The association of sleep difficulties with health-related quality of life among patients with fibromyalgia

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Abstract

Background: Difficulty sleeping is common among patients with fibromyalgia (FM); however, its impact on health-related quality of life (HRQoL) is not well understood. The aim of the current study was to assess the burden of sleep difficulty symptoms on HRQoL among patients with FM.

Methods: The current study included data from the 2009 National Health and Wellness Survey (N=75,000), which is a cross-sectional, Internet-based survey representative of the adult US population. The prevalence of sleep difficulty symptoms among patients with FM (n=2,196) were compared with matched controls (n=2,194), identified using propensity-score matching. Additionally, the relationship between the number of sleep difficulty symptoms (none, one, or two or more) and HRQoL (using the SF-12v2) was assessed using regression modeling, controlling for demographic and health history variables.

Results: Of the 2,196 patients with FM, 11.2% reported no sleep difficulty symptoms, 25.7% reported one sleep difficulty symptom, and 63.05% reported two or more sleep difficulty symptoms. The prevalence of sleep difficulty symptoms was significantly higher than matched controls. Patients with one and two sleep difficulty symptoms both reported significantly worse HRQoL summary and domain scores relative to those with no sleep difficulty symptoms (all p<.05). Further, the relationship between sleep difficulty symptoms and HRQoL was significantly different between those with FM than matched controls, suggesting a uniqueness of the burden of sleep difficulties within the FM population.

Conclusions: Among the FM population, sleep difficulty symptoms were independently associated with clinically-meaningful decrements in mental and physical HRQoL. These results suggest that greater emphasis in the treatment of sleep difficulty symptoms among the FM population may be warranted.

Keywords: Fibromyalgia, Sleep, Insomnia, Health-related quality of life, Pain

Background

Fibromyalgia (FM) is a chronic disorder characterized by widespread pain of the muscle and connective tissues, and pain in response to touch or pressure [1]. Often accompanied by non-specific symptoms, such as fatigue, depressive mood, and sleep difficulties [2], FM affects approximately 5 million Americans [3]. As it largely affects a working-age population, and is associated with increased resource use and disability, FM is responsible for substantial societal costs. Indeed, prior research on managed care patients with FM found an average of $10,911 (standard deviation = $16,860) in healthcare expenses per patient per year during 2001–2004 [4]. Moreover, patients with FM reported short-term disability at a greater rate than patients with rheumatoid arthritis (20% vs. 15% reported any short-term leave) [4]. Costs also increase with severity, with patients with severe symptoms reporting more than three times the costs of patients with mild symptoms [5].

The societal impact of FM is not limited to economic costs, however. Patients report that FM symptoms substantially impact their quality of life by disrupting
relationships, causing social isolation, reducing productivity in activities of daily living, and complicating physical activity [6]. In a recent review of 37 studies, Hoffman & Dukes found patients with FM report mental health-related quality of life (HRQoL) scores 1 standard deviation below the United States (US) population mean and physical HRQoL scores 2 standard deviations below the US population mean [7]. In fact, HRQoL among patients with FM have been found to be similar to or worse than patients with rheumatoid arthritis [8] and other pain conditions [7].

Patients with FM have been found to be significantly more likely to experience difficulties initiating or maintaining sleep than controls (OR=4.56, 95% CI: 4.10-5.06) [9]. In particular, previous studies have identified difficulty falling asleep, staying asleep and waking up too early in the morning as the most common sleep-related symptoms among the FM population [9-12]. Such sleep difficulties have been associated with negative affect and mood, and pain, which, in turn, have been associated with decrements in physical functioning [13-16]. Moreover, in qualitative interviews, patients with FM have reported that sleep disturbances substantially affect their quality of life [5,17]. However, few studies have assessed the direct association of sleep difficulties with decrements in HRQoL among this patient population.

