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ORIGINAL ARTICLE

Fibromyalgia severity and symptoms are associated with the disorders of gut–brain interaction

Sharon Erdrich | **Joanna E. Harnett**

School of Pharmacy, Faculty of Medicine and Health, The University of Sydney, Camperdown, New South Wales, Australia

Correspondence
Sharon Erdrich, School of Pharmacy, Faculty of Medicine and Health, The University of Sydney, Camperdown, New South Wales, Australia.
Email: sharon.erdrich@sydney.edu.au

Abstract

Introduction: Fibromyalgia remains an idiopathic common disorder characterised by widespread pain with no universally accepted treatment. Irritable bowel syndrome is prevalent among women living with fibromyalgia. The prevalence of other disorders of gut–brain interaction (DGBI) and associations with fibromyalgia symptoms and severity is unknown.

Objectives: To evaluate the prevalence of the range of DGBI and associations with the symptoms and severity of fibromyalgia in women.

Methods: A prospective observational study was conducted in New Zealand in 2022. A comprehensive survey included validated measures to identify DGBI (Rome IV) and items assessing the severity of fibromyalgia and pain symptoms, sleep quality, quality of life, mental health and migraine. Analysis was conducted employing Spearman's rho, Mann–Whitney *U*, Kruskal–Wallis and chi-square tests.

Results: A total of 111 adult women with fibromyalgia enrolled in the study. Of these, 98 (93%) met the criteria for at least one DGBI, and 67 (68%) satisfied criteria for more than one. All groups of DGBI, and 11 specific DGBI were significantly associated with measures of pain, fibromyalgia severity, sleep problems and migraine ($p < 0.05$). Severity of pain and symptoms associated with fibromyalgia, including sleep problems, were also significantly associated with the functional bowel disorder severity index.

Conclusion: This study demonstrated that the prevalence of DGBI in women with fibromyalgia extends beyond irritable bowel syndrome. Presence of multiple DGBI correlates with pain, severity indices of fibromyalgia and sleep problems. Further research is required to examine the aetiology of DGBI in this population.

Significance Statement: This observational study has identified important relationships between the broader DGBI, fibromyalgia pain and associated symptoms, particularly migraine and sleep disturbance. Notable correlations between the severity indices of each are demonstrated, suggesting that improvements in one domain may reduce pain and improve overall well-being. These findings

highlight the importance of addressing each clinical feature of the condition when supporting patients with fibromyalgia.

1 | INTRODUCTION

Fibromyalgia is a complex disorder characterized by persistent widespread somatic pain which is strongly associated with a constellation of somatic symptoms. These include poor sleep, fatigue, impaired cognition, headaches, abdominal pain and discomfort, and altered mood. Of these, chronic widespread pain is a pre-requisite for the condition (Wolfe et al., 2016). In addition, fatigue and sleep disturbance are highly prevalent among this population (Cassisi et al., 2008).

After osteoarthritis and chronic back pain, fibromyalgia is the third most common chronic pain condition (Lawrence et al., 2008). Global prevalence of the disorder is estimated at 1.78% (Heidari et al., 2017) to 2.7% (Queiroz, 2013) and is approximately nine times higher in women than men (Heidari et al., 2017). This aligns with the most recent New Zealand/Aotearoa (NZ) data (published in 2002), which estimated overall prevalence in NZ as 1.74%, and just under 1% in the Māori population (Klemp et al., 2002). Since 2002, the diagnostic criteria for fibromyalgia have been updated (Frederick Wolfe et al., 2016), removing the 'tender point' analysis from the diagnostic algorithm which may impact the accuracy or comparability of earlier prevalence data.

It has been suggested that fibromyalgia constitutes one end of a spectrum of polysymptomatic distress (Wolfe et al., 2013), simultaneously affecting multiple body systems and impacting various levels of function (Sarzi-Puttini et al., 2020). A leading theory is that fibromyalgia is a state of centralized pain (Clauw, 2014), implying that peripheral nociceptive stimuli (i.e. the processing of noxious sensations, arising from tissue damage) are amplified in the central nervous system, creating a heightened perception of pain (Armstrong & Herr, 2022). However, associated symptoms are not fully explained by this model, and to date, no clear pathophysiological mechanism nor clinically useful universal diagnostic biomarker has been identified.

While the characteristic pervasive chronic pain and the condition's symptoms are part of the current diagnostic algorithm (Wolfe et al., 2016), fibromyalgia remains idiopathic. Contributory mechanisms are hypothesized to variably include a range of candidates including genetic predisposition (Lukkahatai et al., 2018), stress and emotional triggers, subclinical peripheral neuroinflammation (Sarzi-Puttini et al., 2020), alterations in cerebral levels of glutamate (Pyke et al., 2017) and others, as discussed by Gyorfi et al. (2022). Downstream effects due to disturbances in the gut microbiota (Malatji et al., 2017; Minerbi et al., 2022) have also recently emerged as possible catalysts. However, exact mechanisms have not been elucidated.

Disorders of gut–brain interaction (DGBI), formerly referred to as functional gastrointestinal disorders (FGID), are commonly comorbid with fibromyalgia (Almansa et al., 2009; Erdrich et al., 2020; Guerin et al., 2022). However, we have previously reported a paucity of research examining these relationships beyond IBS (Erdrich et al., 2020). The recent Rome Foundation epidemiological survey (Sperber et al., 2021) ($N = 73{,}076$ in 33 countries) found that some 20%–40% of the global population meet criteria for at least one DGBI. Irritable bowel syndrome (IBS) is the most prevalent DGBI, affecting an estimated 3%–10% of the general population, predominantly women (Sperber et al., 2021), and people with IBS have 80% higher odds of fibromyalgia than a comparator cohort (pooled POR 1.8, 95% CI 1.7–1.9) (Cole et al., 2006).

Sleep disorders are common among individuals with fibromyalgia and are linked to IBS (Duan et al., 2018) and functional dyspepsia, both of which are prevalent disorders within the category of functional gastrointestinal disorders (DGBI). Headaches, which are included in the diagnostic criteria for fibromyalgia (Wolfe et al., 2016), are also associated with gastrointestinal issues and tend to occur more frequently in individuals experiencing these problems (Aamodt et al., 2008).

Despite these associations, a thorough investigation into the relationships among DGBI, sleep disturbances, headaches and other symptoms has not yet been conducted specifically in a fibromyalgia population. Additionally, there has been no in-depth assessment of the overall health and quality of life of individuals with fibromyalgia in New Zealand.

1.1 | Aim

The aim of this study was to conduct a comprehensive evaluation of the relationships between pain and fibromyalgia severity, headache, sleep problems, quality of life, mental health, and the prevalence and severity of DGBI in a cohort of NZ women living with fibromyalgia.

2 | METHODS

2.1 | Study design and participants

This prospective observational study recruited adult women with a physician's diagnosis of fibromyalgia or meeting the diagnostic criteria set by the American College of Rheumatology, 2016 (ACR-2016) and living in New Zealand. Full inclusion and exclusion criteria are reported in the published protocol (Erdrich et al., 2023). Briefly here, women who smoked or used e-cigarettes, or were living with diabetes mellitus, and those with inflammatory conditions were excluded from the study.

The diagnosis of fibromyalgia requires the presence of chronic (at least 3-month duration) widespread pain, in at least 4 of 5 specified body regions, and a minimum of 4 of 19 individual locations. A symptom severity score (SSS) is generated by tallying scores ranging from 0 to 3 based on fatigue, cognitive symptoms and non-refreshing sleep in the past week and binary scores for 'being bothered by' abdominal pain or cramps, headaches or depression in the previous 6 months (Wolfe et al., 2016). Thus, the maximum SSS is 12. Diagnosis is based on a composite score, as presented in Box 1.

2.2 | Procedures

Procedures were conducted as per the published protocol (Erdrich et al., 2023), which included participants visiting the study site for assessment and data collection. A survey instrument that combined the validated questionnaires was used to assess the prevalence of DGBIs and parameters of health. The survey was administered via the secure online platform REDCap® (Research Electronic Data Capture) (Harris et al., 2019), hosted at the University of Sydney.

BOX 1 Fibromyalgia Diagnostic Criteria, as per the American College of Rheumatology, 2016 (Wolfe et al., 2016)

1. Generalized pain, defined as pain in at least 4 of 5 regions, is present.
2. Symptoms have been present at a similar level for at least 3 months.
3. Widespread pain index (WPI) ≥7 and symptom severity scale (SSS) score ≥5 OR WPI of 4–6 and SSS score ≥9.
4. A diagnosis of fibromyalgia is valid irrespective of other diagnoses. A diagnosis of fibromyalgia does not exclude the presence of other clinically important illnesses.

The survey contained the ACR-2016 questionnaire that includes the widespread pain index (WPI) and the symptom severity scale (SSS) (Wolfe et al., 2016). The sum of the WPI plus the SSS forms the fibromyalgia severity scale (FSS), also referred to as the polysymptomatic distress scale (Wolfe et al., 2015). The prevalence of DGBI were assessed employing the Rome IV Survey (Rome IV) (Drossman & Hasler, 2016; Palsson et al., 2016).

