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Poor subjective sleep quality predicts symptoms in Irritable Bowel Syndrome using the Experience Sampling Method

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Abstract

Objectives: Sleep quality may impact symptom experience in Irritable Bowel Syndrome (IBS). Our aim was to investigate the relationship between sleep quality and gastrointestinal (GI) symptoms using actigraphy and the Experience Sampling Method (ESM).

Methods: IBS patients were recruited from a tertiary Neurogastroenterology clinic and the community. GI symptoms and mood were recorded on a smartphone application, ten times per day, over seven consecutive days. Subjective sleep quality was recorded every morning to reflect the night before. Objective measures of sleep quality were estimated from wrist-worn actigraphy. Cross-lagged structural equation models were built to assess the directionality of sleep-symptom relationships over time.

Results: Eighty IBS patients completed the study (mean age: 37 (range 20 – 68), 89% female, 78% community). Sixty-six % had a Pittsburgh Sleep Quality Index (PSQI) score ≥ 8 indicating a clinically significant sleep disturbance. Eighty-two % (95% CI: 72-90) screened positive for a sleep disorder, most commonly insomnia. In cross-lagged analysis, poor subjective sleep quality predicted next day abdominal pain ($0.036 < p < 0.040$) and lower GI symptoms

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(0.030 < p < 0.032), but not vice versa. No significant relationship with GI symptoms was found for any objective sleep measure using actigraphy.

Conclusions: Poor subjective sleep quality was associated with higher next day lower GI symptom levels, but not vice versa. Objective sleep measures did not predict next day abdominal symptoms, potentially supporting the conclusion that it is the perception of sleep quality which is most influential. This study may be used to guide future research into the effect of sleep interventions on GI symptoms.

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WHAT IS KNOWN

- Sleep disturbances are more common in Irritable Bowel Syndrome (IBS) compared to healthy subjects
- Sleep quality is an independent factor affecting gastrointestinal (GI) symptoms

WHAT IS NEW HERE

- Poor subjective sleep quality predicts next day abdominal pain and lower GI symptom scores
- Worse abdominal pain and lower GI symptom scores do not predict subjective sleep quality the following night
- Objective sleep measures are not associated with next day GI symptoms

Keywords: sleep; irritable bowel syndrome; experience sampling method; actigraphy

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Introduction

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Sleep disorders are more common in patients with irritable bowel syndrome (IBS) compared to healthy subjects with a pooled prevalence of 37.6% (1, 2). On average, IBS patients sleep more hours per day but feel less well rested compared to healthy controls (3). However, only 2.4% of patients attribute their sleep disturbances to gastrointestinal (GI) symptoms.

Associations between GI symptoms and sleep quality in IBS patients have been investigated before. Patel *et al.* found that waking episodes during sleep, measured objectively, were associated with greater abdominal pain and lower general and IBS-specific quality of life (QoL) (3). Buchanan *et al.* concluded that poor subjective sleep quality predicts next-day abdominal pain, but not other GI symptoms, and objectively measured sleep efficiency significantly predicts next-day anxiety and fatigue but not abdominal pain (4). Furthermore, GI symptoms measured by end-of-day diaries, did not predict subsequent sleep quality suggesting that sleep is an independent factor affecting GI symptoms (4). Yet most studies are often limited by small sample sizes and fail to assess the directionality of effects between specific sleep quality measures and specific symptoms. Given the well-established association between mood disturbance and IBS (5), the effect of co-morbid anxiety and depression are worth considering when investigating the role of sleep-symptom relationships. Previous studies suggest that anxiety symptoms during the day may predict time taken to fall asleep, as hypervigilance and rumination are psychological processes that are likely to delay sleep onset (6). Whereas depression has been linked to an increased likelihood to awaken early in the morning (7).

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IBS symptom monitoring has traditionally been via single time-point, retrospective questionnaires which by nature are prone to recall bias (8), fail to account for within-day symptom variability (9) and cannot be used to decipher the directionality between symptoms and the factors that influence them. The Experience Sampling Method (ESM) has been used in IBS to overcome these limitations, by quantifying symptom burden repeatedly and randomly throughout the day (10). ESM has demonstrated real-time associations between abdominal pain and stress, underlining the importance of day-to-day variability and longitudinal relationships when interpreting drivers of GI symptoms in IBS (11).

Subjective sleep measures include validated questionnaires and sleep diaries; while objective measures include polysomnography (PSG) – a component of which is comparable to actigraphy (12). An actigraph is an accelerometer worn by a subject to record movements (acceleration; ACC), the nocturnal portion of which is then used to estimate sleep-wake states (13). A study by Rotem *et al.* reports that IBS patients suffer from impaired sleep quality and significant sleep fragmentation on PSG which was supported by actigraphy findings (14). By contrast, Elsenbruch *et al* found that that IBS subjects had significantly increased scores on the Pittsburgh Sleep Quality Index (PSQI) compared to healthy subjects, but no significant group differences on PSG (15). It is widely accepted that there is a mismatch between subjective reporting of sleep quality and objective measurements, which is described as sleep state misperception (16). Studies have yet to conclude whether it is *objective* or *subjective* sleep quality that is associated with GI symptoms in the IBS population, and this is hampered by lack of consistency between studies on the sleep measures they use.