There were several aims of the current study. One aim was to determine the prevalence of sleep difficulty symptoms among those with FM in comparison with those without FM. The second aim was to examine which demographic and health history variables were significantly associated with the presence of these sleep difficulty symptoms. Lastly, the third aim was to examine the relationship between these sleep difficulty symptoms and HRQoL among patients with FM and determine whether these relationships differed from a non-FM control sample.

**Methods**

**Data source**

Data were obtained from the 2009 wave (N=75,000) of the US National Health and Wellness Survey. The NHWS is an annual, cross-sectional, Internet-based survey administered to a sample of adults (18 years and older) identified through a web-based panel. Members of the panel are recruited through emails, Internet newsletter campaigns, website banner placements, and registration with panel partners. All panel members agreed to become panel members and registered through unique email addresses. Of 501,239 persons contacted to participate in the 2009 NHWS, 92,759 responded (an 18.5% response rate). Of those who responded, 75,000 gave their informed consent, met the inclusion criteria (aged 18 or over), and completed the survey instrument. To mimic the demographic composition of the US general population, a stratified random sampling procedure was implemented when recruiting participants for the NHWS. The NHWS sample, US census, and other national surveys have been compared elsewhere [18]. Institutional review board approval for the 2009 US NHWS was granted by Essex IRB (Lebanon, NJ).

**Sample**

All respondents to the 2009 US NHWS were included in the analysis (N=75,000).

**Measures**

**Sleep difficulties**

Although no sleep scale was included in the NHWS, all respondents were asked whether they experienced difficulty falling asleep, difficulty staying asleep, or waking up too early (the response options for each item were either yes or no). These items, which have been shown to be the most common characteristics of sleep difficulties among patients with FM [9-12], were used to operationally define the presence of sleep difficulties. Severity of sleep difficulties was established based on the number of sleep difficulty symptoms reported (see Table 1). Similar operationalizations have been used elsewhere [9,19]. The primary independent variable was a three-level mutually exclusive group variable: no sleep difficulty symptoms, one sleep difficulty symptom, and two or more sleep difficulty symptoms.

### Table 1 Criteria for establishing the presence of sleep difficulties in patients

| No sleep difficulty symptoms | One sleep difficulty symptom | Two or more sleep difficulty symptoms |
|------------------------------|------------------------------|---------------------------------------|
| Reporting none of the following: | Reporting one of the following: | Reporting two or more of the following: |
| • Difficulty falling asleep | • Difficulty falling asleep | • Difficulty falling asleep |
| • Difficulty staying asleep | • Difficulty staying asleep | • Difficulty staying asleep |
| • Waking too early | • Waking too early | • Waking too early |
| • Insomnia | | |
| • Sleep difficulties (any) | | |

**FM**

All respondents in the NHWS were presented with a list of medical conditions and asked to select which ones they had ever experienced ("which of the following..."
conditions have you ever experienced?"). FM (presented as “fibromyalgia” to respondents) was included in this list. All respondents who selected FM were subsequently asked “has your fibromyalgia been diagnosed by a physician?”, with yes/no response options. Only respondents who reported a diagnosis of FM were considered to have FM for the purposes of this study and the remaining respondents were considered controls.

Demographic and health history variables
Age, race/ethnicity (non-Hispanic white, non-Hispanic black, Hispanic, or other race/ethnicity), marital status (married/living with partner versus all else), education (high school graduate or less versus some college or higher), annual household income ($25K or less, $25K to <$50K, $50K to <$75K, $75K or more, or decline to answer), employment (full-time, part-time, self-employed, not employed and not looking for work, not employed but looking for work, on disability, retired, student, or homemaker), health insurance (yes versus no), exercise (no days with 20 minutes or more of exercise in the past month, 1–9 days, or 10 or more days), smoking habits (current smoker versus non-smoker), alcohol consumption (consume alcohol versus abstain from alcohol), body mass index (BMI; underweight, normal weight, overweight, obese, or decline to provide weight), and comorbidity burden (using the Charlson Comorbidity Index; CCI index (BMI; underweight, normal weight, overweight, obese, or decline to provide weight), and comorbidity burden (using the Charlson Comorbidity Index; CCI index (using summary and domain scores of the SF-12 onto the number of sleep difficulty symptoms (none, one, or two or more) among patients with FM. These models were conducted using linear regression for complex survey designs (PROC SURVEYREG in SAS v9.1). For the sake of parsimony, only covariates which differed among the groups were included in the model: age, smoking status (non-smoker served as the reference category), pain severity (no pain served as the reference category), and pain frequency (no pain served as the reference category).