Other items from validated scales were included in the survey instrument to assess symptoms and conditions associated with fibromyalgia including: the Revised Fibromyalgia Impact Questionnaire (FIQR) (Bennett et al., 2009); Headache Symptom Questionnaire (HSQ) (Headache Classification Committee of the International Headache Society (HCC), 2013; van der Meer et al., 2019); Medical Outcomes Study Sleep Scale (MOS-SS) (Hays & Stewart, 1992), Short-Form Survey-36 (SF36) (Hays et al., 1995; McHorney et al., 1994); General Anxiety Disorder-2 (GAD-2) (Plummer et al., 2016); Patient Health Questionnaire-2 (PHQ-2) (Kroenke et al., 2003); and the Functional Bowel Disorder Severity Index (FBDSI) (Drossman et al., 1995). Items to capture other health conditions and current medication use were also included. Diet quality was assessed using the photometric diet quality tool, Diet ID™ (Turner-McGrievy et al., 2022).

The SF36 provides a breakdown of quality of life (QoL) in 8 different domains, with high scores (maximum of 100) indicating higher QoL. For the bodily pain domain, the scores were inverted, such that a high score indicated more severe pain. Extent of pain was evaluated employing the WPI, and intensity and limitations posed by it is represented by the bodily pain (BP) domain of the SF36-BP.

For categorisation of headache, the guidelines set out by the International Headache Society (HCC., 2013) were followed: participants satisfying criteria for probable migraine, and either had a physician's diagnosis of migraine or did not meet definitive criteria for TTH were classified as 'migraine'. If both 'probable migraine' and 'probable TTH' was the outcome, the general rule of hierarchy was applied, thus they were classified as migraine.

2.3 | Statistical methods

A sample power calculation was conducted using G*Power v3.1.9.7 (Faul et al., 2009) to establish that our sample ($n = 113$) was adequately powered (at 89%, $\alpha = 0.05$, effect size = 0.30) for the comparisons of interest in this population of women living with fibromyalgia.

Statistical analysis was conducted using IBM® SPSS® v28. Comparisons of continuous data were conducted

using *t*-test with means, standard deviation (SD) and 95% CI where normally distributed, while non-normally distributed data were analysed using the Mann–Whitney *U*-test (MW-*U*), with *Z*-statistic, median (*Md*) and interquartile range (IQR). Spearman's Rho (ρ) was used to assess correlations. All reported confidence intervals (CI) were reported at the 95% level according to Caruso and Cliff's method.

Comparison of categorical data was undertaken using Pearson's chi-square (X^2), with Fishers' exact test as appropriate. Comparisons between multiple variables were analysed using the Kruskal–Wallis H test with Bonferroni correction for multiple comparisons. After checking for multicollinearity (all VIF <1.10), linear regression was used to evaluate whether the relationships between the FBDSI and measures of pain and severity of fibromyalgia remained significant after controlling for BMI, age and diet quality.

2.4 | Ethics

The study was conducted in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and approved by NZ Health and Disability Ethics Committee (HDEC), reference number: 20/ CEN/197. The study was registered with the Australia and New Zealand Clinical Trials Registry (ANZCTR), registration number ACTRN12620001337965. All participants provided signed informed consent.

3 | RESULTS

One hundred and thirteen adult women (age 18–75) meeting inclusion criteria provided informed consent to participate in the study. The mean age was 46.1 years (SD 12.9 years) and mean BMI 30.6 kg/m^2 (8.0). One-third were overweight and a further 14% ($n=16$) fell into each of the three categories for obesity as defined by the World Health Organization (WHO, 2007). Most participants identified as NZ or European, with 8% ($n=9$) identifying as Māori, 1% ($n=1$) as Pacifica, 1% ($n=1$) as Asian, while 8% ($n=9$) were of other nationalities. All survey items were completed by 111 participants.

3.1 | Prevalence of DGBI

One hundred and three women (93%) met the criteria for at least one DGBI. When evaluated according to the Rome IV DGBI categories, oesophageal disorders were present in 42% ($n=47$), gastroduodenal disorders in 46% ($n=52$), bowel disorders in 87% (98) and anorectal disorders in 31% ($n=35$) of the participants. Multiple DGBI were identified in most participants. Overall, 103 women met the ROME IV criteria for 350 DGBI.

When grouped according to the severity of the functional bowel disorders (FBD) using the FBDSI criteria, 13% ($n=12$) of those with an FBD, the FBDSI was below the threshold for classification; 43% ($n=48$) were classified as mild, 19% ($n=21$) as moderate and 14% ($n=16$) as severe.

3.2 | Measures of pain

Moderate correlations were observed between the number of DGBI per participant and the WPI ($\rho=0.275$, $p<0.004$, 95% CI [0.09, 0.44]) and with the SF36-BP ($\rho=0.239$ $p=0.012$, 95% CI [0.05, 0.41]).

Stronger correlations were seen between the number of DGBI and each of the markers of fibromyalgia severity; FSS ($\rho=0.361$, $p<0.001$, 95% CI [0.18, 0.52]) and the FIQR ($\rho=0.542$ $p<0.001$, 95% CI [0.39, 0.67]), as shown in Figure 1.

Pain scores were significantly associated with FBDSI severity scores and are summarised in Table 2.

The interaction between the FBDSI and indices of pain and severity of fibromyalgia are presented in Table 1. Figure 2 demonstrates the correlation between FBDSI categories and the FSS. Similar patterns were evident for each of the parameters shown in Table 1, demonstrating that worse functional bowel-related symptoms were associated with higher scores on all pain and fibromyalgia severity indices.

Results for the association between the WPI and the FIQR are presented in Table 2. The statistics for the SF36-BP and FSS were similar.

Participants for whom abdominal pain was the most bothersome [digestive] symptom ($n=29$, 26%) (Rome survey Q67) also had higher scores on the WPI: median (IQR) 15 (6), c.f., 12 (5), $Z=-2.42$, $r=-0.23$, $p=0.016$.

A Mann–Whitney *U*-test showed several significant differences in pain scores and fibromyalgia severity in specific DGBI or DGBI groups. These are presented in Table 3. Due to homogeneity of some median and IQR data, means and SD are also presented.

3.3 | Migraine

Thirty-five women (31%) had received a physician's diagnosis of migraine. However, almost twice as many—59% ($n=65$)—met migraine criteria based on the HSQ. Of those with migraine, 25% ($n=16$) were classified as

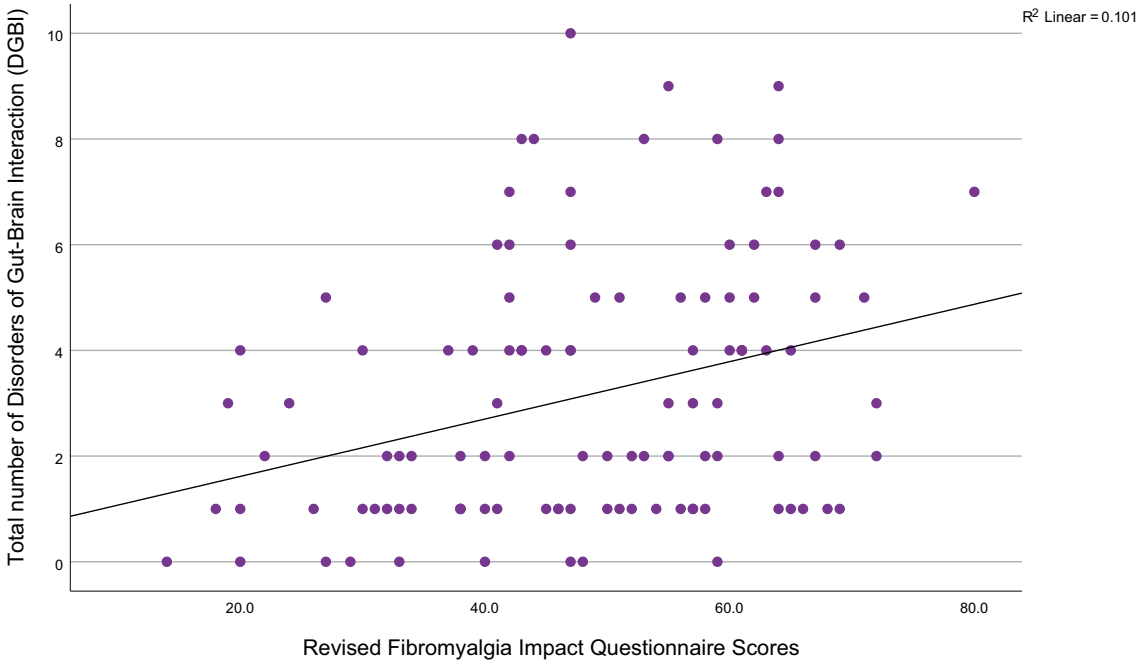

FIGURE 1 Correlation between fibromyalgia severity score and number of disorders of gut–brain interaction.

TABLE 1 Associations between indices of fibromyalgia severity and functional bowel disorder severity groups.

