Pain Duration and Intensity Are Related to Coexisting Pain and Comorbidities Present in Temporomandibular Disorder Pain Patients

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Aims: To investigate the relationships between three pain parameters (duration, intensity, and frequency), the number of pain sites and comorbidities, and the risk of having coexisting pain and/or comorbidities in patients with temporomandibular disorder (TMD) pain. **Methods:** The sample consisted of 198 outpatients attending the Dental Hospital of Chulalongkorn University. TMD pain was determined using the Diagnostic Criteria for TMD. Pain lasting 3 months or longer was defined as chronic pain. Pain intensity was reflected using a 0- to 10-point numeric rating scale, and pain frequency was assessed with the percentage of pain days over a 2-week period. The number of pain sites was evaluated using the Widespread Pain Index. The presence of comorbidities was assessed with a validated diagnostic questionnaire. The associations were analyzed using Spearman rho test, multiple linear regression, and logistic regression, with a significance level of $P \leq .05$. Age and gender were analyzed as confounders. **Results:** The number of pain sites was related to pain duration, pain intensity, and age. The number of comorbidities was associated with pain duration. Neither pain frequency nor gender were related to the number of pain sites or comorbidities. When the pain duration reached 1 month, patients had a 1.045-times higher probability of pain beyond the orofacial area (odds ratio [OR] = 1.045; 95% confidence interval [CI] = 1.024 to 1.066; $P = .001$) and a 1.028-times higher probability of comorbidities (OR = 1.028; 95% CI = 1.005 to 1.05; $P = .008$). For an increase of 1 score on the numeric rating scale, patients had a 1.206-times higher probability of pain presence beyond the orofacial area (OR = 1.206; 95% CI = 1.068 to 1.344; $P = .026$). **Conclusion:** High pain intensity and long pain duration increase the probability of having coexisting pain and comorbidities in TMD pain patients. *J Oral Facial Pain Headache 2019;33:205–212. doi: 10.11607/ofph.2088*

Keywords: *comorbidities, pain parameters, questionnaires, regression analysis, TMD pain*

Temporomandibular disorders (TMD) involve several musculoskeletal problems in the masticatory structures and related tissues.[1] The typical clinical characteristics of TMD include pain and dysfunction localized in the orofacial area[1]; however, recent studies have reported a large prevalence of overlapping health conditions in patients with TMD pain,[2] including pain developing beyond the orofacial area and/or comorbid diseases.[2,3] While the presence of coexisting pain outside the orofacial area is typically reported as a musculoskeletal pain in many other sites of the body,[3–5] the involvement of comorbid diseases is assumed to relate to the maladaptation of the central nervous system.[6] These findings have changed the perception of TMD from an orofacial disorder to a complex illness model.[2]

Of TMD pain patients in the United States, 84% reported the coexistence of TMD pain with shoulder pain, neck pain, back pain, or abdominal pain.[3,7,8] These pain sites can develop in patients who experience pain for a week.[3,9] In addition to the coexisting pain, TMD pain has been reported to be related to the presence of frequent headache, fibromyalgia, chronic fatigue syndrome, irritable bowel syndrome, interstitial cystitis, chronic low back pain, and chronic pelvic pain.[10] These comorbidities are actual diseases and are commonly reported in patients with chronic TMD pain[10]—studies from the United States and Sweden

report that approximately 70% of patients with chronic TMD pain have at least one comorbidity.[11]

Coexisting pain conditions and comorbidities share a similarity: they are both positively related to the duration, intensity, and frequency of the TMD pain.[11–15] Thus, the progression of coexisting pain and comorbidities in TMD patients may share the same pathophysiologic pathway.[2,16,17] So far, the most widely accepted etiology of the appearance of coexisting pain and comorbidities is central sensitization,[6,11,16,18–30] of which there are three mechanisms.[6,31] The first is the anatomico-physiologic connection of the pain pathway; the second is synaptic neuroplasticity, which occurs through long-term potentiation[20]; and the third is that the pain can activate not only the sensory cortex but also other cortical areas that control the functions of different organs[26] (for example, pain can activate the hypothalamus, which controls the heart rate—thus, when we feel pain, the pulse increases). While the first and second mechanisms explain the presence of coexisting pain, the second and third mechanisms are considered to be the cause of the relationship between chronic TMD pain and comorbidities.[20]