The fourth component of the analysis was a comparison of the relationship of sleep difficulty symptoms and pain with FM and matched controls. This was accomplished by entering the case variable (diagnosed FM versus matched control), number of sleep symptoms (none, one, and two or more), and the interaction term into a linear regression model (PROC SURVEYREG) for each summary and domain score. Effects coding was used for all variables. This model tested the main effect (i.e., whether HRQoL was different between those with FM and matched controls) as well as the interaction (i.e., whether the relationship between the number of sleep symptoms and HRQoL differed between patients with FM and matched controls).

All analyses applied sampling weights from the NHWS. Although raw sample sizes are provided in many cases, all other statistical information (unless otherwise specified) were weighted to project to the population. Analyses were conducted using SAS v9.1 (Cary, NC) and statistical significance was set at p<.05.
Results

Frequency of sleep difficulty symptoms
A total of 2,196 patients in the NHWS reported diagnosis of FM (2.81%). Of these, 269 (11.2%) reported no sleep difficulty symptoms, 574 (25.7%) reported one sleep difficulty symptom, and 1353 (63.05%) reported two or more sleep difficulty symptoms. The prevalence of sleep difficulty symptoms was significantly higher when compared with those without FM (none: 40.7%; one: 29.0%; two or more: 30.3%; p<.0001). Indeed, even when comparing patients with FM with matched controls (those matched on age, sex, ethnicity, and comorbidities), the prevalence of sleep difficulty symptoms was significantly higher (none: 11.2% vs. 32.9% for FM and matched control patients, respectively; one: 25.7% vs. 28.22%, respectively; two or more: 63.1% vs. 38.9%, respectively; p<.0001).

Demographic and health history comparisons
Among patients with FM, few demographic and health history variables were related to the number of sleep symptoms experienced (see Table 2). Patients with FM who reported sleep difficulties were younger, less likely to be retired and possess health insurance, and more likely to be on disability and to currently smoke. Levels of severe pain increased concomitantly with the number of sleep symptoms (19.08% vs. 30.77% vs. 43.26% for those with none, one, and two sleep difficulty symptoms, respectively). Similarly, reports of daily pain also increased along with the number of sleep difficulty symptoms (49.21% vs. 59.67% vs. 70.88%).

Association of sleep difficulty symptoms and health-related quality of life
The distributions of all HRQoL summary and domain scores for those with FM are presented in Table 3. Linear regressions were conducted to determine the relationship between the number of sleep difficulty symptoms and HRQoL among those with FM (see Table 4). For all summary and domain scores, the experience of sleep difficulty symptoms was associated with a significant decrement relative to those without any sleep difficulty symptoms. In the case of the normed mental and physical component summary scores, the effects of both one (b’s: -2.79 and -2.42, respectively) and two sleep difficulty symptoms (b’s: -3.91 and -2.84, respectively) approached or exceeded clinically-relevant thresholds (i.e., 3 points).

Similarly, decrements in health utility values (b = -0.04 and -0.05 for one and two sleep difficulty symptoms, respectively) were also above clinically-relevant thresholds (i.e., 0.03 points). The SF-12 domain scores for those with one sleep difficulty symptom were equally affected (generally speaking) compared with those with no sleep difficulty symptoms (b’s ranged from -4.37 to -9.49); similarly, the SF-12 domain scores for those with two sleep difficulty symptoms were also equally affected compared with those with no sleep difficulty symptoms (b’s ranged from -6.64 to -10.84).