	ACR FSS		ACR WPI		ACR SSS		SF36-BP		FIQR	
FBDSI groups	***H* statistic**	***p*-value[a]**	***H* statistic**	***p*-value[a]**	***H* statistic**	***p*-value[a]**	***H* statistic**	***p*-value[a]**	***H* statistic**	***p*-value[a]**
Overall (df = 3)	15.4	**0.001**[b]	12.0	**0.007**[b]	12.8	**0.005**[b]	10.2	**0.02**[b]	10.34	**0.016**[b]
None-mild	−7.0	1.0	−3.2	1.0	−9.3	1.0	−5.4	1.0	−7.0	1.0
None-moderate	−17.4	0.39	−16.4	0.48	−9.7	1.0	−18.0	0.31	−10.4	1.0
None-severe	−37.5	**0.001**	−30.5	**0.016**	−35.3	**0.003**	−28.1	**0.03**	−31.9	**0.011**
Mild-moderate	−10.4	1.0	−13.3	0.68	−0.4	1.0	−12.6	0.76	−3.4	1.0
Mild-severe	−30.5	**0.006**	−27.4	**0.019**	−26.0	**0.025**	−22.7	0.08	−24.9	**0.04**
Moderate-severe	−20.1	0.35	−14.1	1.0	−25.6	0.09	−10.1	1.0	−21.5	0.26

Abbreviations: ACR, American College of Rheumatology; df, degrees of freedom; FIQR, fibromyalgia impact questionnaire; FSS, fibromyalgia severity scale; SF36-BP, short-form 36 bodily pain; SSS, symptom severity score. All *p*-values <0.05 in the tables were presented in bold text.

[a]Adjusted significance using Bonferroni correction.

[b]Unadjusted *p*-value.

having chronic, 60% ($n = 39$) as frequent, and 14% ($n = 9$) had infrequent migraine.

More DGBI were identified in those who met the criteria for migraine compared to those not meeting the criteria (median (IQR) 4 (3), c.f. 1 (3), $Z = -3.15$, $p = 0.002$, $r = -0.30$). Regression analysis with number of DGBI, diet quality, fibre intake, number of comorbidities and medication use showed this was a significant predictor of migraine, X^2 (5, $N = 111$) =16.7, $p = 0.005$ and accurately classified migraine in about 72% of cases. Of the independent variables, only the number of DGBI was significant (OR 1.25) accounting for ~14%–19% of the variance in migraine prevalence.

Meeting any of the criteria for Rome IV category A (oesophageal disorders) was significantly associated with meeting migraine criteria, X^2 (1, $N = 111$) = 6.38, $p = 0.012$. However, no individual disorder in this category was associated with prevalence or type of migraine.

Meeting any criteria in the Rome IV category B (gastroduodenal disorders) was associated with migraine prevalence, X^2 (1, $N = 111$) = 8.50, $p = 0.004$. Significant associations with migraine were seen for post-prandial distress syndrome (PPDS), X^2 (1, $N = 111$) = 5.43, $p = 0.02$, and chronic nausea and vomiting syndrome, X^2 (1, $N = 111$) = 6.45, $p = 0.01$. Noting nausea and vomiting are

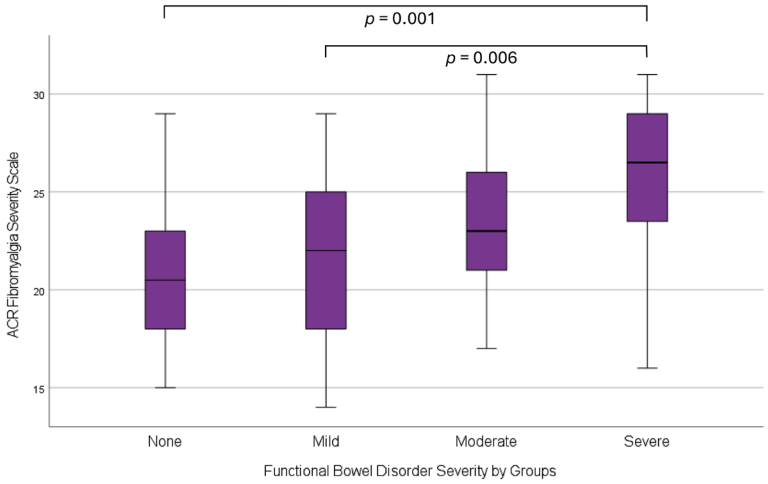

FIGURE 2 Higher scores on the ACR Fibromyalgia Severity Scale were associated with higher scores on the Functional Bowel Disorder Severity Index.

TABLE 2 Summary of linear regression analysis of factors predicted to influence scores of the widespread pain index and revised fibromyalgia impact questionnaire.

Pain parameter	Predictor	Coefficient (*B*)	Standard error	*t*-value	*p*-value	95% CI	Model R^2 (Adj R^2)
Widespread pain index	FBDSI	0.02	0.01	3.60	**<0.001**	0.01, 0.03	0.19 (0.15)
	Age	−0.02	0.03	−0.66	0.513	−0.07, 0.04	
	Healthy eating Index	−0.03	0.02	−1.77	0.08	−0.06, 0.00	
	Body mass index	0.03	0.04	0.74	0.46	−0.05, 0.12	
Revised fibromyalgia impact questionnaire	FBDSI	0.08	0.02	3.35	**0.001**	0.03, 0.13	0.16 (0.13)
	Age	−0.05	0.11	−0.45	0.65	−0.26, 0.17	
	Healthy eating Index	−0.06	0.07	−0.08	0.41	−0.19, 0.08	
	Body mass index	0.41	0.17	2.38	**0.02**	0.07, 0.78	

Abbreviations: BMI, body mass index; FBDSI, functional bowel disorder severity index; HEI, healthy eating index. All *p*-values <0.05 in the tables were presented in bold text.

closely associated with migraine, this was not evaluated further. Two-sided Fisher's exact test showed that type of migraine was associated with Rome B (overall) ($N=111$, $p<0.001$) and PPDS ($N=111$, $p=0.045$).

Overall, the Rome IV category C (bowel disorders) was not associated with migraine, X^2 (1, $N=111$) =2.45, $p=0.12$, but meeting criteria for IBS, X^2 (1, $N=111$)=8.28, $p=0.004$, IBS-mixed type, X^2 (1, $N=111$)=9.50, $p=0.002$, and functional bloating and distension (Fisher's exact $p=0.049$) were.

Using Fisher's exact test, the type of migraine was associated with IBS ($p=0.002$), and with type of IBS ($p<0.001$), in particular IBS diarrhoea ($p=0.03$), and IBS-mixed ($p=0.005$).

As a group, Rome IV F (the anorectal disorders) was not associated with migraine, X^2 (1, $N=111$)=2.11, $p=0.15$, nor with type of migraine, Fisher's exact, $p=0.10$. However, satisfying criteria for any functional anorectal pain disorder was associated with migraine (Fisher's exact, $p=0.03$), but no specific type of migraine. Proctalgia fugax was associated with meeting migraine criteria, X^2 (1, $N=111$)=6.22, $p=0.01$, and with type of migraine (Fisher's exact $p=0.002$).

Chi-square tests of association showed that participants with TTH were significantly less likely to meet criteria for Rome A, B or F: Rome A, X^2 (1, $N=111$)=8.34, $p=0.003$, Rome B, X^2 (1, $N=111$)=12.98, $p<0.001$, and Rome F, X^2 (1, $N=111$)=10.29, $p=0.001$. No differences were observed for Rome IV, group C (Fisher's exact test $p=0.113$).

3.4 | Quality of life

Significant results of pairwise comparisons between categories of FBDSI (Kruskal–Wallis *H*-test with Bonferroni correction) were found for the SF36 domains mental health, bodily pain and general health.

Comparing the FBDSI against the SF36-BP, mean ranks were 74.3 (for severe), 64.2 (moderate), 51.6 (mild) and 46.2 (no FBD). The difference between the 'none' and 'severe' groups was significant: $H(3) = -28.12$, $p = 0.03$.

Similarly, the group in the 'severe' category for FBDSI had significantly lower scores for general health (SF36-GH) than those in 'mild' $H(3) = 28.83$, $p = 0.011$, and no FBD, $H(3) = 32.56$, $p = 0.008$ Mean rank pain scores by FBDSI group were 31.0 (for severe), 56.9 (moderate), 59.8 (mild) and 63.6 for no FBD.

For SF36-MH, mean rank scores were 34.2 (for severe), 56.5 (moderate), 59.0 (mild) and 63.3 for no FBD. Differences between 'severe' were significant compared to no FBD $H(3) = 29.13$, $p = 0.026$ and compared to 'mild' $H(3) = 24.8$, $p = 0.04$. These relationships are demonstrated in Figure 3.

3.5 | Sleep

Less than half (48/113, 43%) of women with fibromyalgia reported getting the amount of sleep considered optimal (~7–8 h per night). For the remaining sleep domains from the MOS-SS, an optimal score is 0, and would indicate no problem with this parameter, while a score of 100 would indicate severe problems. The lowest scores were seen for waking with shortness of breath or headache and the highest score was the sleep disturbance scale, as shown in Table 4.