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In the current literature, studies addressing the relationship between sleep quality and GI symptoms remain limited by small sample sizes, recall bias, heterogeneity between sleep quality measures, and perhaps most importantly, the failure to address directionality of relationships in daily life in a single comprehensive model.

The aim of the present study was therefore to evaluate the directionality of relationships between subjective sleep quality, objective sleep measures and GI symptoms in a well-defined IBS population using actigraphy and ESM as real-time, repeated measurement methods.

Methods

Study design

IBS patients were recruited between March 2020 and June 2021 from the tertiary Neurogastroenterology clinic at The Royal London Hospital, and from the community, in London, UK. The study protocol has been approved by the South Central – Hampshire A Research Ethics Committee (REC reference 19/SC/0236). Data were collected during seven consecutive days and a timeline of the study period is shown in *Figure 1*.

Study patients

We accessed the community group via social media campaigns and the IBS Network, a registered charity for IBS patients. Inclusion criteria comprised of the following: aged 18 – 70 years; IBS diagnosed according to Rome IV criteria (17), including subtype assessment by

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a trained clinical researcher on the first study visit; ability to give informed consent; understand and speak English; and access to smartphone technology. Exclusion criteria comprised of the following: any organic explanation for symptoms; history of abdominal surgery (aside from uncomplicated appendicectomy, cholecystectomy, and / or hysterectomy); new or dose change of regular medication / supplement commenced within the last one month; and / or known allergy to silicone based adhesives / prior skin condition e.g. severe atopic eczema.

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Symptom measures

The following measures were used to report on the directionality of sleep-symptom relationships: subjective sleep and GI symptom measures, objective symptom measures alongside sleep diary, as they were all measured in real-time. Additionally, we measured GI and sleep symptoms at the end of the 7-day study period which were used for descriptive purposes only.

Subjective sleep and GI symptom measures

In order to use ESM, patients were instructed on how to use a digital application (Maastricht Electronic Abdominal Symptom REcording [MEASuRE]) on their smartphone, specifically developed for this purpose (10). The application sends text notifications alongside an auditory signal, ten times per day, at random moments, between the hours of 07:30 and 22:30 with a minimum of 15 minutes and maximum of 3 hours between subsequent signals. The notification prompted completion of an ESM-questionnaire which included the same

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questions each time, over 7 consecutive days, designed to assess: abdominal pain, upper and lower GI symptoms, anxiety, depression, and nocturnal abdominal problems. Each question was scored on an 11-point numeric rating scale (0 = not at all to 10 = very severely) (18, 19). After each notification, the ESM-questionnaire remained available for a 10-minute window, after which it was logged as missing data when not completed. A screenshot of the MEASuRE application for the item 'abdominal pain' is shown in *Figure 2A*.

Subjective sleep quality was reported using the MEASuRE-app in the morning - to reflect the night before - including: the extent to which subjects slept well (***SleptWell***) scored from 0 (none) to 10 (very much); time taken to fall asleep (***SleepOnsetLatency***$_{\text{subjective}}$) and time lying in bed awake before getting out of bed (***EarlyMorningAwakening***$_{subjective}$), scored from 0-5mins; 5-15mins; 15-30mins; 30-45mins; 45mins-1 hour; 1-2 hours; more than 4 hours; and finally, number of awakenings in the night (***NumberofAwakenings***$_{subjective}$) scored from 0 to >5 times.

Objective sleep measures

Patients were sent a wristband alongside a charging cable in the post (see *Figure 2B*). Patients were instructed during the first study visit to wear the wristband on their non-dominant wrist, and as it is not waterproof, they were advised to remove it during heavy exercise, showering or bathing. Apart from these times, patients were instructed to wear it for 24 hours a day, throughout the 7-day study period.

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The wristband is an actigraph designed to record acceleration (ACC) at a sampling rate of 32Hz (2G range; 16 bit resolution; Imec Chill band device). ACC signals were used to estimate physical activity during sleep and an algorithm was developed (incorporating their sleep schedule) to calculate objective sleep variables which included:

- ***SleepEfficiency***$_{objective}$: (TST/TIB) x 100 where TST is the total sleep time in minutes according to the ACC signal and TIB (time in bed) is TST plus time in bed not sleeping according to the ACC signal.
- ***SleepOnsetLatency***$_{objective}$: time between the patient recording getting into bed and the first registered point of sleep according to the ACC signal.
- ***EarlyMorningAwakening***$_{objective}$: time between the last registered point of sleep according to the ACC signal and the patient recording getting out of bed.
- ***WakeAfterSleepOnset***$_{objective}$: total duration of awakening during the night, i.e. time between first and last segment of sleep in minutes on ACC.

