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13 **Abstract**

14 Inflammatory Bowel Disease (IBD) is commonly associated with poor global sleep
15 quality, and has been posited as a modifiable determinant of IBD related outcomes, with
16 recent calls to screen for, and subsequently treat problems sleeping as part of routine IBD
17 care. However, there is little evidence on the specific *types* of problems sleeping (e.g., sleep
18 apnea, insomnia etc.) that might characterize the poor sleep quality experienced by those with
19 IBD. The present research aimed to investigate the severity of seven specific types of
20 problems sleeping in those with IBD vs. a healthy control group. This cross-sectional
21 comparison study recruited $N = 409$ with IBD, and $N = 377$ healthy controls (total sample N
22 $= 786$). The Sleep-50 questionnaire was used to assess the presence of seven types of
23 problems sleeping. Multivariate Analysis of Covariance (MANCOVA) was used to compare
24 the severity of sleep disturbances between the IBD and control groups. Those in the IBD
25 group reported significantly more severe experiences of five of the seven domains of the
26 Sleep-50, including increased; sleep apnea, insomnia, narcolepsy, restless legs, and
27 nightmares. In conclusion, those with a diagnosis of IBD reported significantly more severe
28 symptoms across a range of specific problems sleeping when compared to controls. More
29 research is needed to; i) improve the identification and treatment of problems sleeping in
30 routine care; ii) understand the mechanism(s) of action that links problems sleeping to IBD
31 related outcomes; and iii) develop adapted interventions to improve sleep in those with IBD.

32 Word count: 246

33 *Keywords:* Sleep; Inflammatory Bowel Disease; IBD; Crohn's Disease; Ulcerative
34 Colitis.

35

36 **A Comparative Study of the Nature and Magnitude of Problems Sleeping in**
37 **Inflammatory Bowel Disease (IBD) Compared to Healthy Controls**

38 In recent years, there has been a proliferation of research aiming to better understand
39 the role of sleep in a range of physical (Gallicchio & Kalesan, 2009; O'brien et al., 2010;
40 Pavlova, Ference, Hancock, & Noel, 2017; Wong et al., 2013), and mental health difficulties
41 (Baglioni et al., 2011; Scott, Rowse, & Webb, 2017; Taylor, Lichstein, Durrence, Reidel, &
42 Bush, 2005). The association between problems sleeping and health is particularly apparent
43 in those with Inflammatory Bowel Disease (IBD) - a chronic and incurable disease involving
44 inflammation of the gastrointestinal tract – where poor sleep quality is commonly reported
45 (Kinnucan, Rubin, & Ali, 2013; Swanson, Burgess, & Keshavarzian, 2011; Wilson et al.,
46 2015). Indeed, problems sleeping in those with IBD have been posited as a modifiable risk
47 factor for a number of IBD related outcomes including diagnosis incidence (Ananthkrishnan
48 et al., 2014), disease symptom flares (Ananthkrishnan, Long, Martin, Sandler, &
49 Kappelman, 2013; Uemura et al., 2016), poorer health related quality of life (Keefer,
50 Stepanski, Ranjbaran, Benson, & Keshavarzian, 2006; Ranjbaran, Keefer, Stepanski, Farhadi,
51 & Keshavarzian, 2007; Uemura et al., 2016), and fatigue (Graff et al., 2013). However,
52 despite a growing body of literature further elucidating our understanding of the experience
53 of sleep in those with IBD, there remains a number of opportunities that would facilitate calls
54 to screen for, and subsequently treat problems sleeping in those with IBD (Almedimigh et al.,
55 2018; Kinnucan et al., 2013).

56 **Opportunities for Advancement**

57 To date, the majority of research into the role of sleep disturbances in those with IBD
58 has tended to rely on more global measures of sleep quality (e.g., the Pittsburgh Sleep Quality
59 Index (PSQI); Buysse, Reynolds, Monk, Berman, & Kupfer, 1989), rather than measures able
60 to detect *specific* types of problems sleeping. For example, the PSQI can tell us somebody

61 has poor, or good self-reported sleep quality; however, it cannot tell us this is due to the
62 experience of specific types of problems sleeping (e.g., due to insomnia, sleep apnea,
63 nightmares etc.). Although there is evidence suggesting that those with IBD may experience
64 specific types of problems sleeping more commonly, including symptoms of sleep apnea
65 (Keefer et al., 2006), restless legs (Becker et al., 2018; Keefer et al., 2006), and nightmares
66 (Ranjbaran et al., 2007); the conclusions that can be drawn are limited - in that findings are
67 often reliant on single-item measures of specific problems sleeping, and/or small sample sizes
68 leading to underpowered studies. Consequently, it is important that research also uses multi-
69 item measures of specific sleep disturbances along with larger samples to draw more robust
70 conclusions. Secondly, few studies have compared the problems sleeping seen in IBD to
71 healthy controls (i.e., those without gastrointestinal diagnoses). Consequently, it is unclear
72 whether both the type and magnitude of problems sleeping differ between those with, and
73 without a diagnosis of IBD.