More severe functional bowel disorder scores were significantly associated with higher score for total sleep problems, indicating worse sleep with more severe bowel problems, $H(3) = 10.96$, $p = 0.012$. Mean ranks were 80.4 (for severe), 52.4 (moderate), 50.5 (mild) and 53.9 for those without any FBD. Post hoc comparisons showed that the 'severe' group differed significantly from the 'mild' ($H(3) = -29.87$, $p = 0.008$). Severe vs. moderate and severe vs. no FBD were insignificant after Bonferroni correction ($p = 0.05$ and $p = 0.06$, respectively).

Overall, somnolence scores were significantly different across the FBDSI groups: X^2 (3, $N = 111$) $= 12.02$, $p = 0.007$. Mean rank scores were 81.2 (severe), 54.8 (moderate), 49.6 (mild) and 53.3 (no FBD). Pairwise comparisons between these groups, with Bonferroni correction, were significant for no FBD c.f. severe ($H(3) = -27.90$, $p = 0.04$) and mild c.f. severe ($H(3) = -31.6$, $p = 0.004$).

A Mann–Whitney *U*-test showed that Rome A, *functional heartburn*, was associated with fewer hours sleep, which was not changed when those meeting *possible functional heartburn* criteria were included. Overall, the Rome B group and its individual types were more commonly associated with sleep disturbance, somnolence and overall sleep problems. For Rome groups C and F, the associations were fewer, as shown in Table 5.

Individually, only meeting criteria for Rome B was significantly associated with sleep, ((3, 108) = 8.84, $p = 0.001$), accounting for ~17.6%–19.9% (R^2 0.199) of variance in overall sleep problems (Table 5).

Together, the DGBI groups of interest (A, B, C and F), with WPI and BMI explain approximately 16.5%–21.1% (R^2 0.165) of the variance in overall sleep problems. Overall, the model was significant ($F(6, 105) = 4.63$, $p < 0.001$) as shown in Table 6.

Of the individual DGBI, none of the Rome A were significant predictors of sleep problems. Pooling Rome B disorders together in one model, the overall predicted variance in the sleep problems total score was 18.2%–24.1% (R^2 0.241), ($F(8, 102) = 4.05$, $p = 0.001$), with cyclic nausea and vomiting syndrome significantly associated: (B 9.70, SE 3.65, $t = 2.66$, $p = 0.009$, 95% CI [2.47, 16.9]). None of the functional bowel disorders were significantly associated. The overall model might explain ~7.8%–14.5% ($p = 0.037$) of the overall sleep score. This was similar for Rome F (9.2%–13.3%, $p = 0.01$). In each model, the WPI was the strongest predictor of poor sleep overall.

3.6 | Mental health

As presented in Table 7, results from the PHQ-2 indicated that the criteria for depressive disorder was met by 34 (30.1%) women with fibromyalgia, and 46 (41.4%) met anxiety disorder criteria as per the GAD-2 survey.

As noted above, and shown in Figure 3, significant differences were also seen in mental health scores (SF36-MH) across the four FBDSI groups.

Severity according to the FBDSI was significantly associated with meeting anxiety criteria (Fisher's exact test, $p = 0.03$), but not depression ($p = 0.39$).

Table 8 shows chi-square test results for Rome IV groups and individual DGBI that were present in at least 10% of women with fibromyalgia. Only post-prandial distress syndrome was associated with meeting depression criteria (as indicated on the PHQ-2). Overall, meeting any Rome B criteria and specifically post-prandial distress syndrome and rumination syndrome, and the Rome F disorder, proctalgia fugax were associated with meeting criteria for generalized anxiety disorder (as per the GAD-2).

Mann–Whitney *U*-tests showed that meeting criteria for anxiety was associated with significantly higher scores for total sleep problems ($Z = -3.54$, $r = -0.31$, $p < 0.001$), somnolence ($Z = -2.16$, $p = 0.03$) and waking with shortness of breath or headache ($Z = -3.78$, $r = -0.27$, $p < 0.001$). Depression was also associated with

TABLE 3 Differences in pain and fibromyalgia severity scores by disorders of gut–brain interaction.

		Fibromyalgia severity scale						SF36 bodily pain			
		Mean (SD)		Median (IQR)				Mean (SD)		Median (IQR)	
	n (%)	No	Yes	No	Yes	*Z*	*p*-value[a]	No	Yes	No	Yes
Rome A. Oesophageal disorders	47 (42)	21.8 (4.4)	23.0 (4.2)	22.0 (7)	23.0 (6)	−1.61	0.11	56.6 (16.5)	63.6 (14.8)	60 (28)	70 (20)
Functional chest pain	24 (22)	22.1 (5.4)	23.2 (3.5)	22 (8)	23 (4)	−0.99	0.32	58.0 (16.4)	65.0 (14.1)	60 (20)	70 (18)
Functional heartburn	7 (6)	22.3 (4.2)	22.1 (6.6)	22.5 (7)	23 (13)	−0.16	0.87	58.9 (16.2)	70 (11.5)	60 (20)	70 (20)
Functional heartburn + possible[b]	21 (19)	22.4 (4.2)	22.5 (5.1)	22 (7)	23 (9)	−0.25	0.81	58.9 (16.2)	62.4 (15.8)	60 (20)	60 (20)
Reflux hypersensitivity	8 (7)	22.4 (4.2)	21.0 (5.7)	23 (7)	20.5 (10)	−0.91	0.36	59.2 (7.8)	63.8 (21.3)	60 (20)	70 (25)
Globus	2 (2)	22.3 (4.4)	20 (2.8)	23 (7)	20 (−)	0.39	0.43	59.5 (16.2)	60 (14.1)	60 (20)	60 (−)
Functional dysphagia	22 (20)	20.5 (4.6)	22.8 (4.0)	22 (7)	25.5 (4.0)	−2.51	**0.01**	58.8 (17.0)	62.7 (12.0)	60 (20)	65 (20)
Rome B. Gastroduodenal disorders	52 (47)	21.0 (4.0)	23.7 (4.3)	21 (6)	24.5 (5)	−3.06	**0.002**	57.3 (17.1)	62.1 (14.7)	60 (20)	60 (20)
Any functional dyspeptic disorder	38 (34)	21.7 (4.2)	23.5 (4.4)	22 (7)	23.5 (6)	−2.06	**0.04**	58.8 (17.1)	61.1 (14.3)	60 (20)	60 (20)
Post-prandial distress syndrome	27 (24)	21.6 (4.3)	24.6 (3.7)	22 (7)	25 (5)	−3.14	**0.002**	58.2 (17.0)	63.7 (12.8)	60 (20)	60 (20)
Epigastric pain syndrome	25 (23)	22.0 (4.1)	23.2 (4.9)	22 (6)	23 (9)	−1.21	0.22	59.5 (16.8)	59.6 (14.0)	60 (20)	60 (20)
Belching disorders	4 (4)	22.2 (4.3)	25.0 (5.6)	22 (7)	26.5 (10)	−1.34	0.18	59.4 (16.3)	65 (12.9)	60 (20)	65 (30)
Any Fx nausea and vomiting disorder	18 (16)	21.9 (4.3)	24.3 (4.0)	22 (8)	24 (5)	−2.07	**0.04**	58.2 (16.5)	66.7 (11.9)	60 (20)	70 (15)
Chronic nausea and vomiting syndrome	16 (14)	21.9 (4.3)	24.6 (4.2)	22 (7)	25 (5)	−2.18	**0.03**	58.3 (16.4)	66.9 (12.5)	60 (20)	70 (25)
Cyclic vomiting syndrome	4 (4)	22.2 (4.3)	25.3 (3.3)	22 (7)	25 (6)	−1.42	0.16	59.1 (16.2)	72.5 (9.6)	60 (20)	75 (18)
Rumination syndrome	14 (13)	22.0 (4.3)	24.3 (4.4)	22 (7)	25 (5)	−1.63	0.10	58.7 (15.8)	65.7 (17.4)	60 (2)	70 (23)
Rome C. Bowel disorders	98 (88)	20.4 (4.4)	22.6 (4.3)	20 (7)	23 (7)	−1.68	0.09	54.6 (16.6)	60.2 (16.1)	60 (30)	60 (20)
Irritable bowel syndrome (IBS)	59 (53)	21.4 (4.3)	23.4 (4.3)	21 (7)	24 (6)	−2.13	**0.03**	59.2 (15.4)	59.8 (15.4)	60 (20)	60 (20)
IBS-constipation	15 (14)	22.4 (4.4)	21.7 (4.0)	23 (7)	22 (6)	−0.43	0.67	59.4 (16.1)	60.3 (17.1)	60 (20)	60 (20)
IBS diarrhoea	16 (14)	22.0 (4.3)	24 (4)	22 (7)	24 (6)	−1.60	0.11	59.7 (16.6)	58.7 (13.0)	60 (20)	60 (20)
IBS-mixed type	26 (23)	21.9 (4.3)	23.8 (4.3)	22 (7)	25 (5)	−1.86	0.06	59.8 (16.2)	58.9 (16.3)	60 (20)	60 (20)
IBS-unspecified	2 (2)	22.4 (4.3)	17.5 (0.7)	23 (7)	17.5 (−)	0.10	0.11[b]	59.5 (16.3)	65.0 (7.1)	60 (20)	65 (−)
Functional constipation	5 (5)	22.3 (4.3)	23.2 (5.2)	22.5 (7)	25 (10)	−0.51	0.61	59.3 (16.4)	60 (12.2)	60 (20)	60 (20)
Functional diarrhoea	10 (9)	22.2 (4.4)	23.3 (3.1)	22.0 (8)	24 (6)	−0.88	0.38	59.6 (16.3)	59.0 (15.2)	60 (20)	55 (15)
Functional abdominal bloating and distension	11 (10)	23.3 (4.2)	21.9 (5.8)	23 (7)	21 (9)	−0.31	0.76	59.3 (16.0)	61.8 (17.8)	60 (20)	60 (30)
Unspecified functional bowel disorder	16 (14)	22.4 (4.4)	21.4 (3.6)	23 (7)	22.5 (5)	−0.85	0.40	59.4 (15.6)	60.6 (19.8)	60 (20)	70 (28)
Opioid-induced constipation	7 (6)	22.4 (4.4)	20.3 (3.6)	23 (7)	22 (7)	−1.34	0.18	58.7 (12.5)	72.9 (12.5)	60 (20)	70 (30)
Rome C. Anorectal disorders	35 (32)	21.6 (4.4)	23.8 (3.8)	22 (7)	24 (5)	−2.42	**0.02**	58.2 (16.9)	62.6 (14.2)	60 (20)	60 (20)
Any functional anorectal pain disorder	29 (26)	21.6 (4.3)	24.2 (3.9)	22 (7)	25 (5)	−2.62	**0.01**	57.8 (16.5)	64.5 (14.3)	60 (20)	70 (20)
Faecal incontinence	12 (11)	22.2 (4.2)	23.5 (3.4)	22 (7)	23.5 (4)	−0.82	0.41	59.4 (16.7)	60 (10.4)	60 (20)	70 (30)
Levator ani syndrome & Unsp. Anorectal pain	10 (9)	22.3 (4.4)	22.6 (3.3)	23 (7)	22.5 (5)	−0.25	0.80	59.2 (16.7)	63 (9.5)	60 (20)	60 (30)
Proctalgia fugax	19 (17)	21.7 (4.2)	25 (6)	22 (7)	25 (6)	−2.87	**0.004**	58.4 (15.9)	65.3 (16.5)	60 (20)	70 (30)

