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Systematic review: Physical activity and fatigue in adults with Inflammatory Bowel Disease (IBD) --Manuscript Draft--

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Abstract:	<p>Background: Fatigue is frequently reported in inflammatory bowel disease (IBD). IBD has been shown to have an impact on, and be impacted by, physical activity levels in IBD patients. Yet, to date, there have been no systematic reviews considering the impact of physical activity on levels of IBD fatigue.</p> <p>Aim: This aim of this review is to explore the current body of knowledge of what kind of physical activity interventions are available to treat IBD fatigue.</p> <p>Methods: Systematic database searches (CINAHL, EMBASE, PsychInfo, PsycARTICLES, AMED, Medline) and hand searching were conducted on 03/03/2019. Searches were restricted to 'human', 'adult', 'primary research' and 'English language' publications. No time limit was set. Quality appraisal and data extraction was undertaken by at least 2 reviewers.</p> <p>Results: searches yielded 32 publications; 2 studies were included in the review. Physical activity is inhibited by higher fatigue levels, lowering HRQoL, but also as a means of reducing fatigue, subsequently improving HRQoL.</p> <p>Conclusion: There was very little data eligible for inclusion in this review, and it was not of a high quality. The findings of the review suggest that physical activity may be beneficial for IBD fatigue, but this cannot be definitively stated. Evidence suggests physical activity is safe to undertake in active disease, therefore better-quality studies are needed in this area.</p>
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Systematic review: Physical activity and fatigue in adults with Inflammatory Bowel Disease (IBD)

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Abstract:

Background: Fatigue is frequently reported in inflammatory bowel disease (IBD).

IBD has been shown to have an impact on, and be impacted by, physical activity levels in IBD patients, Yet, to date, there have been no systematic reviews considering the impact of physical activity on levels of IBD fatigue.

Aim: To investigate whether physical activity has the potential to improve levels of IBD fatigue in adults with IBD.

Methods: Systematic database searches (CINAHL, EMBASE, PsychInfo, PsycARTICLES, AMED, Medline) and hand searching were conducted on 03/03/2019. Searches were restricted to 'human', 'adult', 'primary research' and 'English language' publications. No time limit was set. Quality appraisal and data extraction was undertaken by at least 2 reviewers.

Results: searches yielded 32 publications; 2 studies were included in the review. Physical activity is inhibited by higher fatigue levels, lowering HRQoL, but also as a means of reducing fatigue, subsequently improving HRQoL.

Conclusion: Results identified relationships between IBD fatigue and physical activity however, further research is warranted. Exploring this information would allow better understanding of IBD fatigue and inform future work on possible fatigue interventions in IBD.

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Introduction:

Fatigue is one of the **most frequently** experienced symptoms of patients with Inflammatory Bowel Disease (IBD), and **patients report it has some of the largest impact on daily life.**¹ The prevalence of IBD fatigue is reported as 41-48% for patients in remission and 71-86% in patients with active disease.^{2,3} It has been identified as one of the leading concerns of IBD patients.⁴⁻⁸ Recently, the symptom of fatigue has received greater attention as part of overall health-related quality of life (HRQoL) assessments in patients with Long Term Conditions (LTCs), including IBD.^{9,10} IBD has been shown to have an impact on, and be impacted by, physical activity levels in IBD patients,^{11,12} Yet, to date, there have been no systematic reviews considering the impact of physical activity on levels of IBD fatigue.

Fatigue related to IBD, and other LTCs, is defined as an extreme and persistent sense of tiredness, weakness or exhaustion which can be physical, mental or both and is not easily resolved by sleep or rest.^{13,14} The international classification of diseases code presents fatigue as an assortment of physical, cognitive and emotional symptoms affecting undertaking of daily tasks.¹⁵ 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.⁹

Aim:

The aim of this review is to explore **the current body of knowledge of what kind of physical activity interventions are available to treat IBD fatigue.** This is essential in order to better define work streams and possible interventions that are effective at **reducing** IBD fatigue, with the potential of having a positive and lasting impact on HRQoL.