74 **The present research**

75 The lack of research investigating specific types of sleep disturbance in IBD relative
76 to healthy controls serves to inhibit two important avenues; i) the development and adaption
77 of interventions to target specific sleep disturbances experienced by those with IBD as a route
78 to improving IBD related outcomes; and ii) as has been recently suggested, the incorporation
79 of sleep disturbance screening into the routine clinical management of IBD (Almedimigh et
80 al., 2018; Kinnucan et al., 2013). The present research aims to address this by measuring the
81 severity of multiple types of specific problems sleeping in those with diagnosis of IBD
82 relative to healthy controls. We hope that doing so will provide a more comprehensive profile
83 of the types of problems sleeping that are experienced by people with IBD, with each type
84 generally having specific screening and treatment options.

85 **Materials and Methods**

86 **Participants**

87 The IBD group were recruited from three sources; (i) through an advertisement placed
88 on a national IBD charity website in the UK (Crohn's & Colitis UK); (ii) from IBD specific
89 online support groups; and (iii) from volunteer lists maintained by the research team. The
90 healthy control group was recruited from two sources; (i) from volunteer lists maintained by
91 the research team; and (ii) via a social media advertising campaign. Enrolment to the study
92 began in May 2017, and concluded in November 2017. Prior to taking part in the present
93 research, all participants were asked a number of screening and eligibility questions. To be
94 eligible for the IBD group, participants were required to; (i) have a diagnosis of IBD; and (ii)
95 be at least 16 years of age or older. To be eligible for inclusion in the control group,
96 participants were required to; (i) have no diagnosis of any gastrointestinal disorder (e.g., IBD,
97 Irritable Bowel Syndrome, coeliac disease etc.); and (ii) be at least 16 years of age or older.
98 Participants not meeting these criteria, those who did not provide full informed consent, and
99 those who did not start the online survey were excluded.

100 **Procedure**

101 Participants were invited to take part in an online study aiming to investigate the
102 severity of problems sleeping in those with, and without, a diagnosis of IBD. All outcome
103 measures were delivered anonymously online using Qualtrics, a web based survey hosting
104 platform (Qualtrics, 2018). Participants first read an information sheet detailing aspects of the
105 research before confirming eligibility via a series of screening items in line with the studies
106 inclusion and exclusion criteria. If eligible, participants provided electronic consent to
107 participate. The Research Ethics Committee based in the School of Health and Related
108 Research (SchARR), University of Sheffield, granted ethical approval.

109 **Outcome Measures**

110 **Demographics**

111 All participants were asked to provide information relating to their age, gender, and
112 whether they were currently receiving psychological therapy and/or medication for a mental
113 health or sleep related problem. Participants in the IBD group were asked a number of items
114 relating to their IBD, including their IBD diagnosis type (Ulcerative Colitis or Crohn's
115 Disease), number of years living with an IBD diagnosis, whether they had ever undergone
116 IBD related surgery, current and/or previous use of a stoma, and whether they were currently
117 taking medication for their IBD.

118 **The Sleep-50 Questionnaire**

119 The Sleep-50 is a 50 item self-report instrument designed to measure symptoms of
120 seven specific types of sleep disturbances (sleep apnea, insomnia, narcolepsy, restless legs,
121 circadian rhythm disruption, sleepwalking, & nightmares), as well as factors influencing
122 sleep (e.g., low mood, sleep environment not optimal, medication use), and the impact of
123 sleep complaints of daily functioning (e.g., feeling tired on awakening, difficulty
124 concentrating, worrying about sleep). Using a 4-point scale, participants are asked to rate the
125 extent to which they endorse each item over the last 4-weeks, ranging from 'not at all'
126 through to 'very much'. The Sleep-50 has been validated for use in both general population
127 samples, and those with clinically defined sleep disorders, demonstrating a clear factor
128 structure, high internal consistency, and good test-retest reliability (Spoormaker, Verbeek, van
129 den Bout, & Klip, 2005).

130 **The Short Inflammatory Bowel Disease Questionnaire (SIBDQ)**

131 The bowel symptoms subscale of the SIBDQ (Jowett, Seal, Barton, & Welfare, 2001)
132 was used as a proxy measure of disease symptom activity in the IBD group. The bowel
133 symptom subscale of the SIBDQ asks participants to rate the extent to which they endorse

134 three items pertaining to the frequency of IBD symptoms on a 5-point scale, with lower
135 scores indicating more frequent symptom activity. For example, participants are asked, “*How*
136 *often in the last two weeks have you been troubled by pain in the abdomen?*”. The bowel
137 symptoms subscale correlates strongly with several validated measures of disease activity
138 (Jowett et al., 2001), including the Simple Clinical Colitis Activity Index (SCCAI; Walmsley,
139 Ayres, Pounder, & Allan, 1998), and the Seo index (Seo et al., 1992), suggesting its valid use
140 as a proxy measure of disease activity.

141 **Approach to Analysis**

142 A one-way multivariate analysis of covariance (MANCOVA) was conducted to
143 investigate the severity of seven specific types of sleep disturbances measured by the Sleep-
144 50, as well as factors influencing sleep, and the impact of sleep complaints on daily
145 functioning in the IBD group relative to controls. Where the MANCOVA demonstrated
146 significant differences between the IBD and control groups in terms of the type of problem
147 sleeping, a sensitivity analysis in the form of hierarchical linear regression (including only the
148 IBD group) was conducted to investigate whether any IBD related characteristics were
149 significantly associated with the sleep disturbance. G-Power 3.1 (Faul, Erdfelder, Lang, &
150 Buchner, 2007) was used to determine the sample size. For the MANCOVA, based on a
151 small-to-medium sized effect at 90% power, and a strict significance threshold of $p < .001$,
152 the desired total sample size is $N = 560$. Given that the hierarchical linear regression includes
153 only the IBD group, a less conservative alpha level was set; based on a small-to-medium
154 sized effect at 90% power, and a significance threshold of $p < .05$, the desired total sample
155 size is $N = 263$.

