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# **REVIEW ARTICLE**

# A systematic review and meta-analysis of the prevalence of poor sleep in inflammatory bowel disease

# Alex Barnes<sup>1,2,\*,•</sup>, Réme Mountifield<sup>1,2</sup>, Justin Baker<sup>1,2</sup>, Paul Spizzo<sup>1</sup>, Peter Bampton<sup>2</sup>, Jane M. Andrews<sup>4,5</sup>, Robert J. Fraser<sup>1,2</sup> and Sutapa Mukherjee<sup>2,3</sup>

<sup>1</sup>Department of Gastroenterology, Southern Adelaide Local Health Network (SALHN) Flinders Medical Centre, Bedford Park South Australia, Australia, <sup>2</sup>Adelaide Institute for Sleep Health, Flinders Health and Medical Research Institute, College of Medicine and Public Health, Flinders University, Bedford Park, South Australia, Australia, <sup>3</sup>Department of Respiratory and Sleep Medicine, Southern Adelaide Local Health Network (SALHN) Flinders Medical Centre, Bedford Park, South Australia, Australia, <sup>4</sup>Inflammatory Bowel Disease Service, Department of Gastroenterology and Hepatology, (CAHLN) Royal Adelaide Hospital, Adelaide, South Australia, Australia and <sup>5</sup>School of Medicine, Faculty of Health and Medical Sciences, University of Adelaide, Adelaide, South Australia, Australia

\*Corresponding author. Alex Barnes, Flinders Medical Centre, Flinders Drive, Bedford Park, SA 5042, Australia. Email: barn0255@flinders.edu.au.

## Abstract

Study Objectives: Poor sleep-in people with inflammatory bowel disease (IBD) has been associated with worse quality of life, along with anxiety, depression, and fatigue. This meta-analysis aimed to determine the pooled prevalence of poor sleep-in IBD.

**Methods:** Electronic databases were searched for publications from inception to November 1st 2021. Poor sleep was defined according to subjective sleep measures. A random effects model was used to determine the pooled prevalence of poor sleep-in people with IBD. Heterogeneity was investigated through subgroup analysis and meta-regression. Publication bias was assessed by funnel plot and Egger's test.

**Results:** 519 Studies were screened with 36 studies included in the meta-analysis incorporating a total of 24 209 people with IBD. Pooled prevalence of poor sleep-in IBD was 56%, 95% CI (51–61%) with significant heterogeneity. The prevalence did not differ based on the definition of poor sleep. Meta-regression was significant for increased prevalence of poor sleep with increase in age and increased of prevalence of poor sleep with objective IBD activity but not subjective IBD activity, depression, or disease duration.

**Conclusions:** Poor sleep is common in people with IBD. Further research is warranted to investigate if improving sleep quality in people with IBD will improve IBD activity and quality of life.

# Statement of Significance

This meta-analysis of 36 studies, incorporating over 24 000 people with inflammatory bowel disease (IBD), showed that poor sleep quality is common in those with IBD and more frequent than reported estimates for fatigue and mental health conditions in people with IBD. Meta-regression showed that the differences in poor sleep between IBD populations related in part to IBD activity confirmed by objective measures. The presence of IBD related symptoms alone was not found to be significant.

Key words: immune function; insomnia; sleep deprivation

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#### Introduction

Sleep is an important biologic function with increasing attention turning to its role in overall health. Abnormal sleep has been linked to poor health outcomes including cardiovascular disease [1], metabolic syndrome [2] and increased all-cause mortality in some studies [3], in addition to significant economic cost in the form of decreased productivity and increased health care utilization [4]. Sleep has been shown to regulate a number of gastrointestinal functions including gastrointestinal motility and secretion [5]. Sleep disruption has been associated with increased levels of inflammatory cytokines, such as IL-6, and TNF- $\alpha$ , that have been implicated in the pathogenesis of inflammatory bowel disease [6–8]. Poor sleep has been investigated in some chronic inflammatory diseases [9] and found to be prevalent in rheumatoid arthritis [10] and multiple sclerosis [11].