Additional models were then conducted to determine whether the relationship between sleep difficulty symptoms and HRQoL was different among those with FM than a similar cohort without FM. When compared with matched controls, patients with FM reported significantly worse HRQoL across all summary and domain scores of the SF-12 (i.e., “main effects”; see Table 5; all p<.0001).

However, the relationships between the number of sleep difficulty symptoms and HRQoL was significantly stronger among those with FM. In other words, significant interactions were observed for all summary and domain scores (with the exception of emotional role limitations). In most cases, the decrement between no sleep difficulty symptoms and one sleep difficulty symptom was larger among those patients with FM; conversely, the quality of life decrement between one and two or more sleep difficulty symptoms was larger among matched controls.

Discussion

The objective of the current study was to assess the impact of sleep difficulties on HRQoL among patients with FM. Despite the research on the sleep-related symptoms experienced by those with FM, no study to our knowledge has examined the relationship of these symptoms with HRQoL, especially in comparison with a matched control group. Our results suggest sleep difficulties are pervasive among the FM population, as over 88% of patients reported some level of sleep difficulties, as defined by experiencing either difficulty falling asleep, difficulty staying asleep, or waking up too early. Nearly 63% of patients with FM reported experiencing at least two of the above symptoms. These figures were significantly higher than those without FM, even those matched with FM patients.

Replicating past literature, our sample of patients with FM reported significant decrements in both MCS (41.49) and PCS (31.29) scores relative to population norms (50 and 50, respectively). Indeed, the one and two standard deviation differences, respectively, in MCS and PCS compared with the population mean is nearly identical to the results reported by previous literature [6,7]. On an absolute level, these levels of HRQoL are worse than reported in the same survey for patients with severe osteoarthritis, chronic obstructive pulmonary disease, atrial fibrillation, hepatitis C, arthritis, and back pain, among others [24-28]. However, our findings suggest that the presence of sleep difficulties poses an additional burden on patients with FM. Our results suggest that sleep difficulty symptoms has an independent, and significant, clinically-meaningful effect on
Table 2 Demographic and health history differences associated with the number of sleep difficulty symptoms among patients with fibromyalgia