Methods:

This systematic literature review is registered on the PROSPERO database for systematic reviews: CRD42019127730

The review question was developed; “*what is the impact of physical activity on IBD fatigue in adults with IBD?*”

Systematic searches of databases (CINAHL, EMBASE, PsychInfo, PsycARTICLES, AMED, Medline) and hand searching **were conducted on 03/03/2019 by SJR and HJ.**

These databases were selected as they provided a combination of medical and healthcare related databases likely to provide a broad field of search across disciplines without diluting the number of retrieved articles with unrelated articles.¹⁶ Each database was individually searched.¹⁷ Grey literature searching was used to maximise the number of publications retrieved.^{18,19} This was conducted by searching google scholar, reference lists of included publications and registered controlled trial registers. Search terms (Table 1) were determined through consideration of previously reviewed literature and scoping searches of Google Scholar. Searches were performed with the ‘suggested search terms’ and ‘explode’ selection, **and** restricted to ‘human’, ‘adult’, ‘primary research’ and ‘English language’ publications. Studies of any kind, published in English, were considered for the review if IBD fatigue was mentioned in the abstract. Commentary papers and literature reviews were excluded. No time limit was set as there was a limited number of publications retrieved from the systematic search. Due to limited number of publications retrieved, no studies were omitted from the review based on study quality, however quality was considered when reviewing study findings during analysis and discussion. Studies that did not meet the inclusion criteria were retained, if relevant, for background information.

Quality appraisal and Data extraction

Quality assessment of studies and data extraction was completed by two independent reviewers (SJR and HJ), with a third reviewer (GM) available to resolve any deliberations. The use of design specific forms from the Joanna Briggs Institute allowed for comparison of quality across study types.²⁰ 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 limits of time all papers were read in full but only data reflecting the aims of the review were extracted.

Data analysis.

Due to the different study designs being considered in this review and the type of data presented a narrative analysis was undertaken in order to be able to contrast and compare studies effectively.

Results

Searches yielded 32 publications overall, with 2 studies being included in the review. Full text publications were excluded if there was no reference to the interaction between physical activity and IBD fatigue throughout the text. Information is displayed in Figure 1 according to PRISMA²¹ guidelines. A summary of the included papers and data extracted is shown in table 2.

Sample characteristics

Included in the review is one qualitative study²² and one cross sectional study.²³

The review presents data from 202 adults with IBD; 56% of these are female. 65% of participants had CD, 32% had UC and 3% reported undefined IBD. 77% were reported as being in IBD remission. Only 5% of the sample was described as fatigued through the use of a fatigue measuring tool, the remaining authors did not discuss the use of a IBD fatigue measure.²³

Relationship between fatigue and physical activity

Vogelaar *et al*²³ presented data to show that IBD patients with fatigue demonstrated impaired physical fitness and levels of physical activity when compared to non-fatigued IBD patients. However, Vogelaar *et al*²³ did not accurately, and objectively measure levels of

disease activity at baseline. Instead more subjective measures of disease activity, such as the Harvey Bradshaw Index²⁴ were used, possibly leading to the inclusion of patients with variable disease activity.

The Checklist Individual Strength questionnaire (CIS) was used by Vogelaar *et al*³ to determine the fatigued and non-fatigued patient groups. This 20-item self-reported questionnaire has often been used in patients with chronic conditions that also have symptomatic fatigue. However it has not been validated for use in an IBD population.²⁵ Conversely the IBD fatigue scale²⁶ used by Topchiev *et al*²² has been validated for use specifically in IBD cohorts. Yet, there was no mention throughout the study from Topchiev *et al*²², of the fatigue levels of the participants.

Topchiev *et al*²² reported that 26% of participants utilise exercise or physical activity strategies for managing fatigue levels. Interestingly also 26% of participants stated that they believed physical exertion, and inadequate nutrition, were the main cause of their fatigue. No further details regarding the types, frequency or duration of the exercise or physical activity were reported.

Topchiev *et al*²² decided to pool responses from two questions due to the similarity in responses. The authors reported that this allowed for a better overview, indeed the two questions being considered are integral parts of the scale being utilised, however one could hypothesise that by pooling the responses to two questions the original context of the data could diminish.

Discussion.