Inflammatory bowel disease (IBD) is an relapsing-remitting autoimmune disorder that results from a complex interaction between genetics and the environment [12]. IBD leads to a variety of debilitating symptoms such as diarrhea and abdominal pain. It is also associated with so called extra-intestinal manifestations, that include joint pain and skin rashes amongst others [13, 14]. Subjective assessment of the activity of IBD involves patient reported symptoms and utilizes validated scoring systems to ascertain the severity of IBD activity [15]. The reliability of subjective assessment of IBD activity is limited by the high prevalence of so called irritable bowel syndrome (IBS) like symptoms [16]. These IBS-like symptoms are often indistinguishable from the symptoms of active IBD and can occur in the absence of active IBD. Differentiating inactive IBD with IBS-like symptoms from active IBD requires the use of objective measures of IBD activity that directly confirm the presence of inflammation. These objective measures include endoscopic procedures such as colonoscopy, imaging such as magnetic resonance imaging and stool testing for markers of inflammation.

The relationship between IBD activity and sleep quality has been investigated previously with mixed results. A recent metaanalysis on the subject reached the conclusion that subjective sleep quality is worse in those with active IBD [17]. IBD related symptoms themselves, such as diarrhea and abdominal pain, may well disruptive sleep [18], however other studies suggest that endoscopically or histologically active IBD in the absence of any IBD symptoms may be sufficient to disrupt sleep [19, 20]. Extra-intestinal manifestations may also be important with a study suggesting those with enteropathic arthropathy were more likely to have poor sleep than those without [21]. Others suggest that psychosocial factors may be important [22], and in particular depression has been frequently associated with poor sleep [22-29] in an IBD population. Fatigue has also been associated with sleep quality [30-36] and is known to be highly prevalent in people with IBD [37].

Sleep may also be relevant to the development of IBD with data from the Nurses' Health Study showing that sleep duration was associated with the risk of ulcerative colitis, but not Crohn's disease [38]. Sleep quality may also have prognostic value in Crohn's disease with sleep associations seen with increased likelihood of hospitalization and risk of relapse. The effect of IBD therapeutic agents on sleep has been investigated with a prospective study showing improvement in sleep following introduction of biologic therapy [27]—this of course paralleled an improvement in IBD activity. Others have not been able to

demonstrate a relationship between the different IBD therapies and sleep quality [39].

In a recent meta-analysis subjective sleep quality was worse in those with IBD than controls [17]. This may be due to IBD associated symptoms, however there is some literature suggesting that those with inactive IBD also appear to have poor sleep [29, 33, 40, 41], although it is unclear if sleep quality in inactive IBD is worse than that of controls. Much of this data relates to subjective sleep quality with few studies incorporating objective sleep quality. Results from studies incorporating objective sleep quality are so far inconsistent noting a recent meta-analysis unable to establish an associated between objective sleep quality and IBD activity [17]. Furthermore, there was significant heterogeneity present in previous meta-analyses that is not well explained [17, 18].

This meta-analysis aimed to extend the work of the previous meta-analyses [17] by establishing the pooled prevalence of poor sleep-in IBD and exploring any heterogeneity that may be present. To the author's knowledge there has been no previously published estimate of the prevalence of poor sleep-in IBD. An improved understanding of the burden of poor sleep-in IBD may lead to further investigation and interventional studies in this area that may result in improved quality of life for this population.

#### Methods

This systematic review and meta-analysis was prospectively registered with the International Prospective Register of Ongoing Systematic Reviews [42]. It was performed according to the preferred reporting item for systematic reviews and metaanalyses (PRISMA) guidelines [43].

#### Search strategy

Pubmed, MEDLINE, and PsychINFO were searched from inception to November 2021, including articles published in the English language using the following search string: (sleep OR circadian OR insomnia OR apnea) AND [(inflammatory bowel disease) OR (crohn's disease) OR (ulcerative colitis) OR IBD OR crohn's OR colitis)].

#### Eligibility criteria

Studies were included if they met the following criteria: (1) cross-sectional, observational, case control, cohort or randomized controlled trial available (2) included a distinct population of people with inflammatory bowel disease (age  $\geq$  18 years old). Studies with control groups of a healthy population accepted. (3) Sleep quality assessment using a validated subjective patient reported measure of sleep.