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Results

Participants

Of the $N = 498$ participants in the IBD group who started the study procedures, $N = 409$ (82%) were included in the study, with $N = 89$ (18%) excluded. Of those excluded in the IBD group, $N = 9$ (10%) were under the age of 16, $N = 7$ (8%) had no diagnosis of IBD, $N = 22$ (25%) did not provide consent to take part, and $N = 51$ (57%) did not start the online surveys. With regards to the control group, $N = 472$ began the study procedures with $N = 377$ (88%) included in the study. Of the $N = 50$ (12%) who were excluded, $N = 3$ (6%) were under the age of 16, $N = 4$ (8%) had a diagnosis of IBD, $N = 20$ (40%) had diagnosis of Irritable Bowel Syndrome (IBS), $N = 10$ (20%) did not provide consent to take part, and $N = 13$ (26%) did not start the online surveys. Figure 1 describes of the flow of participants through the study, while Table 1 presents the demographic and clinical characteristics of both groups.

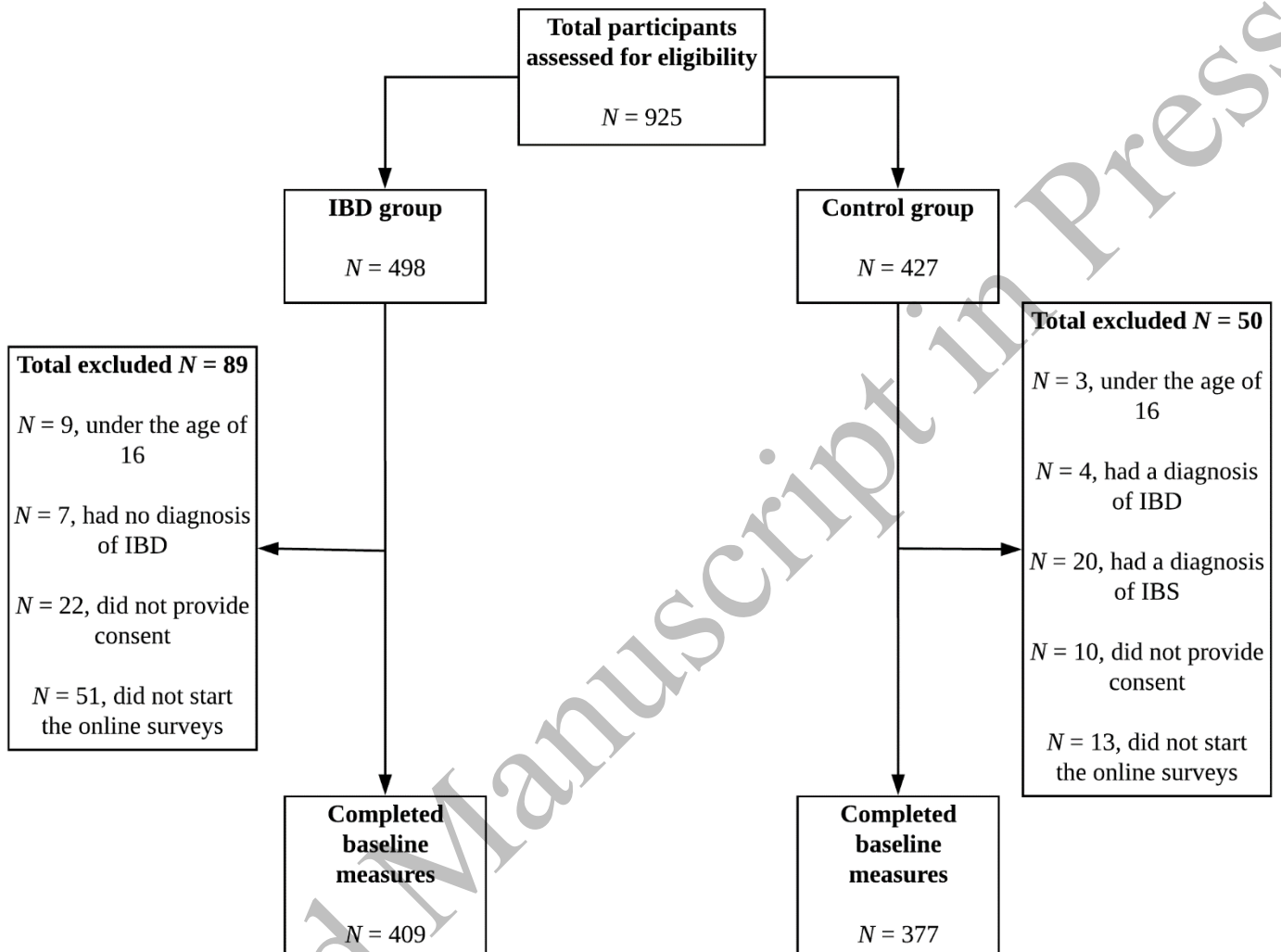
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169 **Figure 1**

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171 *A CONSORT Flow Diagram Showing the Flow of Participants Through the Study*