There is very little evidence regarding exercise or physical activity in IBD fatigue. In the wider literature, introducing higher levels of exercise is associated with feelings of better health status and physically functioning better for patients with LTCs, such as Rheumatoid arthritis, Multiple sclerosis and Cancer.²⁷⁻²⁹ The introduction of an aerobic physical activity

programme has been shown to improve fatigue levels and HRQoL of individuals with LTCs.^{30–32} Regular exercise is recommended to improve IBD fatigue, yet fatigue is often cited by patients as a reason they are unable to undertake exercise.^{33–36} Patients have reported that exercise had positive effects on mood, motivation and physical feelings of fatigue.³⁷ The psychosocial aspects of taking part in exercise need to be explored as well as the physical benefits.³³

Studies have shown that approximately 25% of individuals with CD engage in physical activity, such as daily walking or regular gym based exercise,³⁸ with studies proposing that physical activity may have a beneficial role in reducing disease activity levels.³³ However there are some who express concerns that exercise may exacerbate symptoms, such as fatigue, pain and inflammation, in patients with IBD.^{33,39}

There are no current recommendations on the use of physical activity in IBD. In 1998 guidelines for exercise in IBD were published, these were designed specifically for IBD patients however they were based on the benefits of regular exercise for healthy individuals rather than those with IBD.⁴⁰ There is scope for future research working towards development of specific guidelines regarding physical activity and exercise for people with IBD, with advice for individuals with IBD fatigue.

Although it is increasingly recognised that exercise may have a positive impact on IBD, the literature remains sparse and poorly understood.

Strengths and Limitations:

To increase reliability of this work, author consensus was reached through discussion. Multiple databases were searched, and only relevant publications considered. Each publication was discussed by at least two researchers (SJR, HJ), with a third (GWM) being consulted if there were any discrepancies, however there were none during the review

process. 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 and there is an assurance that possible bias through personal opinions has been ruled out. 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.

The small number of studies included in the review does not allow us to make any firm conclusions. None of the studies included in the review looked directly at the effect of physical activity on IBD fatigue.

There was no use of objective measures of disease activity, nor for levels of fatigue. The fatigue measurement used has not been validated in an IBD cohort. Both studies described are descriptive, with vague IBD inclusions and details regarding the intensity and duration of the physical activity being considered.

Conclusion:

There was very little data eligible for inclusion in this review, and it was not of a high quality. The findings of the review suggest that physical activity may be beneficial for IBD fatigue, but this cannot be definitively stated. There are considerations such as whether physical activity is equally as good at reducing levels of fatigue when disease is active, versus when in remission. Evidence suggests physical activity is safe to undertake in active disease, therefore better-quality studies are needed in this area. The effect of physical activity on fatigue has been explored in other LTCs, however we are still unsure what is feasible in IBD. There are many variables that effect levels of IBD fatigue, these could be investigated independently.