Exclusion criteria included: (1) inappropriate study population such a pediatric or adolescent population. (2) Case report or review

#### Study selection

The first author (AB) performed the literature review and two other authors (PS and JB) independently screened full texts against eligibility criteria, with disagreement resolved by discussion with involvement of another author (RM) when required.

#### Data collection

Data collection was performed by AB. A pre-defined spreadsheet was used for data collection. Items collected for each study population included type of IBD, age, gender, study design, sample size, sleep assessment, outcome of study, disease activity in terms of subjective scores of disease activity or objective measures of disease activity, IBD disease duration, depression in terms of scores assessing depressive symptoms.

#### Study quality assessment

Risk of bias in individual studies was assessed according to study design. Cross-sectional or observational studies were assessed according to modified Newcastle-Ottawa Scale. Cohort or case control studies were assessed according to Newcastle-Ottawa Scale [44]. Statistical analysis was performed using Stata SE 16 (StataCorp, College Station, TX, USA) and the 'metaprop' [45] command to estimate the pooled prevalence of poor sleep-in people with inflammatory bowel disease. Heterogeneity among studies was assessed using the I2 statistic with I2 > 50% considered to indicate substantial heterogeneity. A random effects model was used [45]. A Forest plot was performed to estimate individual and pooled effect sizes with associated 95% CI. Publication bias was assessed using funnel plots with significant visual asymmetry used to indicate publication bias. Egger's test with *p* values less than .05 were considered to indicate significant publication bias. Trim-fill analysis was undertaken. In order to investigate sources of heterogeneity subgroup analysis and meta-regression were conducted.

## Results

The literature search (see Figure 1) identified 519 records following removal of duplicates, which further reduced to 75 records following screening. Following exclusions 36 records

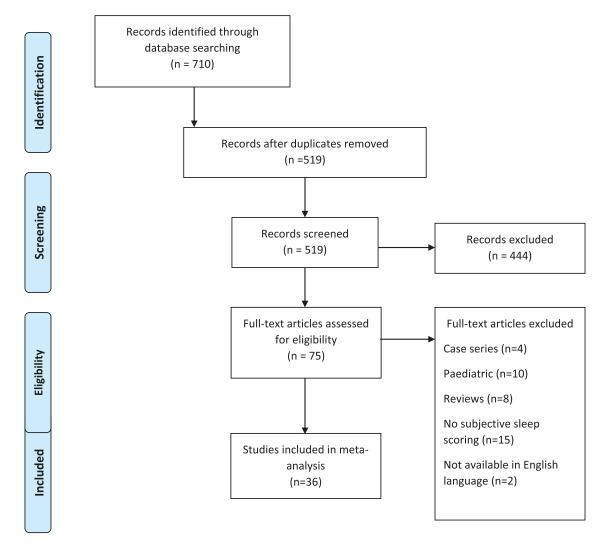


Figure 1. PRISMA flowchart—selection of studies and results of literature search for review and meta-analysis.