In clinical practice, a cut-off at 30 minutes is used to indicate prolonged ***SleepOnsetLatency*** or ***WakeAfterSleepOnset*** (20) and normal ***SleepEfficiency*** is considered to be 85-90% (21).

Periods of time during which there was no change in arm angle larger than 5 degrees over at least 5 minutes, were classed as bouts of sustained inactivity, or potential sleep periods. The sleep period time (SPT) was calculated using a formula by van Hees *et al* (22) - only potential sleep periods that fell within the window of SPT were considered – see supplementary material for more details. We also excluded all patients with ≤ 4 nights of matched ESM and wristband ACC data from the analysis (4).

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Patients were also instructed to self-report on their sleep schedule in a daily sleep diary, including four timings documented in sequential order: (1) time they got into bed; (2) time they intended to fall asleep; (3) time they first awoke and (4) time they got out of bed. These timings were used solely to assist with calculation of actigraphy data. Patients also documented their medication, caffeine, and alcohol intake per day - substances known to impact sleep quality (23).

Descriptive measures

At the end of the 7-day study period, end-of-week questionnaires were automatically emailed to the patient from the electronic system - Castor Electronic Data Capture (24) - designed to assess: baseline demographics; IBS severity (Irritable Bowel Syndrome Severity Scoring System [IBS-SSS]) (25); GI symptoms (Gastrointestinal Symptom Rating Scale – IBS [GSRS-IBS]) (26); Depression symptoms (Patient Health Questionnaire [PHQ-9]) (27); Anxiety symptoms (Generalised Anxiety Disorder-7 [GAD-7]) (28); GI-specific anxiety (Visceral Sensitivity Index [VSI]) (29); Quality of life (Short Form-36 [SF-36]) (30); Sleep quality (Pittsburgh Sleep Quality Index [PSQI]); (31) and Sleep disorder screen (Sleep Disorder Symptom Checklist [SDS-CL-25]); (32). All questionnaires ask participants to report symptoms retrospectively, such that they reflect the same time period over which the MEASuRE-app was used. The PSQI score is a validated retrospective measure of sleep disturbance whereby patients with scores >5 or >8 can be regarded as having poor sleep quality. See supplementary methods for full details on the aforementioned questionnaires.

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Statistical analysis

For all data except for cross-lagged panel analysis, R Studio, version 1.4.1106 (2009-2021, RStudio, PBC) was used to perform analysis. Continuous outcomes are presented as mean (standard deviation, SD) where normally distributed and median (interquartile range, IQR) where not normally distributed.

ESM-questionnaire data was summarised at the individual day-level (i.e. the mean of repeated measurements within the day) for abdominal pain, anxiety, depression, and all subjective sleep quality variables. Lower-GI symptoms (**LGI**) were calculated as the sum of four items: gas, borborygmi, bloating, and urge, then summarised at the individual day-level. Similarly, upper-GI symptoms (**UGI**) were calculated as the sum of four items: nausea, belching, heartburn, and satiety, then summarised at the individual day-level. ESM analysis includes all patients who completed at least one third of the questions over the one week period (i.e. at least 23 out of 70) as has been common standard in ESM protocols (33, 34).

Cross-lagged panel models were built to investigate the following a priori defined associations: (1) ***SleptWell*** and GI symptoms (abdominal pain, **UGI, LGI**) – see figure 4; (2) ***SleepEfficiency***$_{objective}$ and GI symptoms (abdominal pain, **UGI, LGI**); (3) ***SleepOnsetLatency***$_{objective}$ & anxiety; (4) ***EarlyMorningAwakening***$_{objective}$ & depression, while controlling for all auto-regressive coefficients (35) (i.e. the extent to which scores on variable X at time point N, predict scores on variable X at time point N+1) - see supplementary figure 1. Additionally, the following associations were investigated exploratively: ***SleptWell*** & depression, ***SleptWell*** & anxiety, ***SleepEfficiency***$_{objective}$ &

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depression, ***SleepEfficiency***$_{objective}$ & anxiety, ***SleepOnsetLatency***$_{objective}$ & depression, ***EarlyMorningAwakening***$_{objective}$ & anxiety. In all cross-lagged analyses, we controlled for the association between sleep and age by including age as a predictor of the sleep measure at each timepoint (see Figure 4). Since ***EarlyMorningAwakening***$_{subjective}$ *and* ***SleepOnsetLatency***$_{objective}$ were categorical variables and zero-inflated, they were not used in the cross-lagged panel analyses. Cross-lagged panel analysis was performed using SAS software, Version 9.4 (2013v, SAS Institute Inc., Cary, NC, USA). The See supplementary methods for more details.

Linear mixed effect models were used to test the relationship between nocturnal abdominal problems and number of awakenings because both variables were measured on the same night i.e. with no lag between variables, they cannot be compared using cross-lagged panel analysis. Both variables were z-scored within subjects. Models including a random intercept and correcting for repeated measures using an autoregression (AR1) correlation structure. A p-value of ≤ 0.05 was considered statistically significant.