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173 **Table 1**174 *Baseline Sample Characteristics of the IBD and Control Group*

Variable	IBD group (N = 409)	Control group (N = 377)
Age, M (SD)	33.86 (11.57)	39.60 (14.51)
Gender, N (%)		
<i>Male</i>	74 (18%)	100 (27%)
<i>Female</i>	335 (82%)	277 (73%)
Sleep medication use, N (%)		
<i>Yes</i>	96 (23%)	17 (5%)
<i>No</i>	313 (77%)	360 (95%)
Sleep therapy, N (%)		
<i>Yes</i>	21 (5%)	3 (1%)
<i>No</i>	388 (95%)	374 (99%)
IBD type, N (%)		
<i>Ulcerative Colitis (UC)</i>	155 (38%)	-
<i>Crohn's Diseases (CD)</i>	254 (62%)	-
Years with IBD diagnosis, M (SD)	9.12 (8.52)	-
Surgery for IBD, N (%)		
<i>Yes</i>	172 (42%)	-
<i>No</i>	237 (58%)	-
Current stoma, N (%)		
<i>Yes</i>	58 (14%)	-
<i>No</i>	351 (86%)	-
Previous stoma, N (%)		
<i>Yes</i>	64 (16%)	-
<i>No</i>	345 (84%)	-
Immunosuppressant use, N (%)		
<i>Yes</i>	259 (63%)	-
<i>No</i>	150 (37%)	-

176 **Does specific sleep disturbance severity differ between groups?**

177 MANCOVA (controlling for age and gender) was used to examine whether the
178 severity of specific sleep disturbances differed between those in the IBD group vs. the control
179 group (see Table 2 for an overview of these analyses). There was a statistically significant
180 multivariate difference between groups ($F(9, 774) = 50.44, p < 0.001, \text{Eta}^2 = 0.08$), in that
181 participants in the IBD group reported significantly more profound sleep disturbance than the
182 control group. This effect was reflected in significantly more severe sleep disturbance across
183 seven of the eight subscales measured by the Sleep-50, including symptom severity of; **sleep**
184 **apnea** ($F(1, 782) = 12.94, p < 0.001, \text{Eta}^2 = 0.02$), **insomnia** ($F(1, 782) = 31.89, p < 0.001,$
185 $\text{Eta}^2 = 0.04$), **narcolepsy** ($F(1, 782) = 16.01, p < 0.001, \text{Eta}^2 = 0.02$), **restless legs** ($F(1, 782)$
186 $= 17.98, p < 0.001, \text{Eta}^2 = 0.02$), **nightmares** ($F(1, 782) = 13.87, p < 0.001, \text{Eta}^2 = 0.02$),
187 **factors influencing sleep** ($F(1, 782) = 35.81, p < 0.001, \text{Eta}^2 = 0.04$), and the **impact of**
188 **sleep disturbance on daily life** ($F(1, 782) = 63.69, p < 0.001, \text{Eta}^2 = 0.08$). There were no
189 significance differences between groups on the severity of **circadian rhythm disruptions**
190 ($F(1, 782) = 7.34, p = 0.01, \text{Eta}^2 = 0.01$), or **sleepwalking** ($F(1, 782) = 4.48, p = 0.04, \text{Eta}^2 =$
191 0.01).

192 **Table 2**193 *Descriptive Statistics and Between Group Comparisons of Sleep Disorder(s) in the IBD group vs. Controls*

Sleep outcome	IBD group (N = 409)		Control group (N = 377)		F	p	Eta ²
	M	SD	M	SD			
Sleep-50 total	95.47	20.48	84.88	21.38	50.44	< 0.001	0.08
<i>Sleep apnoea</i>	14.03	3.49	13.19	3.99	12.94	< 0.001	0.02
<i>Insomnia</i>	20.33	3.49	17.99	5.57	31.89	< 0.001	0.04
<i>Narcolepsy</i>	7.74	2.34	7.06	2.29	16.01	< 0.001	0.02
<i>Restless legs</i>	6.59	2.47	5.87	2.41	17.98	< 0.001	0.02
<i>Circadian rhythm disruption</i>	5.23	2.01	4.79	1.80	7.34	0.01	0.01
<i>Sleepwalking</i>	3.36	0.99	3.23	0.78	4.48	0.04	0.01
<i>Nightmares</i>	8.29	5.51	6.73	5.65	13.87	< 0.001	0.02
<i>Factors influencing sleep</i>	11.09	2.71	9.94	2.50	35.81	< 0.001	0.04
<i>Impact on daily function</i>	18.89	4.87	16.08	5.18	63.69	< 0.001	0.08

194 *Note: M = mean, SD = standard deviation, p values in bold type represent statistically significant effects at $p < 0.001$.*

195 Clinical correlates of sleep disturbance in the IBD group

196 Where there was a significant difference between the IBD and control group in the
197 preceding analysis, a sensitivity analysis was conducted using only the IBD group to investigate
198 potential clinical correlates of sleep disturbances. Table 3 presents the detailed results of this
199 analysis; however, in short, none of the characteristics of the IBD group were associated with the
200 experience of sleep apnoea ($F(8, 375) = 0.61, p = 0.77$), narcolepsy ($F(8, 375) = 0.46, p = 0.88$),
201 or nightmares ($F(8, 375) = 0.71, p = 0.68$). However, a higher IBD symptom activity as
202 measured by the bowel symptom subscale of the SIBDQ was negatively associated with
203 increased insomnia severity ($\beta = -0.14, p = 0.01$), restless legs symptom severity ($\beta = -0.14, p =$
204 0.03), increased factors influencing sleep, ($\beta = -0.15, p = 0.01$), and increased impact of sleep
205 disturbances on daily function ($\beta = -0.13, p = 0.01$). Furthermore, IBD diagnosis type was
206 associated with the impact of sleep complaints on daily function ($\beta = 0.14, p = 0.01$), with those
207 diagnosed with Ulcerative Colitis reporting more daily impact.

