpatient areas. A total of 1550 participants studied had Crohn's disease (CD) (54.9%), 1182 had ulcerative colitis (UC) (41.9%), 85 healthy volunteers (3%) and 6 with IBD-unclassified (0.2%). Reported fatigue prevalence ranged between 26.4% and 54%. All studies reported data from mixed disease states (active or quiescent).

Through the processes of data extraction and thematic analysis, three themes developed as aspects of IBD fatigue that have the greatest influence on HRQoL; symptom acceptance and management, psychosocial well-being and physical activity. Table 3 displays the distribution and frequency of the main themes throughout the reviewed studies.

Symptom acceptance and management

Ability to accept diagnoses and IBD symptoms can depend on the care patients receive from healthcare professionals. This was particularly highlighted in those of a younger age.³³ One study reports 31% of participants were informed about disease advances, however only 30% of those obtained information from healthcare professionals.³² The same study reports 26% of participants do not discuss their treatment with healthcare professionals, with 40% feeling like healthcare professionals are unsupportive of patients making decisions about their own healthcare.^{7 32}

Participants who report feelings of not having control over IBD symptoms experience higher levels of fatigue than those who feel like they have good levels of control.^{40 41} Altered self-image and fears about stigma caused participants to hold back sharing their diagnosis with friends, family, colleagues and employers.^{7 32–34 40} Negative fatigue perceptions were associated with greater negative impact on daily activities.⁴⁰

'Normalising behaviours' were described in terms of the participants incorporating their management techniques into their daily lives in order to reduce the negative impact that fatigue has on daily functioning. Those patients who used self-help techniques, such as complementary or herbal therapies, were more likely to report higher levels of fatigue than those who engaged in traditional healthcare.³⁸ Participants using poor methods of fatigue management, such as task avoidance and 'all or nothing' behaviours, experienced higher level of fatigue and worse HRQoL than those who did not.^{40 41} Understanding one's own physical and cognitive tolerance limits and being able to adjust lifestyle to manage symptoms were highlighted as important steps for some participants.³⁴ Higher levels of IBD-related distress, namely a lack of symptom