Results

Baseline demographics

Two hundred and fifty-three patients expressed an interest, of whom 80 completed the daily ESM (mean age: 37 (range: 20-68), 89% female) – figure 3. Completion rate of ESM questionnaires was 97.6%, and all patients completed at least one third of the questions. 78% (n=62) of the final cohort were from the community population and 22% (n=18) from

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the tertiary clinic. 22 % (n=17) of patients report taking neuromodulators and 20% (n=16) were on some form of sedating medication – see *Table 1*.

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IBS symptoms

The median IBS-SSS score indicates moderate severity (279 (IQR: 237-350)). The highest subdomain scores on the GSRS-IBS (scored 0-7) were for abdominal pain (median, 4.1 (IQR: 2.8-5.2)) and bloating (median, 4.0 (IQR: 3.0-5.2)). Using ESM (scored 0-10), weekly average group scores tended to be lower than the same symptoms scored on end-of-week questionnaires: abdominal pain (mean:2.6 (SD: 0.4-4.8)), lower GI symptom score (mean, 10.2 (SD: 3.5-16.9)) and upper GI symptom score (mean: 7.6 (SD: 2.0-13.2)) which is an observation supported by previous ESM studies.

Subjective sleep quality

Table 2 presents the results of subjective sleep quality, recorded each morning by ESM.

The median time spent in bed was 9 hours 21 minutes (IQR: 8.7-10.1). Forty-six % of patients reported a prolonged mean ***SleepOnsetLatency***$_{subjective}$ (≥ 30minutes) across the week.

Ninety-five % had a PSQI ≥ 5 indicating a positive screen for a clinically significant sleep disturbance. Sixty-six % had a PSQI score ≥ 8 and this may be a more appropriate cut off for our patient group, as it has a greater specificity at this higher cut-off point (36). Twenty-five % of patients reported reasons for having trouble sleeping during the last month, including

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both ‘internal’ reasons (e.g. worry / anxiety / nightmares) and ‘external’ reasons (e.g. children and pets waking them at night / partners snoring / outside disturbances). Eighty-two % (n=65) screened positive for a sleep disorder according to the SDSCL-25 questionnaire, of which the most common disorder was insomnia.

In cross-lagged panel analysis, ***SleptWell*** predicted worse next-day abdominal pain ($0.036 < p < 0.040$) but worse abdominal pain during the day did not predict ***SleptWell*** during the night *(*all p’s = 0.77; *Figure 4A)*. Similarly, ***SleptWell*** predicted next day lower-GI symptoms ($0.030 < p < 0.032$), but worse lower-GI symptoms during the day did not predict ***SleptWell*** the following night *(*all p’s = 0.90; *Figure 4B)*. Although the direction of the effect was the same as abdominal pain and lower-GI symptoms, it was not significant for the upper-GI symptom model *(Figure 4C)*.

Over the 7-day period, the median number of awakenings was 2 per night (IQR: 1 – 3) and nocturnal abdominal problems was 2 out of 10 severity (IQR: 0-4). Based on individual z-scores, an increase of 1 SD in number of awakenings is predicted by an increase of 0.33 SD of nocturnal abdominal problems the same night. Reverse association demonstrated an increase of 1 SD in nocturnal abdominal problems is predicted by an increase of 0.26 SD of number of awakenings the following night. *Supplementary figure 2* is an effect plot demonstrating the positive association between number of awakenings and nocturnal abdominal problems.

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Objective sleep measures

Fifty-five patients with matched ESM and ACC data were included in the analysis. ***SleepEfficiency***$_{objective}$ was at the lower end of normal range (median, 86% (CI 95%: 85-87) and ***SleepOnsetLatency***$_{objective}$ was at the higher end of normal range (median, 29.9minutes (IQR: 10.5 – 60.7) and 10.8% of patients had a score of zero. ***EarlyMorningAwakening***$_{objective}$ was minimal (median, 5.5minutes (IQR: 11.3 – 40.0)) and 30.7% had a score of zero. ***WakeAfterSleepOnset***$_{objective}$ was within the normal range (median, 22minutes (IQR: 11.3 – 40.0)).

We found no significant cross-lagged paths in the relationship between ***SleepEfficiency***$_{objective}$ and (i) abdominal pain (ii) lower GI symptoms and (iii) upper GI symptoms *(supplementary figure 1).* We found that prolonged SleepOnsetLatency$_{objective}$ predicted *less* anxiety the next day ($0.008 < p < 0.012$), while anxiety during the day did not predict ***SleepOnsetLatency***$_{objective}$ the following night (all p's = 0.76). We found no significant cross-lagged paths between ***EarlyMorningAwakening***$_{objective}$ and next day depression *(supplementary figure 1).*

Exploratory cross-lagged associations

Outside of the main research questions, associations between anxiety and depression on the one hand and sleep quality and efficiency on the other hand were explored using cross-lagged analysis. ***SleptWell*** negatively predicted next-day depression ($p < 0.001$) and anxiety ($p < 0.001$) but not vice versa ($p = 0.95$ and $p = 0.74$, respectively), indicating that better subjective sleep quality was associated with less next-day depressive and anxiety symptoms

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– see figure 4D & 4E. No significant associations were found between ***SleepEfficiency***$_{objective}$ and depression or anxiety, nor between ***SleepOnsetLatency***$_{objective}$ and depression or ***EarlyMorningAwakening***$_{objective}$ and anxiety.