| Variable                        | No sleep symptoms (n=269) | One sleep symptom (n=574) | Two or more sleep symptoms (n=1353) |   |
|---------------------------------|---------------------------|---------------------------|-------------------------------------|---|
|                                 | n | Weighted n | Weighted % | SE | n | Weighted n | Weighted % | SE | n | Weighted n | Weighted % | SE | p  |
| Male                            | 42 | 100791 | 14.27% | 2.24% | 109 | 291061 | 17.96% | 1.71% | 204 | 595728 | 15.01% | 1.08% | 0.2813 |
| Race/ethnicity                  |   |           |           |     |   |           |           |     |   |           |           |     | 0.0701 |
| Non-Hispanic white              | 231 | 579865 | 82.11% | 2.72% | 480 | 1297016 | 80.03% | 1.93% | 1096 | 3060560 | 77.12% | 1.34% |           |
| Non-Hispanic black              | 16 | 44654 | 6.32% | 1.55% | 36 | 95814 | 5.91% | 0.97% | 80 | 207978 | 5.24% | 0.58% |           |
| Hispanic                        | 12 | 51952 | 7.36% | 2.08% | 34 | 160905 | 9.93% | 1.63% | 82 | 396647 | 9.99% | 1.06% |           |
| Other                           | 10 | 29762 | 4.21% | 1.34% | 24 | 66882 | 4.13% | 0.86% | 95 | 303503 | 7.65% | 0.86% |           |
| Greater than high school education | 205 | 548338 | 77.64% | 2.86% | 445 | 1254870 | 77.43% | 1.89% | 1041 | 3115084 | 78.49% | 1.17% | 0.8776 |
| Annual household income         |   |           |           |     |   |           |           |     |   |           |           |     | 0.0906 |
| <$25K                           | 67 | 164262 | 23.26% | 2.91% | 157 | 453920 | 28.01% | 2.06% | 405 | 1194941 | 30.11% | 1.35% |           |
| $25K to <$50K                   | 75 | 209604 | 29.68% | 3.2% | 162 | 450214 | 27.78% | 2.04% | 431 | 1254027 | 31.60% | 1.37% |           |
| $50K to <$75K                   | 59 | 161650 | 22.89% | 2.87% | 125 | 329591 | 20.34% | 1.75% | 234 | 691354 | 17.42% | 1.08% |           |
| $75K or more                    | 47 | 128776 | 18.23% | 2.65% | 100 | 294962 | 18.20% | 1.74% | 228 | 687512 | 17.32% | 1.1% |           |
| Decline to answer               | 21 | 41942 | 5.94% | 1.4% | 30 | 91929 | 5.67% | 1.09% | 55 | 140853 | 5.35% | 0.83% |           |
| Employment                      |   |           |           |     |   |           |           |     |   |           |           |     | <.0001 |
| Full-time                       | 40 | 129881 | 18.39% | 2.69% | 96 | 302795 | 18.68% | 1.78% | 204 | 637364 | 16.06% | 1.06% |           |
| Part-time                       | 21 | 56486 | 8.00% | 1.76% | 58 | 161415 | 9.96% | 1.31% | 132 | 379165 | 9.55% | 0.83% |           |
| Self-employed                   | 17 | 46951 | 6.65% | 1.62% | 30 | 85771 | 5.29% | 0.99% | 81 | 248640 | 6.27% | 0.69% |           |
| Unemployed, looking for work    | 12 | 32426 | 4.59% | 1.35% | 22 | 59646 | 3.68% | 0.8% | 75 | 231083 | 5.82% | 0.68% |           |
| Unemployed, not looking         | 2 | 4421 | 0.63% | 0.48% | 15 | 43845 | 2.71% | 0.7% | 63 | 186145 | 4.69% | 0.59% |           |
| Retired                         | 114 | 258239 | 36.57% | 3.39% | 160 | 391288 | 24.14% | 2.02% | 283 | 715123 | 18.02% | 1.22% |           |
| Disability                      | 40 | 116650 | 16.52% | 2.46% | 133 | 394200 | 24.32% | 1.89% | 379 | 1154974 | 29.10% | 1.31% |           |
| Student                         | 1 | 2271 | 0.32% | 0.32% | 6 | 21302 | 1.31% | 0.56% | 15 | 47148 | 1.19% | 0.31% |           |
| Homemaker                       | 22 | 58909 | 8.34% | 1.81% | 54 | 160354 | 9.89% | 1.34% | 121 | 360946 | 9.30% | 0.83% |           |
| Married/living with partner     | 162 | 420899 | 59.60% | 3.41% | 353 | 968068 | 59.73% | 2.26% | 816 | 2426243 | 61.13% | 1.43% | 0.8299 |
| Possess health insurance        | 252 | 651206 | 92.21% | 1.84% | 517 | 1448371 | 89.37% | 1.38% | 1181 | 3433135 | 86.51% | 0.98% | 0.0153 |
| Exercise behavior               |   |           |           |     |   |           |           |     |   |           |           |     | 0.0624 |
| None in past month              | 118 | 297414 | 42.11% | 3.38% | 265 | 709114 | 43.76% | 2.24% | 674 | 1954071 | 49.24% | 1.46% |           |
| 1-9 days exercise in past month | 59 | 167526 | 23.72% | 2.97% | 157 | 456390 | 28.16% | 2.05% | 306 | 938221 | 23.64% | 1.29% |           |
| 10+ days exercise in past month | 92 | 241295 | 34.17% | 3.25% | 152 | 455112 | 28.08% | 2.06% | 373 | 1076395 | 27.12% | 1.28% |           |
| Alcohol use                     | 140 | 367023 | 51.97% | 3.44% | 299 | 835869 | 51.58% | 2.27% | 672 | 1991970 | 50.19% | 1.46% | 0.8168 |
| Current smoker                  | 58 | 163896 | 23.21% | 2.95% | 171 | 515809 | 31.83% | 2.11% | 405 | 1227589 | 30.93% | 1.34% | 0.0405 |
| Body mass index                 |   |           |           |     |   |           |           |     |   |           |           |     | 0.1211 |
### Table 2 Demographic and health history differences associated with the number of sleep difficulty symptoms among patients with fibromyalgia (Continued)