Because previous studies have separately evaluated three pain parameters (duration, intensity, and frequency) and their relations with comorbidities and coexisting pain, the effect of the interaction among these parameters is unknown. The present study therefore aimed to assess the prevalence of coexisting pain conditions in TMD pain patients (comprising both acute and chronic pain patients) and the prevalence of comorbidities in a group with chronic TMD pain. This study also sought to investigate the associations between the three pain parameters and the coexisting pain and comorbidities. It was hypothesized that: *(1)* In both chronic and acute TMD pain patients, the number of pain sites would be positively associated with pain duration, pain intensity, and pain frequency; and *(2)* In patients with chronic TMD, the number of comorbidities would be positively associated with the level of pain duration, pain intensity, and pain frequency. If the pain parameters proved to be related to the number of pain sites and comorbidities, the probability of spreading pain and comorbidities would then be predicted in this group of patients based on the reported pain parameters and demographic data.

Materials and Methods

Ethical approval was obtained from the Human Research Ethics Committee of the Faculty of Dentistry, Chulalongkorn University, Bangkok, Thailand (Study Protocol and Consent Form Approval number 117/2016).

Study Participants

This study was conducted in the Occlusion and Orofacial Pain Clinic at Chulalongkorn University from January 2017 to August 2017. All outpatients were interviewed and clinically examined using the Diagnostic Criteria for TMD (DC/TMD).[32] According to the DC/TMD, the patients were determined to have TMD pain if they met the following criteria: *(1)* history of pain in the orofacial area within the last 30 days; *(2)* pain modified by chewing, biting, or jaw movement; and *(3)* familiar pain, referred pain, or headache provoked by palpation of the masticatory muscle and/or joint during clinical examination. Because this study concentrated on pain, patients who had fatigue, TMJ dysfunction and abnormalities but no pain, or only tenderness to palpation were not defined as having TMD pain. The age range for inclusion was 16 to 65 years.

The exclusion criteria were self-reported known systemic diseases that had symptoms of pain (eg, orofacial neuropathic pain; autoimmune disease; cancer; diabetes mellitus; neuralgia; persistent pain after stroke, injury, or surgery; hypertension without management) and health problems that could interfere with communication (eg, communication disability, epilepsy). Eligible patients were invited to participate and were provided with a standard consent form. They were asked to complete a questionnaire assessing TMD pain parameters, a widespread pain index (WPI), and comorbidities.

Based on the definition of chronic pain by the International Association for the Study of Pain,[33] participants were divided into two groups: a chronic TMD pain group and an acute TMD pain group. Chronic TMD pain was defined as pain that lasted 3 months or longer.

Pain Parameter Measurement

Pain duration was the number of years, months, and days with pain. According to the criteria of the Graded Chronic Pain Scale (GCPS),[34] pain intensity was the mean intensity of current pain, the intensity of the worst pain, and the mean pain intensity in the past 6 months as rated on a 0- to 10-point numeric rating scale (NRS). Pain frequency was identified as the number of days patients experienced pain over a 2-week period.[35]

Widespread Pain Index

The number of pain sites was determined using the Widespread Pain Index (WPI) (the first part of the American College of Rheumatology fibromyalgia questionnaire, revised in 2016[36]). The patients were asked to mark the area where they felt pain (even at rest) on a mannequin. There were 19 areas on the mannequin, including two facial sides, the neck, two

shoulder sides, two upper arm sides, two lower arm sides, chest, abdomen, upper back, lower back, two hip or buttock sides, two upper leg sides, and two lower leg sides. To evaluate the number of pain sites beyond the orofacial area in patients, the two facial sides were excluded from the WPI; thus, the score could range from 0 to 17.