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Discussion

We present the first study to measure the relationship between real-time reported GI symptoms and sleep quality in IBS patients, utilising both subjective and objective sleep measures. The cohort of moderately severe IBS patients reported high levels of sleep disturbance (PSQI) and most patients met the criteria for at least one sleep disorder (SDSCL-25). Our study demonstrates that firstly, poor subjective sleep quality predicted next day abdominal pain, but the converse was not true. Secondly, poor subjective sleep quality predicted next-day higher scores on abdominal pain, lower-GI symptoms, depression and anxiety, but the converse was not true. Lastly, objectively measured sleep quality did not predict next day abdominal symptom severity.

Sleep quality over the previous month, based on PSQI scores, appeared to be slightly worse for our cohort compared to other studies reporting sleep disturbance in IBS (3). Having sampled the largest IBS cohort in a sleep study to date, this may be a more accurate representation. This was the first study to use the SDSCL-25 score in an IBS cohort and found that a high percentage of our group screened positive for a sleep disorder. The identification of individual sleep disorders is useful to target treatment options however, the scoring system for the SDSCL-25 is highly sensitive e.g. participants who self-report

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snoring on three or more days per week screen positively for obstructive sleep apnoea (OSA) on the SDSCL-25 which is not the only criteria used clinically to diagnose this sleep disorder. It is recommended that results of the SDSCL-25 score should be interpreted within the clinical context of the individual patient (32).

Poor subjective sleep quality predicts next day abdominal pain, but the reverse relationship was not significant. This aligns with previous IBS sleep studies (3) although they did not assess for reverse causality in a single model controlling for the other direction. It is well known that chronic pain and sleep are related in a bidirectional manner, whereby co-morbidity results in greater symptom severity and more disability (37). There is evidence from longitudinal studies to support the notion that sleep disturbance is a stronger, more reliable predictor of pain than pain is of sleep disturbance (38). For instance, in a study that also utilized cross-lagged panel models, increases in monthly insomnia severity ratings were associated with next-month increases in average daily pain in temporomandibular disorder, but not vice versa (37). In one study, the absence of nocturnal abdominal symptoms as an additional symptom marker, has been found to increase the performance of Rome III diagnostic criteria in making a positive diagnosis of IBS (38). Our finding of low levels of nocturnal abdominal symptoms supports this association and may explain the low level of nocturnal awakening in our patients.

Potential common pathways for the effect of sleep on pain include dysregulation of the hypothalamic pituitary adrenal (HPA) axis, which is a known pathophysiological mechanism in IBS (39) and is associated with disrupted sleep (40). One study concluded that poor self-reported sleep quality was significantly associated with greater cortisol reactivity (i.e.

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increases from baseline) following an acute physical stressor i.e. cold pressor task (41). Autonomic nervous system dysregulation as measured by heart rate variability (HRV) has also been demonstrated in IBS patients (42) and is linked to poor sleep efficiency (43). Orr *et al* found that IBS patients have greater sympathetic activity during waking and greater overall sympathetic dominance during rapid eye movement sleep compared to healthy controls (44). Lastly, sensitisation of the central nervous system is an established mechanism of chronic pain in IBS and recent studies suggest that low-grade neuroinflammation, resulting from sleep disturbance, has a role to play in the establishment and/or maintenance of central sensitization (45).

We observed a unidirectional relationship between poor subjective sleep quality and abdominal pain, lower-GI symptoms, depression and anxiety the following day, which contrasts slightly with the findings of Buchanan et al (4) who found that self-reported sleep quality significantly predicted next day abdominal pain and anxiety, but not GI symptoms nor depression. Differences could be accounted for by: lower mean symptom scores, smaller sample size (n=24) and use of different sleep measurement tools (end-of-day diaries) compared to our real-time measurements. Our finding that objectively measured sleep quality did not predict next day symptoms highlights the important role of perception in sleep-symptom relationships.

In our study the relationship between anxiety and ***SleepOnsetLatency***$_{objective}$ was converse to our expectations i.e. prolonged ***SleepOnsetLatency***$_{objective}$ predicted less anxiety the next day. This implies that staying up in bed but not sleeping, has the potential to reduce next day anxiety and could indicate that relaxing activities performed in bed such as reading,

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journaling or talking to a partner may help to reduce next day anxiety which future, qualitative studies should evaluate. People often overestimate their sleep onset latency and underestimate their total sleep time, relative to objective measures, and reasons for this include: inability to distinguish being awake from early sleep stages; worry / anxiety; selective attention toward sleep-related threats and the presence of brief awakenings (46). Therefore future studies will need to consider these factors as possible contributors to the finding observed in our study.