Abbreviations: Fx, functional; unsp, unspecified. All *p*-values <0.05 in the tables were presented in bold text.

[a]Mann–Whitney *U*-test.

[b]Possible functional heartburn.

		ACR widespread pain index						Fibromyalgia impact score (FIQR)					
		Mean (SD)		Median (IQR)				Mean (SD)		Median (IQR)			
Z	*p*-value[a]	No	Yes	No	Yes	*Z*	*p*-value[a]	No	Yes	No	Yes	*Z*	*p*-value[a]
−2.20	**0.03**	12.1 (3.7)	13.1 (3.3)	12 (6)	13 (5)	−1.44	0.15	44.5 (14.3)	52.7 (13.2)	44.5 (25.8)	49 (20)	−1.46	0.14
−1.67	0.09	12.4 (3.7)	13.0 (3.0)	13 (6)	13 (4)	−0.84	0.40	47.1 (14.6)	51 (12.6)	47 (22)	51 (19)	−1.56	0.12
−1.90	0.06	12.5 (3.5)	12.7 (4.4)	13 (5)	12 (8)	−0.1	0.92	47.1 (14.2)	54.5 (15.5)	48 (21)	63 (20)	−1.34	0.18
−1.00	0.32	12.5 (3.5)	12.6 (3.7)	13 (5)	13 (6)	−0.06	0.95	47.2 (14.1)	53.3 (14.5)	47 (20)	59 (21)	−1.94	0.05
−1.02	0.31	12.6 (3.5)	11.5 (4.1)	13 (5)	10.5 (7)	−0.91	0.36	48.3 (14.1)	49.1 (18.4)	48 (20)	55 (33)	−0.47	0.64
1.00	0.99	12.5 (3.6)	11 (2.8)	13 (5)	11 (−)	0.469	0.50	48.2 (14.3)	57 (14.1)	48 (21)	57 (−)	0.35	0.39
−0.90	0.37	12.13 (3.6)	14 (2.9)	12 (6)	14.5 (4)	−2.24	**0.03**	47.9 (15.3)	50.2 (9.3)	50 (22)	47 (17)	−0.54	0.59
−1.52	0.13	11.8 (3.5)	13.4 (3.4)	12 (7)	12.5 (5)	−2.1	**0.04**	44.5 (14.3)	52.7 (13.2)	46 (23)	55.5 (20)	−2.94	**0.003**
−0.57	0.57	12.1 (3.6)	13.3 (3.4)	13 (6)	13.5 (5)	−1.54	0.12	46.4 (14.5)	13.4 (2.2)	47 (22.5)	54 (19)	−1.95	0.05
−1.45	0.15	12.0 (3.6)	14.0 (3.1)	13 (6)	14 (5)	−2.4	**0.02**	46.1 (14.7)	55.3 (10.6)	47 (25)	55 (19)	−2.78	**0.01**
−0.06	0.95	12.3 (3.5)	13.2 (3.7)	13 (5)	14 (7)	−1.12	0.26	48.2 (14.6)	48.9 (13.4)	49 (22)	47 (17)	−0.33	0.74
−0.69	0.49	12.4 (3.5)	14.5 (5.3)	13 (5)	16 (10)	−1.19	0.23	48.4 (14.5)	47.8 (10.3)	48 (21)	48 (19.3)	−0.34	0.73
−2.05	**0.04**	12.3 (3.6)	13.7 (3.1)	13 (6)	13.5 (6)	−1.47	0.14	46.3 (14.2)	58.8 (9.9)	47 (20.5)	60.5 (15.5)	−3.54	**<0.001**
−1.96	0.05	12.3 (3.6)	13.8 (3.2)	13 (6)	13.5 (6)	−1.45	0.15	26.3 (14.1)	60.6 (8.9)	47 (20)	62.5 (11.5)	−3.92	**<0.001**
−1.77	0.08	12.4 (3.6)	15 (2.8)	13 (5)	16 (5)	−1.57	0.12	48.1 (14.4)	53.8 (12.7)	48 (22)	51 (23.8)	−0.64	0.52
−1.52	0.13	12.3 (3.6)	13.8 (3.2)	13 (6)	13.5 (5)	−1.28	0.20	47.5 (14.5)	54.4 (11.8)	47 (22)	56.5 (13.8)	−1.46	0.15
−1.08	0.28	1134 (3.8)	12.7 (3.5)	12 (8)	13 (5)	−1.17	0.24	44.5 (18.9)	48.8 (13.7)	47 (35)	49.5 (19.3)	−0.65	0.52
−0.05	0.96	12.0 (3.6)	13.0 (3.5)	12 (6)	13 (5)	−1.3	0.19	47.1 (15.1)	49.4 (13.6)	47 (24)	50 (19)	−0.63	0.53
−0.01	0.99	12.6 (3.4)	11.9 (2.8)	13 (5)	13 (4)	−0.87	0.38	48.5 (14.4)	47.3 (14.2)	49 (21.8)	47 (15)	−0.60	0.55
−0.40	0.69	12.3 (3.6)	13.8 (3.5)	13 (6)	15 (7)	−1.49	0.14	48.1 (14.4)	49.9 (14.2)	47.5 (20.8)	53 (19)	−0.54	0.59
−0.09	0.93	12.2 (3.5)	13.4 (3.7)	13 (5)	14 (5)	−1.41	0.16	47.9 (14.7)	49.7 (13.3)	48 (21.5)	50 (18.3)	−0.47	0.64
0.62	0.65[b]	12.6 (3.5)	8 (1.4)	13 (5)	8 (−)	0.071	0.07[b]	48.3 (14.3)	52 (21.2)	48 (20)	52 (−)	0.76	05.77[b]
−0.06	0.95	12.5 (3.6)	13.2 (3.6)	13 (5)	14 (7)	−0.51	0.61	48.3 (14.6)	50.2 (4.9)	48.5 (22)	47 (9)	−0.12	0.90
−0.42	0.67	12.4 (3.6)	13.5 (2.5)	13 (6)	13.5 (5)	−0.96	0.34	48.2 (14.7)	49.9 (10.1)	48 (22)	47 (16.8)	−0.14	0.89
−0.59	0.56	12.6 (3.4)	11.3 (5.1)	13 (5)	10 (10)	−1.02	0.31	48.4 (14.7)	47.8 (10.3)	48 (20.8)	52 (18)	−0.39	0.69
−0.58	0.56	12.5 (3.7)	12.6 (2.7)	13 (5)	13 (4)	−0.1	0.92	48.8 (13.6)	45.8 (18.5)	49 (19)	46 (34.8)	−0.39	0.70
−2.14	**0.03**	12.6 (3.6)	10.4 (2.4)	13 (5)	11 (6)	−1.73	0.08	47.8 (14.2)	55.9 (14.8)	47.5 (20.8)	55.9 (24)	−1.15	0.25
−1.31	0.19	12.0 (3.6)	13.6 (3.2)	12.5 (6)	14 (4)	−2.15	**0.03**	46.9 (14.4)	51.5 (13.9)	47 (21.5)	53 (20)	−1.54	0.12
−1.99	**0.046**	12.1 (3.5)	13.8 (3.4)	12.5 (6)	14 (7)	−2.10	**0.04**	46.2 (14.7)	54.4 (11.4)	47 (24.3)	55 (19)	−2.47	**0.01**
−0.01	0.99	12.4 (3.6)	13.6 (2.8)	13 (6)	14 (4)	−1.06	0.29	48.5 (49)	46.9 (16.4)	49 (20)	45 (28.5)	−0.12	0.91
−0.66	0.51	12.5 (3.6)	12.8 (2.8)	13 (6)	12.5 (5)	−0.28	0.78	47.8 (14.7)	53.9 (8.5)	48 (21)	53 (16.3)	−1.32	0.19
−1.82	0.07	12.1 (3.5)	14.3 (3.7)	12.5 (6)	15 (5)	−2.23	**0.03**	47.0 (14.3)	54.7 (12.9)	47 (21)	58 (21)	−1.88	0.06