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209 **Table 3**210 *Clinical Correlates of Specific Sleep Disturbances in the Inflammatory Bowel Disease (IBD)*211 *Group*

Sleep problem	β	<i>t</i>	<i>p</i>
Sleep apnea			
<i>Age</i>	-0.02	-0.31	0.75
<i>Gender</i>	-0.02	-0.40	0.69
<i>IBD type</i>	0.02	0.30	0.76
<i>Years with IBD</i>	-0.01	-0.09	0.93
<i>IBD surgery</i>	0.06	0.91	0.36
<i>Current stoma</i>	0.04	0.74	0.46
<i>IBD medication</i>	0.01	0.27	0.79
<i>IBD symptom activity</i>	-0.02	-0.44	0.66
Insomnia			
<i>Age</i>	-0.10	-1.62	0.11
<i>Gender</i>	-0.05	-0.91	0.36
<i>IBD type</i>	0.02	0.37	0.71
<i>Years with IBD</i>	0.05	0.79	0.43
<i>IBD surgery</i>	-0.07	-1.02	0.31
<i>Current stoma</i>	0.06	1.01	0.31
<i>IBD medication</i>	0.04	0.78	0.44
<i>IBD symptom activity</i>	-0.12	-2.21	0.03
Narcolepsy			
<i>Age</i>	-0.03	-0.55	0.59
<i>Gender</i>	0.02	0.43	0.66
<i>IBD type</i>	0.06	0.98	0.33
<i>Years with IBD</i>	-0.04	-0.65	0.52
<i>IBD surgery</i>	-0.05	-0.81	0.42
<i>Current stoma</i>	-0.03	-0.46	0.65
<i>IBD medication</i>	-0.05	-0.98	0.33

<i>IBD symptom activity</i>	-0.04	-0.65	0.51
Restless legs			
<i>Age</i>	0.04	0.75	0.45
<i>Gender</i>	0.02	0.31	0.75
<i>IBD type</i>	-0.01	-0.19	0.85
<i>Years with IBD</i>	-0.02	-0.24	0.81
<i>IBD surgery</i>	-0.01	-0.20	0.84
<i>Current stoma</i>	0.07	1.13	0.26
<i>IBD medication</i>	0.01	0.10	0.92
<i>IBD symptom activity</i>	-0.12	-2.22	0.03
Nightmares			
<i>Age</i>	0.01	0.19	0.85
<i>Gender</i>	0.04	0.76	0.45
<i>IBD type</i>	0.01	0.12	0.91
<i>Years with IBD</i>	-0.10	-1.53	0.13
<i>IBD surgery</i>	-0.11	-1.76	0.08
<i>Current stoma</i>	0.10	1.67	0.10
<i>IBD medication</i>	-0.02	-0.32	0.75
<i>IBD symptom activity</i>	0.06	1.16	0.25
Factors influencing sleep			
<i>Age</i>	-0.05	-0.81	0.42
<i>Gender</i>	-0.04	-0.80	0.42
<i>IBD type</i>	0.07	1.22	0.22
<i>Years with IBD</i>	0.07	1.11	0.27
<i>IBD surgery</i>	-0.06	-0.92	0.36
<i>Current stoma</i>	0.04	0.71	0.48
<i>IBD medication</i>	0.06	1.13	0.26
<i>IBD symptom activity</i>	-0.15	-2.70	0.01
Impact on daily function			
<i>Age</i>	0.02	0.35	0.73
<i>Gender</i>	-0.03	-0.60	0.55

<i>IBD type</i>	0.14	2.56	0.01
<i>Years with IBD</i>	0.01	0.17	0.86
<i>IBD surgery</i>	-0.06	-0.99	0.32
<i>Current stoma</i>	-0.07	-1.13	0.26
<i>IBD medication</i>	0.01	0.26	0.79
<i>IBD symptom activity</i>	-0.13	-2.48	0.01

212 *Note: p values in bold type represent statistically significant effects at $p < 0.05$*

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Discussion

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The present research aimed to investigate the nature and magnitude of specific types of problems sleeping in those with IBD relative to a healthy control group (i.e., no gastrointestinal diagnoses). Our findings suggest that relative to controls, those with IBD reported significantly more severe symptoms of five of the seven sleep disturbances measured by the Sleep-50, including; sleep apnea, insomnia, narcolepsy, restless legs, and nightmares. Furthermore, those with IBD reported experiencing significantly more factors that are known to influence sleep (e.g., low mood, sleep environment not optimal, medication use), and a greater impact of sleep disturbances on daily life (e.g., feeling tired on awakening, difficulty concentrating, worrying about sleep). Interestingly, only the experience of insomnia, and the impact of sleep disturbances on daily life was associated with some clinical features of IBD. Greater insomnia severity was associated with more frequent IBD symptoms, whereas a diagnosis of Ulcerative Colitis was significantly associated with a greater impact of sleep disturbances on daily life.