We conclude that better subjective sleep quality predicts next day depression, but not vice versa. Although a significant relationship between early morning awakening and depression is highlighted in the literature, to date no studies have examined this relationship in the IBS population. Future research should seek to confirm this finding whilst examining the potential mechanisms of action for this finding.

Strengths of the present study include recruitment of a relatively large number of community IBS patients diagnosed according to Rome IV criteria (78% of our cohort, n=62), who are likely to be representative of the U.K. IBS population, making our findings highly generalisable. Moreover, there were exceptionally high completion rates of ESM, and we were able to simultaneously assess both directions of the sleep-symptom relationship by virtue of using cross-lagged panel models. Further, sleep efficiency was used as the main objective sleep measure, which is the most widely used measure of sleep quality (47, 48) and ought to be replicated as a primary outcome in future studies on sleep and IBS to enable easy comparison between findings.

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Limitations of our study include firstly, subjective sleep variables - ***SleepOnsetLatency***$_{subjective}$ *and* ***EarlyMorningAwakening***$_{subjective}$ - were measured as ordinal variables and response categories crossed the clinically significant threshold of 30 minutes. This was because the ESM questions were designed for measuring IBS symptoms in a multi-centre study, not with sleep measurement in mind. Future studies should consider these variables as continuous to avoid issues with interpretation. Secondly, it must be noted that our algorithm for ACC interpretation is at best, an estimation of sleep / wake states. Actigraphy is unable to detect the difference between awake versus sleep as accurately as PSG, hence our output of ***SleepOnsetLatency***$_{objective}$ and ***EarlyMorningAwakening***$_{objective}$ had high percentages of zero values and could not be easily transformed. Ideally, we would like to have access to PSG in order to validate our findings. Thirdly, IBS sub-type analyses was not performed due our limited sample size, and previous studies examining sleep disorders by IBS sub-type found no significant variation between them (49). Moreover, the present study was underpowered to control for differences in neuromodulator and sedative use; and between the community and the tertiary cohorts. Fourthly, the sum of individual symptoms was used to create the upper-GI and lower-GI symptom scores, however this may not be representative of the different contributions of individual symptoms to upper-GI and lower-GI symptom burden in daily life. Lastly, this study was conducted during the COVID-19 pandemic which has since been demonstrated to have impacted both sleep quality (50) and GI symptoms (51) alongside mood symptoms. However, if symptoms were influenced, then the present findings simply represent the more severe end of the spectrum and should be interpreted in this context.

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The main findings of this study support subjective sleep quality influencing next-day GI symptoms but not vice versa. Objective sleep measures did not predict next-day symptoms, potentially supporting the conclusion that it is the perception of sleep quality that is most influential on next-day abdominal pain. Our findings suggest gastroenterologists should consider sleep as a lifestyle factor influencing GI symptoms, highlighting the role of assessing subjective sleep quality / screening for sleep disorders in the clinical consultation and to guide future research into whether interventions aimed at improving sleep also impact GI symptom severity.

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Tables

Age, y	37 (20-68)
BMI, kg/m2	23 (21-28)
Gender, F	71 (89%)
Ethnicity	
Caucasian	66 (83%)
Employed	58 (73%)
Caffeine, cups/day	1 (0-2)
Alcohol, units/day	0 (0-0)
IBS-SSS score	279 (237-350)
GSRS-IBS score*	
Abdominal pain	4.1 (2.9-5.3)
Bloating	4.0 (3.0-5.2)
Diarrhoea	3.3 (2.3-4.3)
Constipation	3.5 (1.5-4.0)
Satiety	2.5 (1.5-4.0)
PHQ-9 score	9.0 (5.0-12.0)
GAD-7 score	8.4 (3.5-13.3)
VSI score	55 (49-64)
SF-36 score	
Physical subscale	39.5 (34.7 – 44.3)
Mental subscale	28.8 (22.5 - 35.1)
Neuromodulator use	
TCAs	
Amitriptyline	5 (6.3%)
SSRIs	
Sertraline	4 (5.1%)
Fluoxetine	1 (1.3%)
Citalopram	3 (3.8%)
Other	
Duloxetine	1 (1.3%)
Mirtazapine	3 (3.8%)
Total	17 (21.3%)
Anti-psychotic use	
Atypical (Quetiapine)	2 (2.5%)
Sedating mediation use	
Hypnotics	
Zopiclone	3 (3.8%)
Analgesia	
Zomorph	1 (1.3%)
Oramorph	1 (1.3%)
Gabapentin	2 (2.5%)
Pregabalin	1 (1.3)
Antihistamines	
Promethazine	1 (1.3%)
Sleep aids	
Nytol	1 (1.3%)
Herbal Aids	1 (1.3%)