worse total scores for sleep problems overall ($Z = -4.00$, $r = -0.31$, $p < 0.001$), sleep disturbance scale ($Z = -2.80$, $p = 0.005$), somnolence ($Z = -3.01$, $p = 0.003$) and waking with shortness of breath or headache ($Z = -2.65$, $r = -0.27$, $p = 0.008$).

To confirm the relative influence of the SF36-BP vs. WPI scores, partial least square analysis was conducted. Using 2 latent factors, SF36-BP was the strongest predictor, thus it was used in a simple regression model to evaluate associations between pain and mental health. Variable importance in the project data is included in Table 9.

To evaluate the influence of gastrointestinal function on depression, a logistic regression model with the number of DGBI and the FBDSI, controlling for measures of pain, HEI, sleep problems overall, number of comorbidities and BMI revealed that only pain was significantly predictive of meeting PHQ-2 depression criteria, as shown in Table 9. While the odds ratio is low (1.10), together the overall model was predictive of 33.4%–47.2% of the variance in meeting criteria for depression, as per Cox and Snell and Nagelkerke R^2 values.

For estimating the influence of GI function on anxiety in the study population, the same analysis, without BMI (Eik-Nes et al., 2022), was conducted. SF36-BP remained the most significant predictor, while diet quality was associated with a small but significant reduction in the likelihood of meeting anxiety criteria. Overall, the model was significant and predictive of 23.3%–31.4% of likelihood of meeting anxiety criteria (per Cox and Snell and Nagelkerke R^2 values). Values for each predictor in the model are reported in Table 9. For the FBDSI, Helmert contrast method was used in the model.

These results demonstrate that while some specific DGBI were associated with mental health, overall, body pain is a predictor of depression and anxiety. The risk of anxiety is slightly but significantly reduced by a diet of higher quality.

TABLE 4 Sleep scores from the medical outcomes study sleep survey in women with fibromyalgia.

	Fibromyalgia ($N = 111$)	
	Mean (SD)	**Median (IQR)**
Sleep quantity (hours)	6.9 (1.3)	7 (2)
Sleep disturbance scale	53.7 (22.4)	53.8 (34)
Sleep adequacy	47.8 (15.5)	50 (20)
Somnolence	45.3 (22.7)	40 (33)
Snoring	38.2 (31.3)	40 (40)
SOB or headache on awakening	23.24 (24.5)	20 (40)
Sleep problems overall	49.12 (13.7)	50 (18)

Abbreviation: SOB, shortness of breath.

4 | DISCUSSION

The principal findings of this study are women living with fibromyalgia have multiple DGBI that are significantly associated with multiple extra-intestinal conditions and symptoms. Further, the number of DGBIs was a significant predictor of the severity of pain and poor sleep health. These findings suggest the aetiology and clinical management of fibromyalgia requires an integrative physiological lens that considers fibromyalgia as a gastrointestinal-mediated condition. In all, 93% of women with fibromyalgia met criteria for at least one DGBI. This is slightly lower than the 98% reported by Almansa's group (Almansa et al., 2009). In contrast, 18% of our controls also met criteria for at least one DGBI, which is notably lower than the 39% reported in the only other study examining the totality of the DGBI published to date (Almansa et al., 2009). While accurate comparison is thwarted by different criteria in the survey tools used in Almansa's study compared to ours (Rome II vs Rome IV), several differences were noted: the prevalence of oesophageal disorders (Rome II, group A) in Almansa's study was 27%, lower than our 42%. Thirty-four percent of Almansa's cohort met the criteria for a gastroduodenal disorder (Rome II, group B), which is also lower than the 46% in our study. The prevalence of the functional

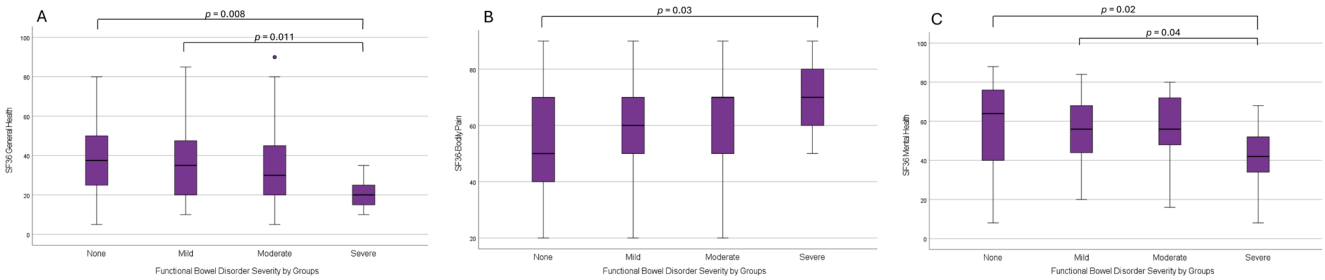

FIGURE 3 Measures of quality of life as evaluated using the short-form 36 survey, by groups of functional bowel disorder severity groups. Scores for fig 3B are inverted such that high values are consistent with more severe pain.

TABLE 5 Associations between sleep indices and selected disorders of gut–brain interaction in women with fibromyalgia.

		Sleep disturbance scale		Sleep inadequacy		Number of hours sleep		Somnolence		Wake SOB or w/ headache		Sleep problems overall	
	n	*Z*	*p-value*	*Z*	*p-value*	*Z*	*p-value*	*Z*	*p-value*	*Z*	*p-value*	*Z*	*p-value*
Rome A. Oesophageal disorders	47	−0.44	0.66	−0.96	0.34	−0.41	0.68	−0.61	0.55	−0.65	0.52	−0.73	0.47
Functional heartburn	7	−0.11	0.92	−1.36	0.17	−2.47	**0.01**	−1.04	0.30	−0.34	0.73	−0.25	0.80
Functional heartburn + possible*	21	−0.50	0.62	−0.66	0.51	−2.80	**0.005**	−1.83	0.07	−1.05	0.29	−0.08	0.93
Functional dysphagia	22	−0.33	0.74	−0.83	0.41	−0.05	0.96	−1.59	0.11	−1.97	**0.049**	−1.09	0.28
Rome B. Gastroduodenal disorders	52	−2.21	**0.03**	−1.33	0.19	−0.82	0.42	−3.23	**0.001**	−2.33	**0.02**	−3.58	**<0.001**
Any functional dyspeptic disorder	38	−1.46	0.15	−0.70	0.49	−0.84	0.40	−2.25	**0.02**	−2.86	**0.004**	−2.51	**0.01**
Post-prandial distress syndrome	27	−1.50	0.14	−0.02	0.98	1.09	0.27	−2.33	**0.02**	−3.08	0.002	−2.69	**0.01**
Epigastric pain syndrome	25	−1.69	0.09	−0.38	0.70	−0.13	0.90	−2.38	**0.02**	−1.96	0.050	−2.12	**0.03**
Any functional nausea & vomiting disorder	18	2.14	**0.03**	−1.50	0.13	−1.20	0.23	−3.11	**0.002**	−1.31	0.19	−3.36	**<0.001**
Chronic nausea & vomiting syndrome	16	−2.52	**0.01**	−1.26	0.21	−0.92	0.36	−3.33	**<0.001**	−1.32	0.19	−3.74	**<0.001**
Rumination syndrome	14	−1.09	0.28	−0.99	0.33	−0.62	0.53	−2.62	**0.01**	−1.51	0.13	−2.25	**0.03**
Rome C. Bowel disorders	98	−0.11	0.92	−0.76	0.45	−0.93	0.35	−1.31	0.19	−0.43	0.67	−0.29	0.78
Chronic functional abdominal pain	13	−1.67	0.10	−0.22	0.83	−1.01	0.32	−3.00	**0.003**	−1.53	0.13	−2.56	**0.01**
IBS (Any)	59	−0.37	0.71	−0.09	0.93	−1.24	0.22	−1.72	0.09	−1.33	0.18	−1.34	0.18
IBS-mixed	26	−1.25	0.21	−0.02	0.99	−0.38	0.70	−1.78	0.08	−1.53	0.13	−1.96	0.05
Functional constipation	5	−0.07	0.94	−1.06	0.29	−0.58	0.56	−0.18	0.89	−1.97	**0.049**	−0.57	0.57
Functional diarrhoea	10	−0.62	0.53	−1.07	0.29	−0.19	0.85	−1.19	0.23	−2.04	**0.04**	−0.62	0.54
Functional bloating & distension	11	−0.90	0.37	−1.75	0.08	−2.01	**0.045**	−0.22	0.82	−0.81	0.42	−0.18	0.86
Rome F. Anorectal disorders	35	−0.82	0.41	−0.38	0.70	−0.50	0.62	−1.97	**0.048**	−1.86	0.06	−1.49	0.14
Proctalgia fugax	19	−1.27	0.20	−0.43	0.67	−0.48	0.63	−1.51	0.13	−2.01	**0.04**	−1.72	0.09
Faecal incontinence	12	−0.39	0.69	−0.40	0.69	−0.19	0.85	−1.92	0.06	−0.92	0.36	−0.85	0.40

Abbreviation: SOB, short of breath. All *p*-values <0.05 in the tables were presented in bold text.