| Weight Category        | No Pain     | Pain Frequency | Pain Severity |
|-----------------------|-------------|----------------|---------------|
| Underweight           | 9180        | 1.30%          | 3.57          |
| Normal                | 144538      | 20.47%         | 41.07         |
| Overweight            | 208488      | 29.52%         | 42.98%        |
| Obese                 | 309173      | 43.78%         | 49.30%        |
| Decline to answer weight | 34856  | 4.94%          | 52824         |

| Pain severity         | No pain     | Daily pain     | Moderate pain |
|-----------------------|-------------|----------------|---------------|
| No pain               | 217295      | 347542         | 113            |
| Mild pain             | 32456       | 44232          | 113            |
| Moderate pain         | 295400      | 44232          | 113            |
| Severe pain           | 134783      | 44232          | 113            |
| Missing severity      | 26300       | 44232          | 113            |

| Pain frequency        | No pain     | Daily pain     | Weekly pain   |
|-----------------------|-------------|----------------|---------------|
| No pain               | 217295      | 347542         | 6227          |
| Daily pain            | 140         | 44232          | 27264         |
| 4-6 days per week     | 11852       | 11852          | 27264         |
| 2-3 days per week     | 37374       | 37374          | 37374         |
| Weekly pain           | 2           | 6227           | 27264         |
| 2-3 days per month or less | 9     | 27264          | 27264         |

| Missing frequency     | 26300       | 44232          | 13782         |

| Mean Weighted Mean SE | Mean Weighted Mean SE | Mean Weighted Mean SE | p  |
|-----------------------|-----------------------|-----------------------|----|
| Age                   | 57.56                 | 56.04                 | 1.07 | 53.36 | 51.90 | 0.7 | 52.47 | 51.63 | 0.39 | 0.0006 |
| Charlson comorbidity index | 1.1        | 1.11             | 0.11 | 1.3 | 1.34 | 0.13 | 1.18 | 1.17 | 0.05 | 0.3475 |

### Table 3 Descriptive statistics of summary and domain scores of the SF-12 among patients with fibromyalgia

| Summary scores          | Min | % at Min | Q1 | Median | Mean | Q3 | Max | % at Max |
|-------------------------|-----|----------|----|--------|------|----|-----|----------|
| Mental component summary| 3.57| 0.05%    | 31.98| 41.07  | 41.49| 51.22| 71.53| 0.05%    |
| Physical component summary| 7.25| 0.05%    | 23.99| 31.29  | 31.29| 39.88| 63.16| 0.05%    |
| Health utilities        | 0.35| 1.50%    | 0.49 | 0.57   | 0.57 | 0.64 | 1.00 | 0.23%    |