The key finding reported in the present research is that those with IBD reported more severe experiences of a variety of specific problems sleeping, including; sleep apnea, insomnia, narcolepsy, restless legs, and nightmares, as well as more disruptions to factors known to influence sleep, and a greater impact of sleep disturbances on daily life. Although the majority of extant research reports the association between global sleep quality and IBD, the few studies that have examined specific types of problems sleeping are supported by the present research. For example, the findings reported here support previous research suggesting that those with IBD experience sleep disordered breathing (i.e., a core symptom of sleep apnoea, Keefer et al., 2006), restless legs (Becker et al., 2018; Keefer et al., 2006), and nightmares (Ranjbaran et al., 2007). As well as strengthening existing findings using a larger sample size, and a multi-item measure

236 *specific* problems sleeping, the findings reported here also extend previous work by reporting an
237 increased severity of insomnia, and narcolepsy symptoms in the IBD group relative to controls.
238 Although more research is warranted, these findings suggest that the routine care of those with
239 IBD might consider incorporating assessments to screen for the presence a variety of specific
240 types of problems sleeping.

241 **Future directions**

242 It seems clear that problems sleeping are associated with IBD, and may even represent a
243 core experience of IBD itself (Keefer et al., 2006). However, *how* problems sleeping are related
244 to IBD, and the direction that best explains this association is currently unclear. Consequently,
245 future research might seek to elucidate the mechanisms of action that can explain how problems
246 sleeping can exert an effect on IBD related outcomes, using designs able to inform the direction
247 of effect. Research that is well placed to disentangle the impact of mediators and the direction of
248 association between sleep and IBD outcomes are those that employ longitudinal designs (i.e.,
249 designs that measure variables over time, so that the temporal relationship between variables can
250 be investigated), research that is currently lacking (for notable exceptions, see Ananthakrishnan
251 et al., 2014; Ananthakrishnan et al., 2013; Graff et al., 2013; Uemura et al., 2016). Problems
252 sleeping have been posited as a possible modifiable environmental risk factor that can adversely
253 affect IBD outcomes. However, despite recent calls to screen for, and subsequently treat
254 problems sleeping in those with IBD (Almedimigh et al., 2018; Kinnucan et al., 2013), there are
255 relatively few guidelines to facilitate clinical decision making in this area (National Institute for
256 Health and Care Excellence, 2015; Kinnucan et al., 2013). Therefore, future research might
257 profitably seek to understand the barriers and facilitators to effective sleep management in
258 routine IBD care, from both the patients', and healthcare professional's perspectives as a route to

259 developing effective guidelines to facilitate the detection and subsequent treatment of specific
260 sleep disturbances in those with IBD.

261 **Limitations of the present research**

262 Firstly, the present study recruited participants based on a self-reported IBD diagnosis.
263 Although recent research has demonstrated that self-reported diagnosis in online research has a
264 high concordance rate with physician diagnoses (Kelstrup, Juillerat, & Korzenik, 2014; Randell
265 et al., 2014), this should be taken into account when considering the present findings. Secondly, a
266 large proportion of the participants from which the present findings are based are female. This is
267 perhaps not surprising given that there is evidence to suggest that there is a greater prevalence of
268 IBD in women when compared to men (Bernstein, Blanchard, Rawsthorne, & Wajda, 1999;
269 Brant & Nguyen, 2008). Indeed, findings based on majority female participants are a common
270 occurrence in the sleep-IBD literature (Ananthakrishnan et al., 2014; Ananthakrishnan et al.,
271 2013; Graff et al., 2013), and in epidemiological research more broadly (Dunn, Jordan, Lacey,
272 Shapley, & Jinks, 2004; Galea & Tracy, 2007; Smith, 2008). The large sample size in the present
273 research does mitigate some of the effects of sample representativeness, and the analyses
274 controlled the effects of gender (gender was not associated with outcomes). That being said, the
275 gender distributions in the present research need to be taken into account when interpreting the
276 findings.

277 **Conclusions**

278 The present research found that, relative to controls, those with a diagnosis of IBD
279 reported significantly more severe experiences of sleep apnea, insomnia, narcolepsy, restless
280 legs, and nightmares, as well as more factors that influence sleep, and a greater impact of sleep
281 complaints on daily life. We recommend that future research should explore three possible

282 avenues; i) investigation of the barriers/facilitators to the effective management of problems
283 sleeping in the routine care of those with IBD; ii) research aiming to elucidate the directional
284 association between sleep and IBD related outcomes, as well as any mechanisms of action; and
285 iii) the effectiveness and efficacy of interventions designed to improve sleep as a route to
286 improving IBD related outcomes. We hope that the present research will highlight the nature and
287 magnitude of problems sleeping in those with IBD, and facilitate more research in this area.