*Includes those meeting criteria for functional heartburn, plus those classifed as "possible heartburn"

TABLE 6 Regression model showing influence of DGBI by groups on total sleep problems score in women with fibromyalgia, controlling for widespread pain and BMI.

	β-coefficient (SE)	Std *β*	*t*-statistic	95% CI	*p*-value
Rome A. Oesophageal disorders	-the 2.91 (2.5)	−0.11	−1.15	−7.93, 2.11	0.252
Rome B. Gastroduodenal disorders	8.70 (2.7)	0.32	3.21	3.32, 14.01	**0.002**
Rome C. Bowel disorders	−1.78 (3.8)	−0.04	−0.47	−9.30, 5.74	0.640
Rome F. Anorectal disorders	−0.40 (2.8)	−0.01	−0.01	−5.97, 5.18	0.888
WPI	1.17 (0.4)	0.30	3.34	0.47, 1.86	**0.001**
BMI	0.06 (0.15)	0.03	0.37	−0.24, 0.36	0.711

All *p*-values <0.05 in the tables were presented in bold text.

TABLE 7 Pain and fibromyalgia severity differences in women with fibromyaglia with and without anxiety and depression.

	Anxiety (GAD-2)				Depression (PHQ-2)			
	No	Yes	*Z*	*p*-value*	No	Yes	*Z*	*p*-value*
Widespread pain index	12 (6)	14 (5)	−1.66	0.10	12 (6)	14 (3)	−2.12	**0.03**
Short-form 36. Body pain	50 (20)	70 (20)	−3.93	**<0.001**	50 (30)	70 (20)	−4.90	**<0.001**
Fibromyalgia severity scale	22 (7)	24.5 (6)	−2.35	**0.02**	21 (7)	25 (4)	−3.03	**0.002**
Revised fibromyalgia impact questionnaire	43 (20)	59 (17)	−5.03	**<0.001**	44 (20)	61 (10)	−5.41	**<0.001**

Note: Values shown are median (interquartile range). All *p*-values <0.05 in the tables were presented in bold text.

Abbreviations: GAD-2, generalized anxiety disorder, 2-question survey, PHQ-2; patient health questionnaire, 2-question survey.

*Mann–Whitney *U*-test.

bowel disorders (Rome II, group C) was similar at 82%, c.f. 86%, while the anorectal disorders (Rome II, group F) were higher in Almansa's cohort at 59% compared to 31% in this study. Another notable difference between our study and Almansa's is the use of the ACR 1990 diagnostic criteria in the latter. These criteria were based on physical assessment of tender points (Wolfe et al., 1990), the majority of which are myofascial trigger points (Gerwin, 2011) that are sensitive in multiple pain disorders (Aggarwal et al., 2012; Medina et al., 2013).

4.1 | Migraine

The finding that those meeting the criteria for migraine was twice as high as the number of participants reporting a doctor's diagnosis (31%), suggests that under-reporting and/or underdiagnosis is common in this population. Of those with migraine, 60% of attacks were classed as frequent and almost 25% as chronic. Chronic migraine is defined as having 15 or more days in a month with headache, at least 8 days of which include features of migraine (HCC., 2013), indicating a significant quality of life burden for those experiencing this malady.

Most investigations into comorbidity of headache (as distinct from migraine) and fibromyalgia have been unidirectional, with evaluation of the prevalence of fibromyalgia in those diagnosed with headache. This was the case in de Tommaso et al.'s, 2009 study (de Tommaso et al., 2009), in which the prevalence of fibromyalgia in people with primary headache was 36%.

Migraine, also considered a central sensitization disorder (Penn et al., 2019), is strongly associated with fibromyalgia, with research indicating this association is bidirectional (Lin et al., 2022; Penn et al., 2019; Stuginski-Barbosa et al., 2012). Additionally, migraine correlates with the impact (de Tommaso et al., 2011) and severity of fibromyalgia such that migraine is proposed as a triggering factor (Giamberardino et al., 2016). The detrimental impact of migraine on quality of life is not insignificant, with acute and debilitating symptoms and diminished functioning on physical, social and emotional levels (Domitrz & Golicki, 2022; Stuginski-Barbosa et al., 2012). Independent of fibromyalgia, migraine is strongly associated with increased rates of depression and suicidal ideation (Chang & Lu, 2013), Galvez-Sanchez et al. (2019) reported that around 16.7% of fibromyalgics attempt suicide—which aligns with the rate in other chronic diseases. Alarmingly, this rate rises to over 58% when migraine is comorbid. Thus, migraine is a critically important consideration through the lens of mental health in fibromyalgia.

TABLE 8 Chi-square analysis of associations between the DGBI and anxiety and depression in women with fibromyalgia.

	Depression (PHQ-2)		Anxiety (GAD-2)	
	X^2	*p*-value	X^2	*p*-value
Rome A. Oesophageal disorders (any)	1.177	0.28	0.968	0.33
Functional chest pain	3.331	0.07	0.924	0.34
Functional heartburn, incl. 'possible'	1.822	0.18	0.021	0.88
Functional dysphagia	0.146	0.70	1.942	0.16
Rome B. Gastroduodenal disorders (any)	2.823	0.09	6.203	**0.01**
Post-prandial distress syndrome	5.153	**0.02**	6.810	**0.01**
Epigastric pain syndrome	0.105	0.75	2.818	0.09
Chronic nausea & vomiting syndrome		0.25[a]	3.416	0.07
Rumination syndrome	0.195	0.76	5.936	**0.02**
Rome C. Bowel disorders (any)		0.55[a]	0.691	0.41
Irritable bowel syndrome	0.147	0.70	0.358	0.55
IBS constipation		0.77[a]	0.015	0.90
IBS diarrhoea		0.55[a]	0.470	0.49
IBS mixed	0.254	0.61	1.025	0.31
Functional bloating & distension		0.73[a]		0.76[a]
Unspecified functional bowel disorder		0.25[a]	0.041	0.84
Rome F. Anorectal disorders (any)	0.321	0.57	3.475	0.06
Faecal incontinence	0.046	0.99	0.364	0.76
Proctalgia fugax	3.022	0.08	6.876	**0.01**

All *p*-values <0.05 in the tables were presented in bold text.

[a]Fisher's exact test.

Here, migraine was strongly associated with fibromyalgia severity regardless of which assessment tool was used—the FSS, the FIQR, the WPI and the SF36-BP. A study in 2009 by, de Tommaso et al. (2009) demonstrated a correlation between tender point pain and frequency of headaches, suggesting the possibility of a unifying mechanism in both. Giamberardino et al. (2016) reported that in those suffering both migraine and fibromyalgia, having a migraine was predictive of a flare of fibromyalgia pain within 12 h. They also found that prophylactic migraine medication significantly reduced the number of flares of fibromyalgia pain ($p < 0.001$), suggesting cross-sensitization may be a factor. Only six women with fibromyalgia in our study reported use of specific migraine-aborting medication.

Women with migraine had higher prevalence of DGBI, which remained significant after controlling for likely confounders. There is currently a limited amount of research examining this relationship, despite the consideration that migraine and the DGBI may have a common basis. What data there is, has examined the presence of migraine in people presenting with DGBI (Di Stefano et al., 2019), mainly functional dyspepsia, cyclic vomiting syndrome (Aurora et al., 2021), and IBS (Ohlsson, 2022). A recent systemic review reported similar co-prevalence of IBS and migraine across the included studies, also noting bi-directionality (Todor & Fukudo, 2023). Interestingly, IBS is also considered a hypersensitization disorder (Adams & Turk, 2018), with effects demonstrable peripherally and centrally (Farmer & Aziz, 2014). Severity of IBS is strongly linked to fibromyalgia pain (Lubrano et al., 2001), and migraine, fibromyalgia and depression are seen at around 40%–80% higher prevalence rates in people with IBS than those without IBS (Cole et al., 2006).