| Domain scores          | Bodily pain* | General health* | Vitality* | Social functioning* | Mental health** | Emotional role limitations** | Physical role limitations** | Physical functioning* |
|------------------------|--------------|-----------------|-----------|---------------------|-----------------|-----------------------------|---------------------------|----------------------|
| Min                    | 0.00         | 0.00            | 0.00      | 0.00                | 0.00            | 0.00                        | 0.00                      | 0.00                 |
| % at Min               | 20.49%       | 13.34%          | 30.78%    | 12.66%              | 2.73%           | 8.24%                       | 21.04%                    | 29.96%               |
| Q1                     | 25.00        | 25.00           | 25.00     | 25.00               | 37.50           | 37.50                       | 12.50                     | 0.00                 |
| Median                 | 25.00        | 25.00           | 25.00     | 25.00               | 50.00           | 50.00                       | 25.00                     | 25.00               |
| Mean                   | 50.00        | 60.00           | 50.00     | 50.00               | 75.00           | 87.50                       | 50.00                     | 50.00               |
| Q3                     | 100.00       | 100.00          | 100.00    | 100.00              | 100.00          | 100.00                      | 100.00                    | 100.00              |
| % at Max               | 2.41%        | 1.55%           | 1.14%     | 1.82%               | 13.93%          | 21.36%                      | 4.74%                     | 10.75%               |

*Note these domains scores from the SF-12 are based only on a five-point range (0, 25, 50, 75, 100).

**Note these domains scores from the SF-12 are based only on a 9-point range (0, 12.5, 25, 37.5, 50, 62.5, 75, 87.5, 100).
HRQoL among the FM population. Past research has suggested a three-point between-groups difference in MCS and PCS is often associated with a clinically-meaningful difference [21]. The comparison between one sleep difficulty symptom and no sleep difficulty symptoms approached this threshold while the comparison between two sleep difficulty symptoms and no sleep difficulty symptoms exceeded it, even after adjusting for confounding variables.

It is particularly important to note that these models controlled for pain severity and frequency. Naturally, severe pain and frequent pain (as confirmed in Table 2) would be expected to have a significant effect on sleep symptoms, as also demonstrated in prior research [14,16,20,22]. Yet, even accounting for the higher prevalence of pain severity and frequency among those with more sleep difficulty symptoms, worse HRQoL summary and domain scores were observed. This suggests that

| Dependent variable | No symptoms (reference) | One symptom | Two or more symptoms |
|--------------------|--------------------------|-------------|----------------------|
| Mental component summary | b = -2.786 | -3.905 |
| 95% CL | (-4.448, -1.124) | (-5.461, -2.35) |
| R² | 0.174 |
| Physical component summary | b = -2.415 | -2.835 |
| 95% CL | (-4.144, -0.686) | (-4.467, -1.202) |
| R² | 0.241 |
| Health utilities | b = -0.041 | -0.064 |
| 95% CL | (-0.06, -0.022) | (-0.072, -0.035) |
| R² | 0.284 |
| Bodily pain | b = -5.770 | -8.555 |
| 95% CL | (-9.729, -1.811) | (-12.239, -4.87) |
| R² | 0.312 |
| General health | b = -6.349 | -8.411 |
| 95% CL | (-10.358, -2.34) | (-12.222, -4.66) |
| R² | 0.153 |
| Vitality | b = -5.943 | -6.637 |
| 95% CL | (-9.994, -1.893) | (-10.447, -2.827) |
| R² | 0.097 |
| Social functioning | b = -7.327 | -10.838 |
| 95% CL | (-11.741, -2.913) | (-14.906, -6.771) |
| R² | 0.205 |
| Mental health | b = -4.366 | -8.658 |
| 95% CL | (-7.71, -1.021) | (-11.805, -5.511) |
| R² | 0.184 |
| Emotional role limitations | b = -8.094 | -7.546 |
| 95% CL | (-12.802, -3.387) | (-11.847, -3.245) |
| R² | 0.120 |
| Physical role limitations | b = -9.485 | -10.416 |
| 95% CL | (-14.043, -4.928) | (-14.683, -6.148) |
| R² | 0.194 |
| Physical functioning | b = -6.015 | -6.915 |
| 95% CL | (-11.315, -0.715) | (-11.867, -1.963) |
| R² | 0.177 |

Regression coefficients represent the difference in HRQoL for those with one and two symptoms relative to those without any (e.g., those with one symptom and two or more symptoms reported mental component summary scores 2.786 and 3.905 points less, respectively, than those without symptoms). All models controlled for age, smoking status, pain severity, and pain frequency.
sleep difficulties have an independent effect on HRQoL among those with FM, beyond any potential effect of the pain experience.