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5-HT	3 (3.8%)
Melatonin	2 (2.5%)
Total	16 (20.3%)

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Table 1: Baseline Demographics and clinical characteristics (N=80). All results represent median (IQR) except for age: mean (range) and unless stated as numbers (proportions). IBS-SSS: Irritable Bowel Syndrome Symptom Severity Score. GSRS-IBS: Gastrointestinal Symptom Rating Scale for Irritable Bowel Syndrome *scored on a visual analogue scale from 0 - 10. PHQ-9: Patient Health Questionnaire-9. GAD-7: General Anxiety Disorder Assessment-7. VSI: Visceral Sensitivity Index. SF-36: Short-Form 36. TCAs: Tricyclic Antidepressants. SSRIs: Selective Serotonin Reuptake Inhibitors.

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Morning ESM questionnaire±	
Sleep Latency, mins	15-30 (5-45)
Number of Awakenings	2 (1-2)
Early Morning Awakening, mins	15-30 (5-45)
Slept well*	6 (5-7)
Abdominal Pain at night*	2 (1-3)
End-of-day questionnaire	
Time in Bed, hours	9.2 (8.71-10.13)
PSQI score	
Total score	9.2 (5.92 - 12.38)
Clinically significant score(>8)	53 (66.3%)
SDSCL-25 score	
Insomnia	46 (58.2%)
Circadian Rhythm Disorder	10 (12.7%)
Excessive Daytime Sleepiness	5 (6.3%)
Sleep Apnoea	40 (50.6%)
RLS / PLMD	28 (35.4%)
Narcolepsy	17 (21.5%)
Parasomnias	9 (11.4%)
Overall Suspected Sleep Disorder	65 (82.3%)

Table 2: Subjective sleep data (N=80). All results represent median (IQR) except the PSQI: Pittsburgh Sleep Quality Index which is reported as mean (SD) and the SDSCL-25: Symptom Disorder Symptom Checklist-25 which is reported as number (proportion). *scored on a visual analogue scale from 0 to 10. ±based on weekly averages for each patient.

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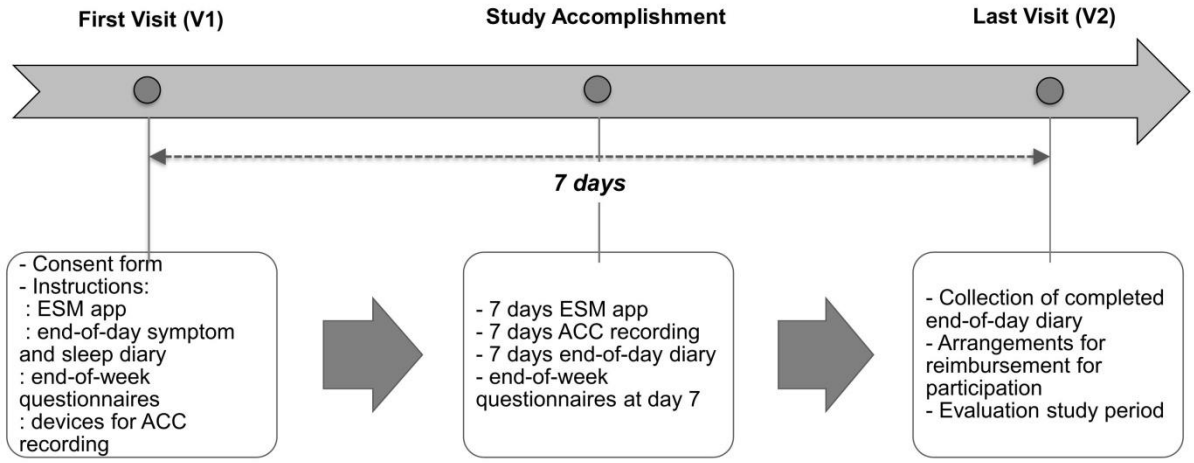

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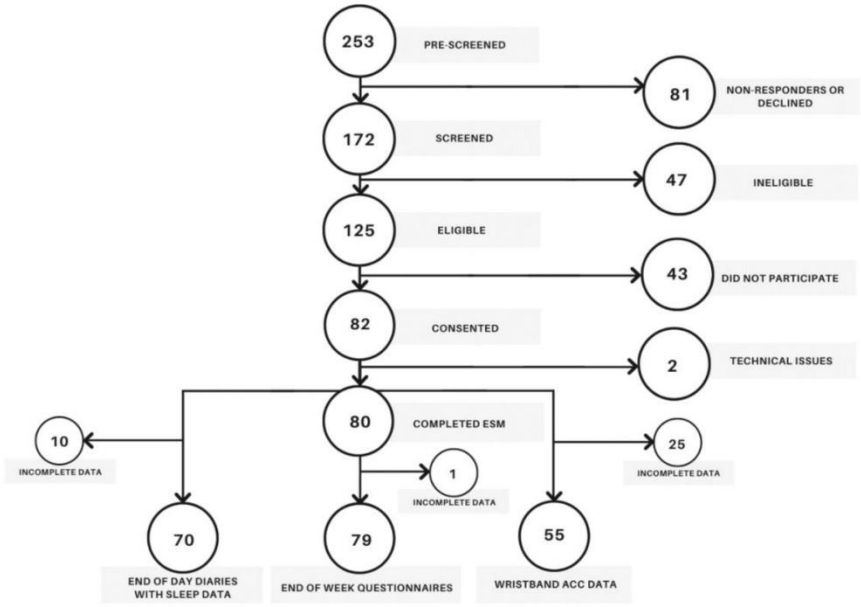