Study	Year Country	Year Country Poor sleep definition	Study population	Sam Population size	mple P če fi	Sample Percentage size female (%) Age	Number with Crohn's ge disease	Proportion with poor sleep	Study summary
Abdalla et al. [49]	2017 USA	PROMIS-SD t score > 5	PROMIS-SD t score > 50 Patients within Crohn's colitis foundation of America Partners Co- hort	IBD 63	6309 7	71 44	3947	0.54	IBD-IBS diagnosis was associated with in- creased narcotic usage and poor sleep
Ali et al. [ <b>20</b> ]	2013 USA	PSQI > 5	Single centre—clinic	IBD	41 6	66 37	23	0.87	Clinically active IBD was associated with poor
Ananthakrishnan et al. [29]	2013 USA	PROMIS-SD t score > 5	PROMIS-SD t score > 50 CCFA partners cohort	IBD 3.	3173 7	72 44	2079	0.6	Sleep Sleep disturbance was associated with an increased risk of disease flares in Crohn's discosobut not ubcosting colifie
Ballou et al. [62]	2018 USA	PSQI > 5	Single centre—clinic	IBD	44 7	71 42	22	0.54	ubease out not utestative contus IBD patients at a tertiary clinic have poorer sleen than healthy controls
Bazin et al. [63]	2019 France	PSQI > 5	Single centre—clinic	Crohn's disease	34 4	44 40	34	0.35	Sleep efficiency is lower in those active Crohn's disease than in remission
Bucci et al. [64]	2018 Italy	PSQI > 5	Single centre—clinic	IBD	47 5	53 38	28	0.38	Bruxism was associated with pathological
Calvo et al. [26]	2020 Spain	PSQI > 5	Single centre—clinic	IBD	102 4	43 45	51	0.54	Poor sleep quality is present in more than half
Chakradeo et al. [65]	2018 USA	PSQI > 5	Single centre—clinic	IBD	115 6	62 41		0.63	of people with JDD Later chronotype and markers of circadian misalignment were associated with IBD specific complications and lower quality
Chrobak et al. [ <mark>3</mark> 1]	2018 Poland	PSQI > 5	Single centre—clinic	IBD	72 4	42 42	34	0.68	of life Chronotype preferences contribute to fatigue
Frigstad et al. [ <b>32</b> ]	2018 Norway	BSNQ	Multi-centre	IBD 4	405 4	49 40	227	0.19	III IBU Sleep and depressive symptoms were associ-
Gîlc-Blanariu et al. [22]	2020 Romania PSQI > 5	PSQI > 5	Single centre—clinic	IBD	110 4	47 44	34	0.75	ateu with total laugue scores Poor sleep is frequent in IBD and associated with psychological distress
Gingold-Belfer et al. [66] 2014 Israel	] 2014 Israel	PSQI > 5	single centre—clinic	Crohn's disease	108 4	47 40	108	0.37	Poor sleep is associated with active Crohn's disease but not inactive disease
Graff et al. [ <mark>33</mark> ]	2011 USA	PSQI > 5	Manitoba IBD cohort		318 6	60 43	160	0.49	Poor sleep is prevalent in those with active IBD but also in those with inactive IBD
Habibi et al. [67]	2019 Iran	PSQI > 5	Single centre—clinic	IBD	68 6	63 38	24	0.32	Poor sleep is prevalent in those with IBD including those in remission
Hashash et al. [34]	2016 USA	PSQI > 5	Single centre—registry	IBD	685 5	53 44	418	0.54	Fatigue was associated wit poor sleep and
Hood et al. [24]	2018 USA	PSQI > 5	Multi-centre—clinic	IBD	47		0	0.59	psychopaulougy Poor sleep is prevalent in ulcerative colitis
IsHak et al. [48]	2017 USA	PROMIS-SD t score > 5	PROMIS-SD t score > 50 Single centre—clinic	IBD	110 4	43 42	62	0.6	and related to uppression Patient's with Crohn's disease demonstrated worse impairments in quality of life and
Iskandar et al. [68]	2020 USA	PSQI > 5	Single centre—clinic	Crohn's disease	61	32	61	0.57	tunction than those with ucertative courts Crohn's disease patients reported more dis- turbed sleep than controls but this was not confirmed with objective measures

Table 1. Studies with people with inflammatory bowel disease with subjective sleep quality assessment