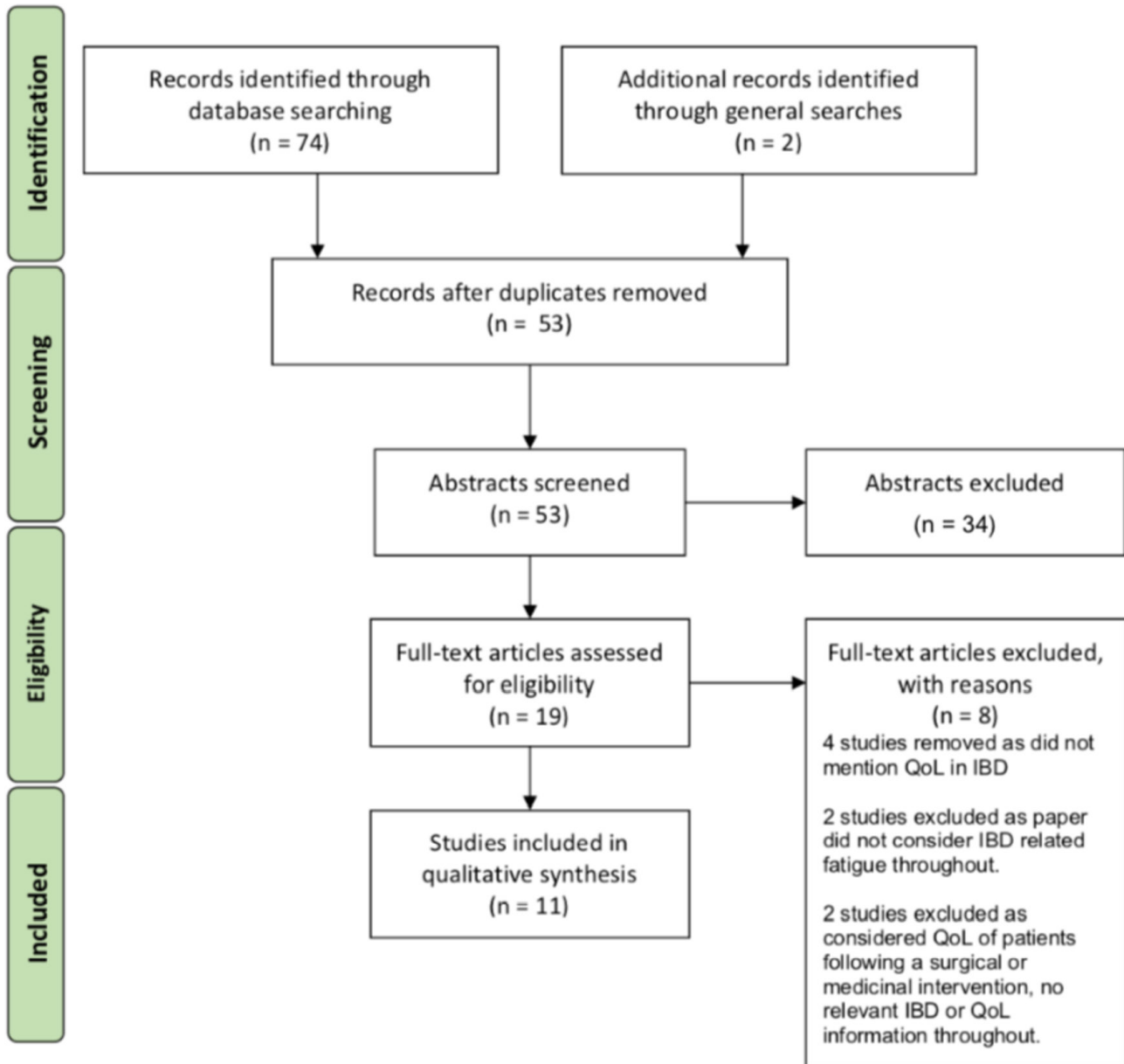


Figure 1 Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow chart of literature search and selection. IBD, inflammatory bowel disease; QoL, quality of life.

acceptance or ability to manage symptoms, have been shown to be associated with diminished HRQoL.⁴⁰

Psychosocial well-being

Anxiety and depression were the factors most frequently associated with high levels of fatigue,^{7 32 34–37 39–41} contributing to higher psychological distress.³⁶ Patients reported low mood (60%) or anger (25%) because of IBD and symptoms interfering with their social life.³² Both, UC and CD patient populations affected by fatigue exhibit higher anxiety and depression and lower HRQoL than those without IBD.^{41 42}

Fatigue burden was frequently reported by study participants as a reason for limited or missed social interactions.^{7 32 33} Family and friends have been

presented as being supportive, however others, such as employers or colleagues, were reported as lacking in understanding of IBD fatigue.³⁴ Participants reported that they were mindful about depending heavily on family support while also recounting they would feel more supported if the people around them were better informed about IBD fatigue.⁷ Support from family and friends may compensate for the gaps in support from healthcare professionals as reported by participants.³²

Interestingly, none of the studies considered the impact of fatigue on intimate relationships. Only one study touched on the subject of personal relationships, with participants feeling unable to disclose IBD to a new partner for the fear of stigma related to symptoms.³³ Two studies reported participants views

Table 2 Summary of data extracted from the reviewed literature (in ascending chronological order)

Study	Year	Geographic location	Study design	Sample size and characteristics	Disease activity	Fatigue questionnaires and measurements	HRQoL questionnaires and measurements	Study findings	Quality
Castillo-Cejas, et al ³⁹	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 levels of fatigue related to low HRQoL.	High
Czuber-Dochan, et al ⁷	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. Participants described fatigue in terms of how it affected life. High levels of fatigue affected physical and cognitive abilities, impacting on everyday life.	High
Viazis, N. et al ³²	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.	Low
Cohen, B. L. et al ³⁵	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.	High
DeIVEN, J. et al ³³	2014	USA	Qualitative	27 participants (four focus groups), 10 1:1 interviews) (21 UC, 6 CD)	Active disease; 22% (CD/UC not specified)	No questionnaires used, focus group study		21/27 participants were in disease remission. Patient reported key burdens of IBD fatigue were impact on lifestyle, impact on daily activities, impact on relationships and psychological impact.	Medium
Opheim, R. et al ³⁸	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, working and higher income were less likely to report high fatigue interference. 43% CD and 33% UC reported severe fatigue interference with everyday life.	Medium