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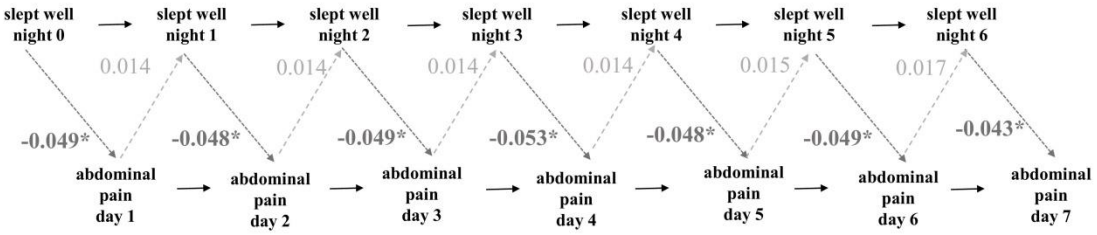

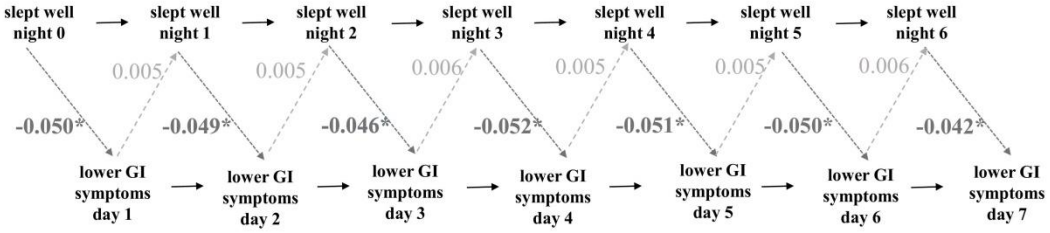

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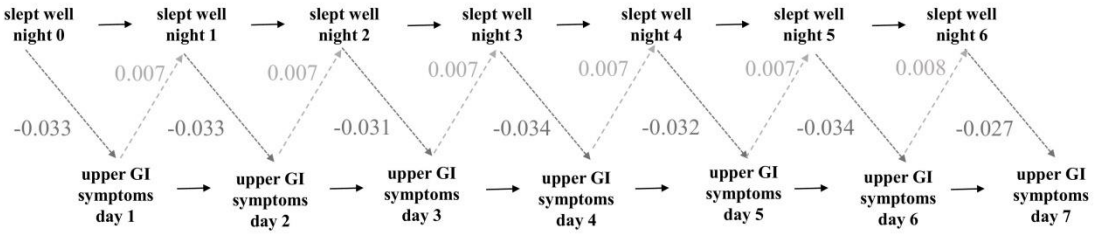

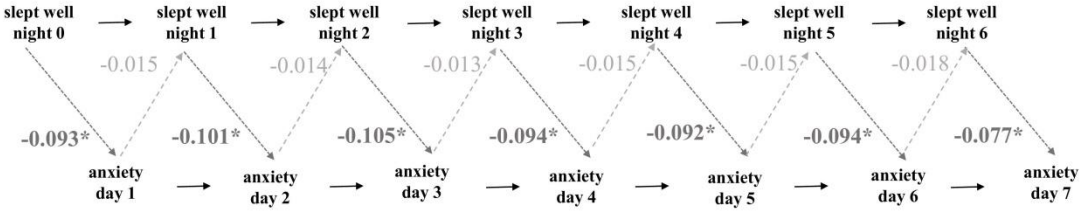

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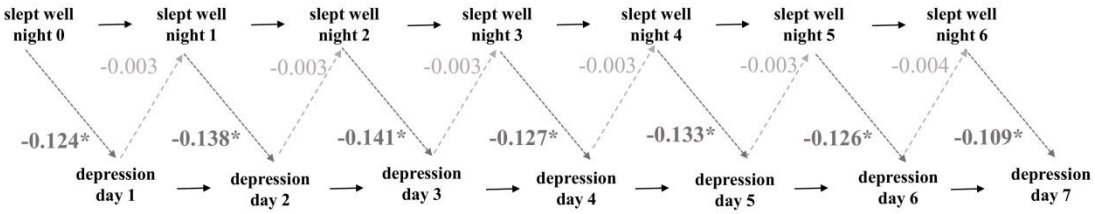

ACCEPT

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