Table 1. Continued

Study Year Countr Kani et al. [69] 2019 Turkey Kappelman et al. [47] 2014 USA						with I	Proportion	
t al. [69] Iman et al. [47]			Comp	Samula Darrantara		uquyo	with noor	
	Year Country Poor sleep definition	Study population	Population size	female (%)	Age		sleep	Study summary
	ey PSQI > 5	Single centre—clinic	IBD 136	5 58	39	72 (	0.59	Dream anxiety may lead to sleep disturbance in patients with IBD
		PROMIS-SD t score > 50 internet cohort multi-	IBD 10634	ł 71	44 66	6689 (	0.58	Health outcomes measures differ between pa-
Kaskin at al [70] 2020 Turkav	PSOI > 5	centre Single centre—clinic	IRD 80	26	37	41	051	tients with IBD and the general population IBD risk factor for slean disturbance with
					5		4	eveningness more common than in controls
Lee et al. [39] 2018 USA	PSQI > 5	Single centre—clinic	IBD 56	5 66	45	39 (	0.82	Treatment with immuno-modulators or
								biologics does not appear to improve sleep quality
Marinelli et al. [25] 2020 Italy	PSQI > 5	Single centre—clinic	IBD 166	5 47	44	87 (	0.67	Sleep quality was not associated with IBD ac- tivity but with mood, disability and quality of life
Michalopoulos et al. [19] 2018 Greece	ce PSQI > 5	Single centre—clinic	IBD 90	) 46	40	54 (	0.45	In IBD in clinical remission endoscopic find-
					!			ings was associated with poor sleep
Schindlbeck et al. [36] 2016 Germ	2016 Germany PSQI > 5	Single centre—clinic	IBD 43	3 72	47	30	0.61	Restless leg syndrome in inflammatory dis- ease with associated with worse quality of life
Sobolewska-Włodarczyk 2018 Poland et al. [71]	nd PSQI > 5	Single centre—clinic	IBD 65	5 43	40	30	0.69	Poor sleep-in IBD related to IBD activity
Sobolewska-Włodarczyk 2020 Poland et al. [72]	nd PSQI > 5	Single centre—clinic	IBD 65	5 47	40	30	0.57	Specific adipokine profiles are associated with circadian rhythms
Sochal et al. [23] 2020 Poland	nd PSQI > 5	Single centre—clinic	IBD 133	3 55	37	68 (	0.43	Poor sleep-in IBD is common and related to mood
Sofia et al. [73] 2019 USA	PSQI>5	Single centre—clinic	IBD 92	2 62	43	92 (	0.77	Poor sleep is common in Crohn's disease and
Stevens et al [27] 2016 IISA		PROMIS-SD t score > 50 Single centre—registry	IBD 160	48	35	94	0.44	associated with adverse outcomes Vedoliznmah and anti-TNF hiologics were as-
					)			sociated with improvement in sleep quality
Takahara et al. [74] 2016 Japan	n PSQI > 5	Single centre—clinic	IBD 80	) 42	42	34 (	0.4	Restless leg syndrome occurs frequently in
Uemura et al. [75] 2016 Japan	n PSQI > 5.5	Single centre—clinic	IBD 136	5 44	42	48 (	0.44	Japanese patients with IBD Sleep disturbance common in Japanese IBD
								patients and associated with poor quality of life
van Langenberg et al. 2017 Austr [76]	2017 Australia PSQI > 5	Single centre—clinic	IBD 49	9 58	44	49 (	0.63	Crohn's disease patients demonstrated subtle cognitive impairment
Wilson et al. [28] 2014 USA		PROMIS-SD t score > 50 single centre—registry	IBD 131	l 55	25	78 (	0.44	High CRP associated with poor sleep irre- spective of night-time disruptions
		Single centre—clinic			38	30 (	0.51	IBS may worsen sleep disturbance in IBD
Zhang et al. [21] 2020 China	PSQI >	Single centre—clinic	IBD 120	0 50	36		0.99	Sleep quality in those with peripheral arthropathy and IBD was worse than those without

Characteristics of studies included in the meta-analysis of poor sleep prevalence. See Supplementary Table 1 for further details. USA, United States of America; IBD, inflammatory bowel disease; PSQI, Pittsburgh Sleep Quality Index; BSNQ, Basic Nordic Sleep Questionnaire—first question used.

	Number of studies	Coefficient	Standard error	P value	Residual heterogeneity (I2%)
Crohn's disease	31	0.0147	0.10	.88	96.8
Age	36	0.017	0.006	.005	95.6
Female gender	33	0.002	0.002	.28	96.5
IBD disease duration	18	0.005	0.007	.54	97.6
Objective IBD activity	8	0.64	0.17	.001	30.5
Subjective IBD activity	25	0.013	0.21	.95	98.0
Depression	15	0.13	0.17	.43	95.6

Table 2. Meta-regression performed for prevalence of poor sleep

IBD, inflammatory bowel disease.

were included in the meta-analysis incorporating 24 209 people with IBD.