Continued

Table 2 Continued

Study	Year	Geographic location	Study design	Sample size and characteristics	Disease activity	Fatigue questionnaires and measurements	HRQoL questionnaires and measurements	Study findings	Quality
Van Langerberg, D.R. and Gibson, P.R. ⁸	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 significantly higher scores on all global and dimensional fatigue indices compared with controls. Improved physical fatigue was associated with establishing a regular exercise routine. Improvement was seen in cognitive fatigue when immunomodulator therapy ceased.	High
Artom, M. <i>et al</i> ⁴⁰	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	There was a significant difference in fatigue and HRQoL according to employment, education, marital and smoking status. Negative fatigue perceptions, 'all-or-nothing' and avoidance behaviours were significantly associated with worse HRQoL.	High
Habibi, F. <i>et al</i> ⁴¹	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.	Medium
Skrautvoll, K. and Naden, D ³⁴	2017	Norway	Qualitative	13 (7 CD, 6 UC)	Not disclosed	No questionnaires used, face-to-face interview study		Participants reported tolerance limits might be reflected in a lack of energy. Participants reported the importance of balancing regular physical activity with regular rest.	Medium
Villoria, A. <i>et al</i> ³⁶	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 than those without fatigue. A strong negative correlation was seen between HRQoL and fatigue. Those patients with more severe IBD fatigue had worse anxiety and depression and worse quality of life.	Medium

CD, Crohn's disease; DFIS, Daily Fatigue Impact Scale; EQ-5D-5L, EuroQual 5-dimension questionnaire (five level); FACIT-F scale, Functional Assessment of Chronic Illness Therapy-Fatigue; FSS, Fatigue Severity Scale; IBD, inflammatory bowel disease; IBD-F, Inflammatory Bowel Disease-Fatigue scale; IBDQ-9/IBDQ-32, Inflammatory Bowel Disease Questionnaire 9(shortened)/32; MFI, multidimensional fatigue inventory; SF-36, 36-item Short Form survey; UC, ulcerative colitis.

Table 3 Main themes from the reviewed literature

Reviewed studies	Year published	Main themes		
		Symptom acceptance and management	Psychosocial well-being	Physical activity
Castillo-Cejas, M. <i>et al</i> ³⁹	2013			x
Czuber-Dochan, <i>et al</i> ⁷	2013	x	x	x
Viazis, N. <i>et al</i> ³²	2013	x	x	
Cohen, B. L. <i>et al</i> ³⁵	2014	x	x	x
Devlen, J. <i>et al</i> ³³	2014	x	x	x
Opheim, R. <i>et al</i> ³⁸	2014	x	x	x
Van Langenberg, D.R. and Gibson, P.R. ³⁷	2014			x
Artom, M. <i>et al</i> ⁴⁰	2017	x	x	x
Habibi, F. <i>et al</i> ⁴¹	2017	x		x
Skrautvol, K. and Naden, D. ³⁴	2017	x	x	x
Villoria, A. <i>et al</i> ³⁶	2017		x	

regarding children; fatigue has impacted their decisions to delay having any children, having more children or not to have children at all.^{7,33}

IBD fatigue was found to interfere with working capability in 40% of study participants, with more than half taking time off work for IBD-related reasons.³² Patients report not progressing in their careers at the same rate as colleagues without IBD fatigue. Participants report choosing not to take on more responsibility or reducing the working hours due to IBD fatigue.^{7,33-35}

Physical activity

Participants reported IBD fatigue impacted on their daily living by increasing absence from work or school, cancelling trips or events and avoiding undertaking certain activities such as sports or travelling.³³ Avoidance and ‘all or nothing’ behaviours associated with high levels of fatigue, such as decisions regarding not being in employment, were linked to the negative impact on HRQoL.^{7,40}