Migraine intensifies sensitivity to peripheral stimuli (Penn et al., 2019), and mitigating migraine improves

TABLE 9 Linear regression model showing odds of depression and anxiety relative to body pain, sleep and DBGI in women with fibromyalgia.

	Depression (PHQ-2)						Anxiety (GAD-2)					
	B (coefficient)	**SE**	**Wald**	***p*-value**	**OR (95% CI)**	***VIP***	**B (coefficient)**	**SE**	***Wald***	***p***	**OR (95% CI)**	***VIP***
SF36-bodily pain	0.10	0.03	13.26	**<0.001**	1.10 (1.05, 1.16)	1.93	0.04	0.02	4.95	**0.03**	1.04 (1.01, 1.07)	1.56
Number of DGBI	0.14	0.12	1.27	0.26	1.15 (0.90, 1.45)	0.81	0.19	0.11	3.04	0.08	1.21 (0.98, 1.51)	1.31
FBDSI (0)			4.46	0.22		0.30–0.58			0.73	0.87		0.43–0.48
FBDSI (1)	0.35	0.83	0.18	0.67	1.42 (0.28, 7.3)		0.17	0.66	0.06	0.80	1.18 (0.32, 4.34)	
FBDSI (2)	1.41	0.69	4.13	**0.04**	4.10 (1.1, 15.8)		−0.14	0.57	0.06	0.80	0.87 (0.29, 2.63)	
FBDSI (3)	−0.29	0.97	0.10	0.76	0.75 (0.11, 4.98)		−0.62	0.86	0.52	0.47	0.54 (0.10, 2.91)	
Diet quality (HEI)	−0.02	0.01	1.95	0.16	0.98 (0.96, 1.01)	1.19	−0.02	0.01	4.01	**0.045**	0.98 (0.96, 1.0)	1.21
Sleep problems total	0.04	0.24	3.11	0.08	1.04 (1.0, 1.1)	1.40	0.02	0.02	0.67	0.41	1.02 (0.98, 1.06)	1.26
Number of ICD dx	0.16	0.13	1.53	0.22	1.18 (0.91, 1.51)	0.43	0.06	0.10	0.39	0.53	1.07 (0.88, 1.30)	0.43
Body mass index	0.05	0.03	2.62	0.11	1.06 (0.99, 1.13)	0.72	–	–	–	–	–	–

Note: FBDSI 0, Reference; Contrast 1: None versus mild, moderate, severe. Contrast 2: Mild versus moderate, severe, Contrast 3: Moderate versus severe. All *p*-values <0.05 in the tables were presented in bold text.
Abbreviations: DGBI, disorders of gut–brain interaction; Dx: diagnoses, FBDSI, functional bowel disorder severity index; HEI, healthy eating index. SF36: short-form 36; ICD, international classification of disease.

fibromyalgia pain (Giamberardino et al., 2016). Thus, fibromyalgia, migraine and DGBI may represent distinct examples of a common mechanism affecting both peripheral and central pain sensitization.

These data highlight the need for encouraging the use of migraine-mitigating strategies and treatments and supporting patients and the totality of their symptoms at a clinical level.

4.2 | Sleep

Contextualizing our study's findings, perhaps one of the most confounding contributors to the spectrum of symptoms in fibromyalgia is sleep disturbance. Disturbed sleep is generally considered to be an artefact of chronic pain. As noted above, 'waking unrefreshed' is a component of fibromyalgia's diagnostic algorithm (Wolfe et al., 2016), sleep quality extends beyond feeling refreshed on awakening. Poor sleep quality is a harbinger of multiple problems, including (but not limited to) impaired cognitive function, fatigue, lower rates of exercise and social inadequacy (Choy, 2015).

Prolonged periods of sleep deprivation also cause muscle pain, perpetuate fatigue and headache (particularly migraine), and increases pain sensitivity and psychological distress—even in otherwise well people (Moldofsky, 2015), Enkvist et al. (2023) studied sleep disturbance over a 3-year period and observed higher levels of somatic symptoms, stress, 'burnout', anxiety and depression in participants with sleep disturbance. They found that chronicity of sleep problems was generally associated with stronger relationships between poor mental health and functional somatic syndromes (including fibromyalgia, IBS and migraine).

Our findings align with other reports (Andrade et al., 2020; Lima et al., 2023) where pain, and increased severity of pain and other symptoms (including fatigue, depression, anxiety and cognitive problems), were strongly associated with poor quality sleep.

Overall sleep quality has also been demonstrated to consistently predict next-day pain (Kothari et al., 2015; Tang et al., 2012), and Bigatti et al. (2008) demonstrated that onset of sleep disturbance is predictive of pain. When chronic, this initiates a cascade of consequences, resulting in mood disturbance. Other studies have demonstrated that reductions in quality and quantity of sleep are associated with a 2-3-fold increase in risk of developing a pain-related condition, with worse pain outcomes over time (Afolalu et al., 2018).

Insomnia is associated with increased central sensitization and pain catastrophizing in people without fibromyalgia (Husak & Bair, 2020), which is an interesting

consideration in view of the current thinking around central sensitization as a key component of fibromyalgia (Cohen, 2017).

Together, it appears that sleep is likely a major contributing—and ultimately modifiable—factor in the pain-fatigue-obesity-depression-pain cycle in people with fibromyalgia. Strategies to improve and monitor sleep quality deserve a stronger focus in this condition.

4.3 | Mental health

Almost one-third of our cohort met criteria for depression and 40% met anxiety disorder criteria. These results are lower than reported by Wolfe et al. (2013) using the same assessment tools in a German cohort with fibromyalgia (63.5% and 50%, respectively).

Depression and anxiety were significantly associated with pain, as evaluated by the SF36. This was not seen for the WPI.

Severity of the functional bowel disorders (but not prevalence of the disorders themselves) was associated with prevalence of anxiety and overall mental health as calculated by the SF36. Three specific DGBI (post-prandial distress syndrome, rumination syndrome and proctalgia fugax) were associated with anxiety, while none were associated with depression.

Relationships between sleep difficulties, depression and pain in people with fibromyalgia are well established (Bigatti et al., 2008), thus the strong associations seen here are not unexpected. Independent of fibromyalgia, sleep disturbance has recently emerged as a likely factor mediating the depression–pain relationship (Karimi et al., 2023), with insomnia predictive of depression developing within 1–3 years (Riemann, 2003). Its relationship with chronic pain aside, impaired quality of sleep is a known risk factor for poor mental health (Enkvist et al., 2023), with more severe depression, anxiety (Husak & Bair, 2020) and increased rates of suicidal ideation (Varallo et al., 2023) all associated with sleep problems.

4.4 | Limitations

Several limitations in the study warrant comment. The survey data are all self-reported, and while this has the potential to introduce bias, the tools used were validated for gathering self-reported data. There is currently a deficit of clinically applicable biomarkers for fibromyalgia (Warren & Clauw, 2012) to which more attention is required. While objective measures would strengthen the confidence of the associations reported here and enhance the robustness of data, studies have shown that physician diagnosis of fibromyalgia is also heavily influenced by bias (Walitt et al., 2016). Similarly, as a diagnosis of a DGBI is generally reached by exclusion, with notable cost implications to rule out organic digestive disorders (Camilleri & Yang, 2024), the Rome IV survey is considered robust for self-report (Sperber et al., 2021). There is potential for multiple confounders in a study such as this, including physical activity, marital status, number and types of medications, dietary supplement use, and so on, which we did not attempt to control for. Our study only included women living in NZ, measured at a single time-point, and may not be generalizable to men, or to those living elsewhere. This limitation would be well-addressed in larger, multi-centred studies, designed to include a broader demographic population. Associations and correlations observed between the clinical features do not imply causal relationships, which would only be possible through experimental manipulation of the variables or by undertaking a prospective longitudinal study to determine the interaction of these associations.

4.5 | Conclusion

This study provides new insights to the interconnectedness of the severity of key symptoms of women living with fibromyalgia and the burden of gastrointestinal dysfunction. In addition to chronic nociplastic pain, the relationship of gastrointestinal dysfunction with other clinical features, particularly sleep disturbance, migraine and overall quality of life, are noteworthy. Clinicians working with fibromyalgia patients are encouraged to explore beyond the presenting pain and adopt a holistic approach to the assessment and management of this multifaceted condition. Continued exploration of putative mechanisms linking these pain hypersensitization disorders in the research setting is of paramount importance. Future research should build on these findings, with a view to developing integrative approaches to improve patient outcomes.

AUTHOR CONTRIBUTIONS

This study was designed by S.E. and J.E.H. Data collection and analysis were performed by S.E. The first draft of the manuscript was written by S.E., and J.E.H. edited and contributed to subsequent drafts. Both authors read and approved the final version of the manuscript and agreed to be accountable for all aspects of the work.

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CONFLICT OF INTEREST STATEMENT

Neither Sharon Erdrich nor Joanna Harnett has any financial disclosures or conflicts of interest to declare.

ORCID

Sharon Erdrich https://orcid.org/0000-0002-8448-5644
Joanna E. Harnett https://orcid.org/0000-0001-9904-2144

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