#### Subgroup analysis

#### Study characteristics

Characteristics of included studies can be seen in Table 1 and further data in Supplementary Table 1. Publication dates ranged from 2011 to 2020. Most of the studies were single centre (n = 20), two were multi-centre, three recruited from an existing IBD registry, two recruited from a longitudinal cohort study, three used internet survey data, and two used data from a nationwide IBD cohort. The majority incorporated a cross-sectional design. No study included sample size calculations for prevalence estimates, and no study incorporated a population sampling regimen. Sample size ranged from 34 to 10 634 participants. The mean age of participants ranged from 42 to 72%.

#### Measurement of sleep quality

The Pittsburgh Sleep Quality Index (PSQI) was reported in the majority of included studies (n = 29) (see Table 2).The PSQI is a validated measure to assess perceived sleep quality [46]. The index consists of subscales on sleep duration, sleep disturbance, sleep latency, daytime dysfunction, sleep efficiency, overall sleep quality and medications for sleep. The score ranges from 0 to 21, with a PSQI > 5 considered to represent poor sleep quality. PSQI sub-scores were reported in seven studies and consequently this was not investigated further.

The Patient Reported Outcomes Measurement Information Systems sleep disturbance (PROMIS-SD) questionnaire was used by six studies [27–29, 47–49]. The PROMIS-SD questionnaire was developed by the National Institute of Health [50]. The PROMIS-SD has comparable performance to the PSQI in identifying poor sleep [51]. A PROMIS-SD t score over 50 is referred to as poor sleep. A single study [32] used the Basic Nordic Sleep Questionnaire [52] (BNSQ), utilizing the first dimension of the BNSQ and a score above 3 considered significant.

#### Prevalence of poor sleep-in IBD

The prevalence of poor sleep varied from 32 to 99%, with random effects model derived pooled prevalence of 55%, 95% CI (51–59) with substantial heterogeneity (Forest plot in Figure 2), outliers were removed [21, 32]. Funnel plot was symmetric (Supplementary Figure 1) and Egger's test not significant (p = .49). The Trim-fill method did not suggest any additional studies.

Subgroup analysis was performed for definition of poor sleep, study of origin and publication date. There was no difference in the prevalence of poor sleep by definition of poor sleep (PSQI or PROMIS-SD sleep, p = .75). Most studies were from the United States of America (n = 15), followed by Europe (n = 12), and others including Australia, Japan, Turkey and Iran. The pooled prevalence was similar between Europe (56% [49–63]), and the USA (58% [53–64], both of which were significantly different to other (Australia, Japan, Turkey, Iran) (44% [36–52]) (p = .01)(see Supplementary Figure 2). Publication date subgroups were considered from 2011 to 2016 (n = 10), and 2017 to 2020 (n = 23). The prevalence of poor sleep was higher in the 2017 to 2020 subgroup (p = .03, 58% [53–63] v 50% [44–55]). However, altering the publication date subgroups by a single year resulting in no effect seen, discounting the above result.

#### Meta-regression

Meta-regression was performed for demographics and IBD related data (see Table 2 and supplementary Table 3). Age was significant (p = .005) with increasing proportion of poor sleep associated with increase in age, however residual heterogeneity remaining significant (I2 95.6%). Meta-regression was not significant for gender (p = .28), IBD type (p = .88), and IBD disease duration (p = .54).

#### IBD activity

IBD activity was reported in 25 studies (n = 23 229) in the form of subjective disease activity scores such as the Harvey Bradshaw Index [15] or the Crohn's disease activity index [53] (see Supplementary Table 2). The meta-regression incorporated the number of people with active IBD as per these subjective disease activity scores. Meta-regression for subjective disease activity was not significant (p = .95). Objective IBD activity was reported in eight studies (n = 1931), with objective measures including C-reactive protein, fecal calprotectin, endoscopic findings and histology (see Supplementary Table 3). On meta-regression objective IBD activity was significant (p = .001), increasing proportion of poor sleep was associated with increase in objective disease activity. Residual heterogeneity was I2 30.5%, this is as compared to heterogeneity for these eight studies at I2 of 82.6%, suggesting that objective disease activity may explain much of the inter-study heterogeneity.