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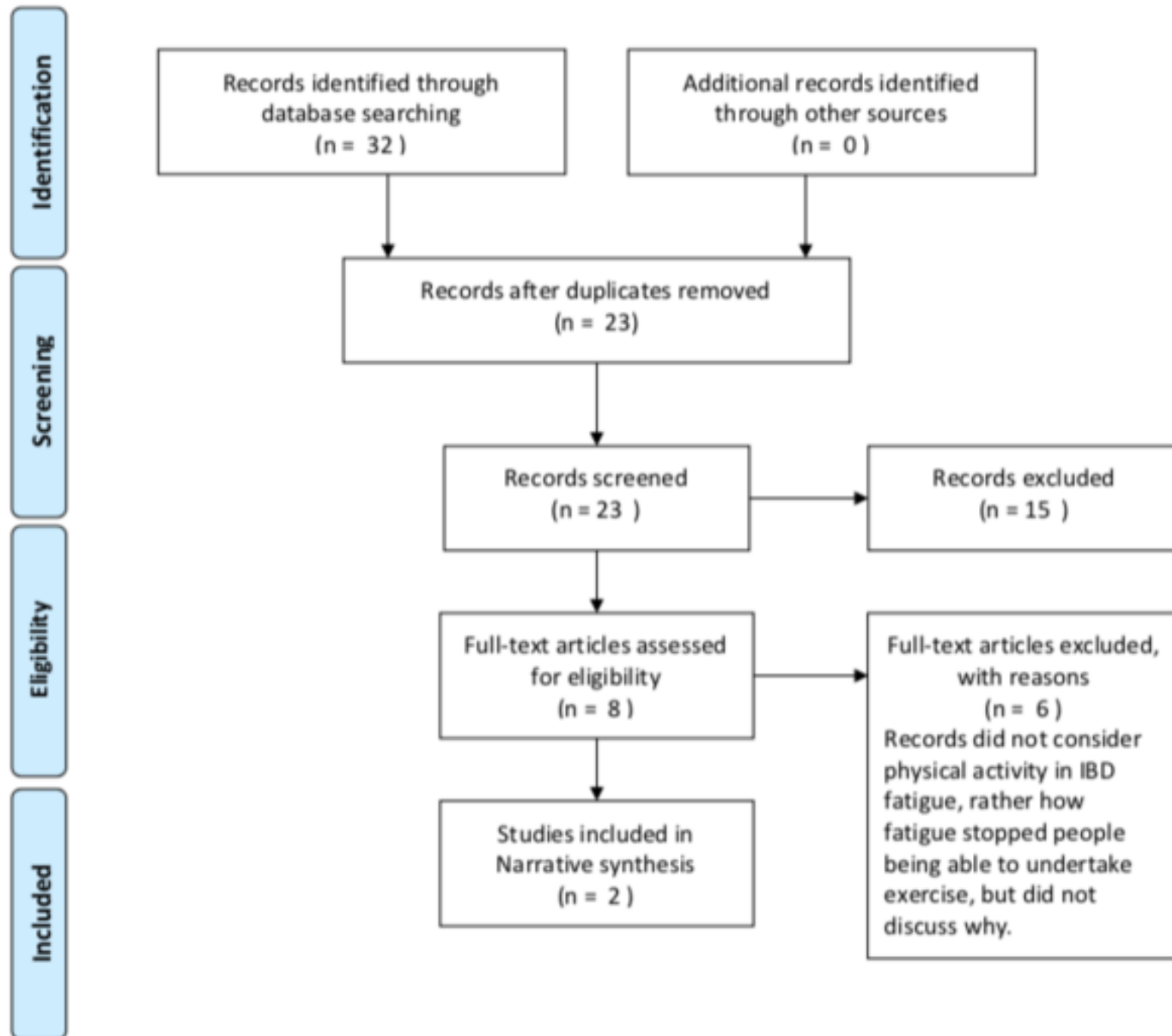


Table 1: Key Search Terms.		
Fatigue	IBD	Exercise
Fatigue (MeSH)	Inflammatory Bowel Disease *	Exercise*
Fatigue*	IBD	Physical Activity*
Lethargy (MeSH)	Ulcerative Colitis*	
Lethargy	UC	
Low energy*	Crohn's Disease*	
Vigour*	CD	
Vitality*		
Exhaustion*		
Key=* free search term for truncation		

Table 2: Summary of data extracted

Author(s)	Title	Year	Geographical Location	Study Type	Participants and setting, sample size.	Summary of data extracted	Quality.
Vogelaar, L., van den Berg-Emons, R., Busmann, H., Rozenburg, R., Timmna, R., and van der Woude, C.J.	<i>Physical Fitness and Physical Activity in Fatigued and Non-Fatigued Inflammatory Bowel Disease Patients</i>	2015	Netherlands	Cross sectional	n=20 (10 fatigued, 10 non fatigued adults with IBD)	Fatigued IBD patients show impaired physical fitness and physical activity compared with non-fatigued patients. Unclear causality direction. Further research in exercise in IBD is warranted.	Medium
Topchiev, H., Norton, C., Czuber-Dochan, W., Black, S., and Artom, M	<i>What Causes and What Helps with Fatigue in Inflammatory Bowel Disease : A Qualitative Analysis of Patient Perspectives'</i>	2017	UK	Qualitative	182 (57% female, 64% CD, 4.9 % stoma, 74% remission)	26% of sample exercise was a cause of fatigue. Some though that the lack of exercise was the cause whilst others felt the problem was overexertion (lack of exercise) 4% said they could not explain the cause of their fatigue. 26% (Of 137) reported increasing exercise or activity levels as a method for managing fatigue. (keeping on the move)(regular exercise)(exercise energises me)	Medium