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288 **References**

- 289 Almedimigh, A., Szeto, S., Dave, J., Alsulaimi, N., Myint, A., & Borum, M. L. (2018). P108
290 Sleep disorders in inflammatory bowel disease: The forgotten discussion.
291 *Gastroenterology*, *154*(1), S56. Doi: <https://doi.org/10.1053/j.gastro.2017.11.154>.
- 292 Ananthakrishnan, A. N., Khalili, H., Konijeti, G. G., Higuchi, L. M., de Silva, P., Fuchs, C.
293 S., . . . Chan, A. T. (2014). Sleep duration affects risk for ulcerative colitis: A prospective
294 cohort study. *Clinical Gastroenterology and Hepatology*, *12*(11), 1879-1886.
295 Doi:10.1016/j.cgh.2014.04.021.
- 296 Ananthakrishnan, A. N., Long, M. D., Martin, C. F., Sandler, R. S., & Kappelman, M. D. (2013).
297 Sleep disturbance and risk of active disease in patients with crohn's disease and ulcerative
298 colitis. *Clinical Gastroenterology and Hepatology*, *11*(8), 965-971. Doi:
299 10.1016/j.cgh.2013.01.021.
- 300 Baglioni, C., Battagliese, G., Feige, B., Spiegelhalder, K., Nissen, C., Voderholzer, U., . . .
301 Riemann, D. (2011). Insomnia as a predictor of depression: A meta-analytic evaluation of
302 longitudinal epidemiological studies. *Journal of Affective Disorders*, *135*(1), 10-19. Doi:
303 <https://doi.org/10.1016/j.jad.2011.01.011>.
- 304 Becker, J., Berger, F., Schindlbeck, K. A., Poddubnyy, D., Koch, P. M., Preiß, J. C., . . . Maul, J.
305 (2018). Restless legs syndrome is a relevant comorbidity in patients with inflammatory
306 bowel disease. *International Journal of Colorectal Disease*, 1-8. Doi:
307 <https://doi.org/10.1007/s00384-018-3032-8>.
- 308 Bernstein, C. N., Blanchard, J. F., Rawsthorne, P., & Wajda, A. (1999). Epidemiology of Crohn's
309 disease and Ulcerative Colitis in a central Canadian province: A population-based study.

- 310 *American Journal of Epidemiology*, 149(10), 916-924. Doi:
311 <https://doi.org/10.1093/oxfordjournals.aje.a009735>.
- 312 Brant, S. R., & Nguyen, G. C. (2008). Is there a gender difference in the prevalence of crohn's
313 disease or ulcerative colitis? *Inflammatory Bowel Diseases*, 14, S2-S3. Doi:
314 <https://doi.org/10.1002/ibd.20540>.
- 315 Buysse, D. J., Reynolds, C. F., Monk, T. H., Berman, S. R., & Kupfer, D. J. (1989). The
316 pittsburgh sleep quality index: A new instrument for psychiatric practice and research.
317 *Psychiatry Research*, 28(2), 193-213. Doi: [https://doi.org/10.1016/0165-1781\(89\)90047-](https://doi.org/10.1016/0165-1781(89)90047-4)
318 4.
- 319 Dunn, K. M., Jordan, K., Lacey, R. J., Shapley, M., & Jinks, C. (2004). Patterns of consent in
320 epidemiologic research: Evidence from over 25,000 responders. *American Journal of*
321 *Epidemiology*, 159(11), 1087-1094. Doi: <https://doi.org/10.1093/aje/kwh141>.
- 322 Faul, F., Erdfelder, E., Lang, A.-G., & Buchner, A. (2007). G* power 3: A flexible statistical
323 power analysis program for the social, behavioral, and biomedical sciences. *Behavior*
324 *Research Methods*, 39(2), 175-191. Doi: <https://doi.org/10.3758/BF03193146>.
- 325 Galea, S., & Tracy, M. (2007). Participation rates in epidemiologic studies. *Annals of*
326 *Epidemiology*, 17(9), 643-653. Doi: <https://doi.org/10.1016/j.annepidem.2007.03.013>.
- 327 Gallicchio, L., & Kalesan, B. (2009). Sleep duration and mortality: A systematic review and
328 meta-analysis. *Journal of Sleep Research*, 18(2), 148-158. Doi:
329 <https://doi.org/10.1111/j.1365-2869.2008.00732.x>.
- 330 Graff, L., Clara, I., Walker, J., Lix, L., Carr, R., Miller, N., . . . Bernstein, C. (2013). Changes in
331 fatigue over 2 years are associated with activity of inflammatory bowel disease and

- 332 psychological factors. *Clinical Gastroenterology and Hepatology*, 11(9), 1140-1146. Doi:
333 <https://doi.org/10.1016/j.cgh.2013.03.031>.
- 334 Jowett, S. L., Seal, C. J., Barton, J. R., & Welfare, M. R. (2001). The short inflammatory bowel
335 disease questionnaire is reliable and responsive to clinically important change in
336 ulcerative colitis. *The American Journal of Gastroenterology*, 96(10), 2921. Doi:
337 [10.1111/j.1572-0241.2001.04682.x](https://doi.org/10.1111/j.1572-0241.2001.04682.x)
- 338 Keefer, L., Stepanski, E. J., Ranjbaran, Z., Benson, L. M., & Keshavarzian, A. (2006). An initial
339 report of sleep disturbance in inactive inflammatory bowel disease. *Journal of Clinical*
340 *Sleep Medicine*, 2(4), 409-416.
- 341 Kelstrup, A. M., Juillerat, P., & Korzenik, J. (2014). The accuracy of self-reported medical
342 history: A preliminary analysis of the promise of internet-based research in inflammatory
343 bowel diseases. *Journal of Crohn's and Colitis*, 8(5), 349-356. Doi:
344 <https://doi.org/10.1016/j.crohns.2013.09.012>.
- 345 Kinnucan, J. A., Rubin, D. T., & Ali, T. (2013). Sleep and inflammatory bowel disease:
346 Exploring the relationship between sleep disturbances and inflammation.
347 *Gastroenterology & Hepatology*, 9(11), 718-727.
- 348 National Institute for Health and Care Excellence (NICE). (2015). Inflammatory bowel disease
349 quality standard (qs81). Retrieved from <https://www.nice.org.uk/guidance/qs81>
- 350 O'Brien, E. M., Waxenberg, L. B., Atchison, J. W., Gremillion, H. A., Staud, R. M., McCrae, C.
351 S., & Robinson, M. E. (2010). Negative mood mediates the effect of poor sleep on pain
352 among chronic pain patients. *The Clinical Journal of Pain*, 26(4), 310-319. Doi:
353 [10.1097/AJP.0b013e3181c328e9](https://doi.org/10.1097/AJP.0b013e3181c328e9).