High levels of physical fatigue impacted participants’ ability to have a fulfilling life.⁷ Patients with IBD fatigue reported having problems undertaking usual daily activities when compared with those without fatigue.⁴² Very few participants reported issues with self-care regardless of fatigue level.⁴² Patients who commenced a regular exercise programme had greater improvement in the fatigue scores than those who did not.³⁷ Improvements in physical fatigue associated with the introduction of regular exercise were also associated with reduction of depression scores.³⁷ Establishing a regular routine between activity and rest helped some participants establish physical fatigue limits.³⁴ Introducing a healthy average amount of daily activity was important to participants.³⁴

DISCUSSION

The symptom of fatigue across long-term conditions all share characteristics; persistent, reduced energy and reduced muscle strength which is disproportionate to

the level of activity, impacting daily physical and cognitive functioning and leading to impaired HRQoL.^{1,43-49} IBD fatigue has been shown to have a predominantly negative impact on every aspect of an individual’s life.^{34,50-54}

The well-established link between increased disease activity and increased levels of fatigue is presented in many of the included studies.^{7,32,34-37,39-41} However, disease activity cannot independently explain the presence, or severity, of fatigue as IBD fatigue is also reported in disease remission.⁵⁵⁻⁵⁷ This is also true in other long-term conditions.

Symptom acceptance and management

Patients with IBD often feel it is important to remain ‘in control’ of their health.^{34,52,58}

Unpredictability and uncertainty concerning IBD relapses, treatment options and possible side effects contribute to low HRQoL.⁵² On the contrary, a diagnosis of a long-term condition can, after time, build an individual’s resilience and can sometimes be a relief, such as eventually getting an answer to questions regarding symptoms.^{59,60} Symptoms are reported more frequently when the patient has difficulty in coping with the demands of the disease.^{26,61} Acceptance of IBD and using effective coping strategies, such as task management and pacing, seem to have positive impact on symptom activity and higher levels of HRQoL, whereas negative attitude and ineffective strategies, such as task avoidance, worsens HRQoL.^{26,58,61,62}

Psychosocial support

Stigma is found to be independent of level of disease activity and seems to affect the lives of patients with IBD in multiple ways.⁶³ Stigma related to ill-health has been shown to be connected with the perceived views of employers, coworkers and friends.^{52,63} In the case of IBD fatigue, like in other long-term conditions, stigma

results from perceived physical weakness, cognitive limitations, reduced social activity and the inability to fulfil certain roles within an individual's personal and professional life.^{64–68}

Lack of support from colleagues negatively impacts on an individual's HRQoL.^{52 53} Often the steps taken to adjust the work environment to accommodate IBD symptoms can lead to feelings of loneliness, such as adjusting the working day to accommodate more frequent rest breaks.^{52 62} Patients in full-time work experience significantly higher HRQoL, than those in part-time work, unemployed or absent due to sickness.^{62 69} Sick leave and work absence was reported to reduce HRQoL.^{7 32 33 35 38 53 69} This could be attributed to enhanced interaction in those individuals who work or are in education, consequently improving HRQoL.⁷⁰

A study in multiple sclerosis showed a cycle of depression; social isolation leading to a reduction in social support, contributing to increased depression.⁷¹ Similar cycle has been also observed in IBD fatigue.^{26 57} Social support has been found to be important to individuals and help encourage good coping strategies, while disengagement from social activity had negative affect on HRQoL.^{26 52 54 62} It is reported that 68% of patients with IBD have experienced social constraint in some way, such as an inability to undertake hobbies or leisure activities.^{52–54 62} Patients worry that their fatigue restricts their own, and their families' social activities.⁵² Close relationships with friends and social support groups are evidenced to positively impact on HRQoL by improving fatigue management.^{54 58} IBD fatigue has been reported to be a daily concern of 66% of patients; however, only 44% of family and friends and 36% of healthcare professionals demonstrated agreement with the patients' perceived fatigue levels.⁷² This kind of discrepancy may result in patients feeling misunderstood and isolated, leading to under-reporting of symptoms. Family and friends occasionally express disbelief that symptoms of IBD are real, causing feelings of hurt and anger in patients.^{52 62} Some healthcare professionals consider some IBD symptoms as psychological in nature, causing emotional distress among patients due to feelings of lack of support and understanding.⁶² This is echoed in other long-term conditions, such as chronic fatigue syndrome, where there has been converse viewpoints regarding the origins of fatigue from healthcare professionals and patients.²