Study	Prevalance of poor sleep with 95% CI	Weight (%)
Abdalla et al	0.55 [ 0.53, 0.56]	3.64
Ananthakrishnan et al	0.60 [ 0.58, 0.62]	3.63
Ballou et al	0.55 [ 0.40, 0.69]	2.48
Bazin et al	0.35 [ 0.19, 0.51]	2.34
Bucci et al	0.38 [ 0.24, 0.52]	2.57
Calvo et al -	0.55 [ 0.45, 0.65]	3.04
Chakradeo et al	- 0.63 [ 0.55, 0.72]	3.13
Chrobak et al	0.68 [ 0.57, 0.79]	2.92
Gilc-Blanariu et al	0.75 [ 0.67, 0.83]	3.20
Gingold-Belfer et al	0.37 [ 0.28, 0.46]	3.10
Graff et al	0.49 [ 0.44, 0.55]	3.43
Habibi et al	0.32 [ 0.21, 0.43]	2.88
Hashash et al	0.54 [ 0.50, 0.58]	3.55
Hood et al	- 0.60 [ 0.46, 0.74]	2.56
IsHak et al	- 0.60 [ 0.51, 0.69]	3.09
Iskander et al	- 0.57 [ 0.45, 0.70]	2.74
Kappelman et al	0.59 [ 0.58, 0.60]	3.65
Kani et al -	0.59 [ 0.51, 0.67]	3.18
Keskin et al	0.52 [ 0.41, 0.62]	2.96
van Langenberg at al	0.61 [ 0.48, 0.75]	2.60
Lee et al	0.82 [ 0.72, 0.92]	3.00
Marinelli et al -	- 0.67 [ 0.60, 0.75]	3.29
Michalopoulos et al	0.46 [ 0.35, 0.56]	2.97
Schindlbeck et al	0.60 [ 0.46, 0.75]	2.50
Sobolewska-Włodarczyk et al, 2020	0.57 [ 0.45, 0.69]	2.78
Sobolewska-Włodarczyk et al, 2018	0.69 [ 0.58, 0.80]	2.87
Sochal et al -	0.44 [ 0.35, 0.52]	3.17
Sofia et al	0.77 [ 0.69, 0.86]	3.15
Stevens et al	0.44 [ 0.36, 0.51]	3.24
Takahara et al	0.40 [ 0.29, 0.51]	2.92
Uemura et al -	0.44 [ 0.36, 0.52]	3.17
Wilson et al	0.44 [ 0.36, 0.53]	3.16
Zargar et al	0.52 [ 0.43, 0.61]	3.09
Overall 🔶	0.55 [ 0.51, 0.59]	
Heterogeneity: $\tau^2 = 0.01$ , $I^2 = 96.28\%$ , $H^2 = 26.92$		
Test of $\theta_i = \theta_i$ : Q(32) = 240.07, p = 0.00		
Test of θ = 0: z = 26.33, p = 0.00	.8 1	
.2 .4 .6 Random-effects REML model	.8 1	

Figure 2. Forest plot of the prevalence of poor sleep-in those with inflammatory bowel disease.

#### Depression

Assessment of depression was performed in 15 studies (n = 10744) (see Supplementary Table 4). Eight of these studies reported a significant association between poor sleep quality and depression [22–29]. Scoring systems included the Hospital

Anxiety and Depression Scale [54] (n = 6), PROMIS [55] depression score (n = 4), Beck's Depression Inventory II [56] (n = 3), depressive symptoms (n = 1) and depression under treatment (n = 1). On meta-regression depression was not significant (p = .43).

#### Discussion

This is the largest and only meta-analysis to date providing prevalence estimates for poor sleep-in IBD. The pooled prevalence for poor sleep-in IBD was high (55%), eclipsing that reported in a recent meta-analysis of fatigue (47%) [37], and of symptoms of anxiety (32%) and depression (25%) [4]. The prevalence of poor sleep reported here is of a higher magnitude than the prevalence of sleep disorder in IBS with a recent meta-analysis reporting a pooled prevalence of 37.6% [57]. This highlights the importance of poor sleep-in IBD and suggests further resources should be allocated to investigate this area.