- 354 Pavlova, M., Ference, J., Hancock, M., & Noel, M. (2017). Disentangling the sleep-pain
355 relationship in pediatric chronic pain: The mediating role of internalizing mental health
356 symptoms. *Pain Research and Management*, 2017. Doi:
357 <https://doi.org/10.1155/2017/1586921>.
- 358 Qualtrics. (2018). Provo, Utah, USA. Retrieved from <https://www.qualtrics.com/>
- 359 Randell, R., Long, M., Cook, S., Wrennall, C., Chen, W., Martin, C., & Anton, K. (2014).
360 Validation of an internet-based cohort of inflammatory bowel disease (CCFA partners)
361 Inflammatory Bowel Disease. 2014; 20 (3): 541–544. Doi: 10.1097/01. *MIB*, 441348, 34.
- 362 Ranjbaran, Z., Keefer, L., Stepanski, E., Farhadi, A., & Keshavarzian, A. (2007). The relevance
363 of sleep abnormalities to chronic inflammatory conditions. *Inflammation Research*, 56(2),
364 51-57. Doi: 10.1007/s00011-006-6067-1.
- 365 Scott, A. J., Rowse, G., & Webb, T. L. (2017). A structural equation model of the relationship
366 between insomnia, negative affect, and paranoid thinking. *PLOS ONE*, 12(10), e0186233.
367 Doi:10.1371/journal.pone.0186233
- 368 Seo, M., Okada, M., Yao, T., Ueki, M., Arima, S., & Okumura, M. (1992). An index of disease
369 activity in patients with ulcerative colitis. *American Journal of Gastroenterology*, 87(8).
- 370 Smith, W. G. (2008). Does gender influence online survey participation? A record-linkage
371 analysis of university faculty online survey response behavior. *ERIC Document*
372 *Reproduction Service No. ED 501717*.
- 373 Spoomaker, V. I., Verbeek, I., van den Bout, J., & Klip, E. C. (2005). Initial validation of the
374 sleep-50 questionnaire. *Behavioral Sleep Medicine*, 3(4), 227-246. Doi:
375 https://doi.org/10.1207/s15402010bsm0304_4.

- 376 Swanson, G. R., Burgess, H. J., & Keshavarzian, A. (2011). Sleep disturbances and inflammatory
377 bowel disease: A potential trigger for disease flare? *Expert Review of Clinical*
378 *Immunology*, 7(1), 29-36. Doi:10.1586/eci.10.83
- 379 Taylor, D. J., Lichstein, K. L., Durrence, H. H., Reidel, B. W., & Bush, A. J. (2005).
380 Epidemiology of insomnia, depression, and anxiety. *Sleep*, 28(11), 1457-1464. Doi:
381 <https://doi.org/10.1093/sleep/28.11.1457>.
- 382 Uemura, R., Fujiwara, Y., Iwakura, N., Shiba, M., Watanabe, K., Kamata, N., . . . Arakawa, T.
383 (2016). Sleep disturbances in japanese patients with inflammatory bowel disease and
384 their impact on disease flare. *Springerplus*, 5(5), 1792. Doi:10.1186/s40064-016-3408-6
- 385 Walmsley, R., Ayres, R., Pounder, R., & Allan, R. (1998). A simple clinical colitis activity index.
386 *Gut*, 43(1), 29-32. Doi: <http://dx.doi.org/10.1136/gut.43.1.29>.
- 387 Wilson, R. G., Stevens, B. W., Guo, A. Y., Russell, C. N., Thornton, A., Cohen, M. A., . . .
388 Ananthkrishnan, A. N. (2015). High c-reactive protein is associated with poor sleep
389 quality independent of nocturnal symptoms in patients with inflammatory bowel disease.
390 *Digestive Diseases and Sciences*, 60(7), 2136-2143. Doi:10.1007/s10620-015-3580-5
- 391 Wong, M. L., Lau, E. Y. Y., Wan, J. H. Y., Cheung, S. F., Hui, C. H., & Mok, D. S. Y. (2013). The
392 interplay between sleep and mood in predicting academic functioning, physical health
393 and psychological health: A longitudinal study. *Journal of Psychosomatic Research*,
394 74(4), 271-277. Doi: 10.1016/j.jpsychores.2012.08.014.