Also noteworthy was that the relationship between sleep difficulties and HRQoL varied between those with FM and matched controls. In many cases, the introduction of a single sleep difficulty symptom was associated with a larger decrement in HRQoL among patients with FM, however, the introduction in a second sleep difficulty symptom was associated with larger decrement in HRQoL among matched controls. Further research may be necessary to ascertain the cause of the discrepancy.

One possibility is that sleep difficulties are generally more burdensome for patients with FM, however, given the nature of the disease, a floor effect is reached upon the introduction of the second sleep difficulty symptom. In other words, patients with FM are so burdened already by their condition that the introduction of an additional sleep difficulty symptom does not affect their HRQoL as much as it would a patient without FM. Regardless, our preliminary evidence suggests that the pattern of the relationship between sleep difficulty symptoms and HRQoL is unique among those with FM.

The effect of sleep difficulty symptoms extended beyond HRQoL. In unadjusted comparisons, patients who reported sleep difficulties showed higher rates of disability than those without sleep difficulties. Although beyond the scope of the present analysis, the effect of sleep difficulties on participation in the labor force and productivity at work may also need to be considered in future research.

In sum, the results suggest patients with FM experience considerable difficulty initiating and maintaining sleep. The presence of these sleep difficulty symptoms have a significant and clinically-meaningful impact on HRQoL, even after accounting for a range of confounding variables. The study results suggest the improved management of these sleep difficulty symptoms among patients with FM may lead to clinically-relevant improvements in HRQoL. The alleviation of pain could have an important effect of improving sleep, but more research would be necessary to establish this causal pathway. Indeed, the relationship between pain and sleep does appear bidirectional [29]. Of course, since the effect of sleep difficulty symptoms on HRQoL was observed even after controlling for pain, the management of sleep difficulties likely extends beyond the mere alleviation of pain.

Limitations
Several limitations should be noted from the results of this study. Given the cross-sectional design of the study, the causal inference cannot be determined. Although alternative
explanations have been included (such as comorbidities and, demographic confounders), it is possible other unmeasured variables might explain the relationship between sleep difficulties and HRQoL. Because of the self-reported nature, recall bias may have introduced additional error into the observed associations. As described before, the sleep difficulty groups were not defined by a sleep scale but rather using three symptoms of initiating and maintaining sleep to operationalize sleep difficulty severity. It should also be emphasized that although the NHWS is demographically representative of the US population, the sample in the current study of FM patients may differ with respect to healthcare attitudes or healthcare engagement (among other variables) that could affect the size and direction of the relationships observed here.

Conclusions
Sleep difficulties were found to have significant and clinically meaningful deleterious effects on HRQoL among the FM population. Effective treatment of sleep difficulties may improve HRQoL among the FM population.

Abbreviations
FM: Fibromyalgia; SD: Standard deviation; HRQoL: Health-related quality of life; US: United States; NHWS: National Health and Wellness Survey; IRB: Institutional review board; BMI: Body mass index; CCI: Charlson comorbidity index; SF: Short Form; MCS: Mental component summary; PCS: Physical component summary.

Competing interests
This study was conducted by Kantar Health on behalf of Pfizer Inc, which funded the study. JSW and MD are full-time employees of Kantar Health who were paid consultants to Pfizer in connection with the analysis and the development of this manuscript. AC and JCC are full-time employees of Pfizer, Inc.

Authors' contributions
JSW participated in the design, coordination, and analysis of the study, and drafted the manuscript. MD was engaged in the conception and design of the study and participated in the manuscript's drafting and editing. AC was involved in the conception, design, and coordination, of the study, and critically evaluated and provided input to the manuscript. JCC was involved in the design of the study, provided oversight on the analyses, critically evaluated and provided input to the manuscript. All authors read and approved the final manuscript.

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