Sources of heterogeneity in the prevalence estimate of poor sleep included age, geographic location, and objective disease activity. Age-related sleep changes have been well described with decreasing sleep quality accepted [58], with a similar association between age and sleep quality seen in a rheumatoid arthritis population [59, 60]. It was considered that the significance of age may also relate to IBD disease duration, however this was not significant on meta-regression.

Objective IBD activity did vary between studies and was a significant source of heterogeneity. A recent meta-analysis was unable to elicit a significant relationship between objective IBD activity and sleep [17], which may in part be due to the small number of studies utilizing objective measures of IBD activity. It did however find that subjective IBD activity was associated with poor sleep quality—a finding not replicated here despite the variance between different studies. This suggests that the underlying inflammatory response may be more significant than the associated symptoms, consistent with studies associated histology activity and endoscopic activity in the absence of symptoms with poor sleep [19, 20]. IBD activity is likely not the only driver of poor sleep quality with several studies reporting frequent poor sleep-in those with inactive disease [29, 33, 40, 41].

Depression was not a significant source of heterogeneity despite varying between studies and despite several positive findings in the literature [22–29]. Low physical activity [31, 61] and the presence of extra-intestinal IBD manifestations [21] have also been associated with poor sleep, unfortunately these were reported a minority of studies making further investigation impractical.

#### Limitations

As a result of the paucity of studies incorporating objective sleep assessments, we used a definition of poor sleep based on selfreported sleep quality. There is a suggestion in some studies [25] that people with IBD will report significantly worse sleep than can be substantiated objectively, and consequently the true prevalence of poor sleep may be lower. This supports the need for objective sleep assessments in people with IBD. Other limitations include most studies being single centre, although results were similar to multi-centre or nationwide studies. Although we note that prevalence from nationwide studies was similar to other single centre studies. No study incorporated sample size calculations or included a rigorous sampling approach. There was a general lack of demographic data reported in studies, such as race, that may have a significant influence on the prevalence of poor sleep-in this population. The differentiation between gender and sex was not well defined in most studies. Finally, a single reviewer was responsible for data collection.

#### Future work

Further work should consider studies incorporating objective disease and sleep quality measurements to understand the relationship and type of sleep disorders in this population. There are few interventional studies in this area, with a need to establish if the potential benefit of improving sleep-in people with IBD would extend beyond quality of life to incorporate IBD related outcomes such as IBD activity, and surgery. There is also the lack of simple IBD specific screening tool for use in IBD clinic to identify those with poor sleep who would benefit from referral onto a sleep physician.

#### Conclusions

This meta-analysis has demonstrated that the prevalence of poor sleep-in IBD is significant, although there was substantial heterogeneity between studies. Meta-regression demonstrated that age and objective IBD activity were significant, with subjective IBD activity not significant. Objective IBD activity explained most of the heterogeneity between studies. Further research is required in this area to establish the relationship between IBD activity and sleep quality and to consider sleep targeted interventions in an IBD population.

#### Supplementary material

Supplementary material is available at SLEEP Advances online.

#### Funding

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#### **Disclosure Statement**

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#### Data Availability Statement

The data underlying this article are available in the Harvard Dataverse Digital Repository at https://doi.org/10.7910/DVN/FVLPYA

#### **Author Contributions**

A.B.: responsible for study concept and design, data acquisition, analysis and data interpretation, drafting of manuscript, critical revision of the manuscript. P.S.: responsible for data acquisition, data interpretation, drafting of manuscript, critical revision of the manuscript. J.B.: responsible for data acquisition and critical revision of the manuscript. P.B.: responsible for critical revision of the manuscript. J.A.: responsible for study conception. R.J.F.: responsible for study conception. R.M.: responsible for critical revision of the manuscript. S.M.: responsible for study concept and design, critical revision of the manuscript.

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