Physical activity

There is very little evidence regarding exercise or physical activity in IBD fatigue. The benefit of exercise on an individual level of fatigue was identified in a recent randomised controlled trial.⁷³ The pilot study compared exercise advice, dietary advice, dietary supplementation of omega-3 fatty acids and placebo. It was found that fatigue was considerably reduced in the exercise group.⁷³ Evidence from the review demonstrates that those who commenced a regular exercise programme

generally had greater improvement in fatigue scores than those who did not undertake regular exercise.³⁷ This is supported in the wider literature, where introducing regular exercise was associated with more positive feelings, improved HRQoL and better functioning by patients with long-term conditions, such as cancer or multiple sclerosis.^{74–76}

LIMITATIONS

There are potential limitations to this work. The use of thematic analysis may be limited by the subjective nature of the reviewer, influencing the repeatability of data analysis. This may introduce an element of inter-observer variability, which might limit the reliability of the themes chosen. Thematic analysis may as well be overly reductive and emphasise on less important themes. To increase reliability of this work, the categories and subcategories were reached through discussion with multiple authors.

Multiple databases were searched, and only relevant publications considered. Each publication was discussed by at least two researchers, with a third or fourth being consulted if there were any discrepancies. The outcomes represent an accurate response to the research question. Continuous conversations between authors occurred throughout to ensure a unanimous decision regarding article searches and quality appraisal criteria, thus limiting any potential bias.

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.

Contribution to knowledge

This is the first systematic review considering the impact of IBD fatigue on HRQoL. This review has highlighted the areas of HRQoL identified by individuals with IBD, to be most impacted by IBD fatigue. Uncovering these compounding factors of HRQoL has identified areas for further research and has begun a pathway to better understanding of the patient's experience of living with IBD fatigue.

Clinical implications

The clinical implications of this work include permitting healthcare professionals to better understand the lived patient experience of IBD fatigue. Healthcare professionals will be better able to consider IBD fatigue holistically taking into consideration factors that have been raised throughout this review. Researchers will be more efficient in designing and conducting targeted research for interventions for both IBD fatigue and IBD-related HRQoL.

CONCLUSION

This work identified the experiences of fatigue were significantly related to three HRQoL linked themes: symptom acceptance and management, psychosocial

well-being and management and physical activity. Individuals with IBD fatigue who exhibit better coping and management mechanisms were shown to have higher levels of HRQoL than those with IBD fatigue who adopted maladaptive behaviours.

Good social support from friends, family and colleague was found to be important to individuals with IBD fatigue and was shown to meaningfully impact on HRQoL. Findings from the review suggest that patients who are more physically active have higher levels of HRQoL than those who are comparatively sedentary.

This would suggest that a psychosocial and/or exercise intervention for fatigue management would be beneficial. Further exploration of the impact of IBD fatigue on HRQoL is warranted in order to better understand patient experiences. There is a need for prospective long-term studies with serial measures of IBD fatigue alongside other key measures, such as HRQoL, anxiety and depression, physical activity, disease activity and measures of disease burden. Exploring this information would allow better understanding of IBD fatigue. Further work with use of validated fatigue and HRQoL measures, and clearer characterisation of disease activity is needed to define a diagnostic cut-off for IBD fatigue that requires an intervention.

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Contributors SJR: whole manuscript preparation, literature searching, data appraisal and extraction, analysis and write up. JMcG: literature searching, data appraisal and extraction and analysis. WC-D: review of manuscript and supervision of data extraction and analysis. GM: whole manuscript review, supervision of data extraction and analysis.

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