Comorbidities

Seven comorbidities were identified: fibromyalgia; chronic fatigue syndrome; irritable bowel syndrome; interstitial cystitis; frequent headache; chronic low back pain; and chronic pelvic pain. The presence of frequent headache, chronic pelvic pain, and chronic low back pain were determined using the corresponding questions on the Comprehensive Pain Symptom Questionnaire (CPSQ) (respectively: 36, 40C, 40D, 40E, and 40F; 50S; and 51A and 51C), following criteria from the studies of Chen et al. Frequent headache was diagnosed if it occurred every week for at least 3 months or every month for at least 10 months.[3,10] The presence of chronic low back pain was determined if there were at least 11 episodes of pain in the past 12 months in the relevant area.[3,10] Chronic pelvic pain was defined as recurrent or continuous pain below the umbilicus that lasted for at least 6 months.[37] The validity coefficients of the CPSQ ranged from 0.85 to 1.0 when compared to the expert interview (Ohrbach et al, unpublished data).[3,10]

To evaluate the presence of fibromyalgia, chronic fatigue syndrome, irritable bowel syndrome, and interstitial cystitis, the following validated diagnostic questionnaires were used: the American College of Rheumatology fibromyalgia questionnaire (fibromyalgia),[36] the Schedule of Fatigue and Anergia/General Physician (chronic fatigue syndrome) scale,[38] the Rome III questionnaire* (irritable bowel syndrome),[39] and the Pelvic Pain and Urgency/Frequency symptom scale (interstitial cystitis).[40,41] All four questionnaires have good sensitivity (70% to 90%) and specificity (76% to 95%).[36,38,39,41] The Thai version of the Rome III questionnaire was employed, supplied by the Rome Foundation.* Other questionnaires were translated into Thai by a Thai expert who can speak English fluently, then back-translated into English by an English native speaker who can speak Thai fluently. To validate the details in the Thai version, every back-translated version was revised with the authors of each questionnaire. The final Thai version was tested in a small group of patients to check their understanding and cultural acceptance.

Data Collection

Gender and age were recorded for all participants. The three pain parameters and WPI were evaluated in both the acute and chronic TMD groups. The seven comorbidities were determined only in the chronic TMD pain participants.

Statistical Analyses

Dependent variables were WPI and the number of comorbidities, and the independent variables were the three pain parameters. Pain duration was converted from year, month, and/or day to month to be consistent for all patients. According to the aforementioned definition of chronic pain, the pain duration variable in the chronic pain group was at least 3 months. Pain frequency was calculated as the percentage of pain days in the past 2 weeks. For the patients who had pain duration shorter than 2 weeks, the percentage of pain days out of the total pain duration was assumed to be their pain frequency.

The bivariate association between WPI or the number of comorbidities and each pain parameter was analyzed using the Spearman rank correlation coefficient. Because women tend to have a higher risk of comorbid pain than men[11] (with a 1.5:1 ratio) and elderly people are more susceptible to pain,[42] age and gender were considered possible confounders. Spearman rank bivariate correlation was used to test the relationship between WPI or the number of comorbidities with gender and age; to be considered a confounder, the level of significance had to be less than 0.25.[11] The pain parameters and confounders that had significant associations with WPI or the number of comorbidities were included in a multiple linear regression model to analyze the association between TMD pain and the dependent variables. Finally, the probability of the presence of coexisting pain and comorbidities was predicted using binary logistic regression, with the pain parameters and confounders that had associations with the number of comorbidities or WPI in the multiple linear regression model being the dependent variables. The significance level was set at $P \leq .05$. Statistical analyses were conducted with SPSS for Mac software version 22 (IBM).

Results

From January 2017 to August 2017, 496 outpatients came to the Occlusion Clinic; of these patients, 198 with TMD pain were recruited (88 chronic TMD pain, 110 acute TMD pain) (Fig 1). Patients were aged 16 to 65 years (mean ± standard deviation [SD] age was 36.6 ± 14.1 years), and 72.6% were female. Most of the participants had muscle pain; only 13.6% had no muscle pain (Table 1). Except for pain duration, data were not significantly different between the chronic and acute pain groups. The mean pain duration for the acute pain group was 0.75 ± 0.74 months and for the chronic pain group was 31.4 ± 49.2 months. The

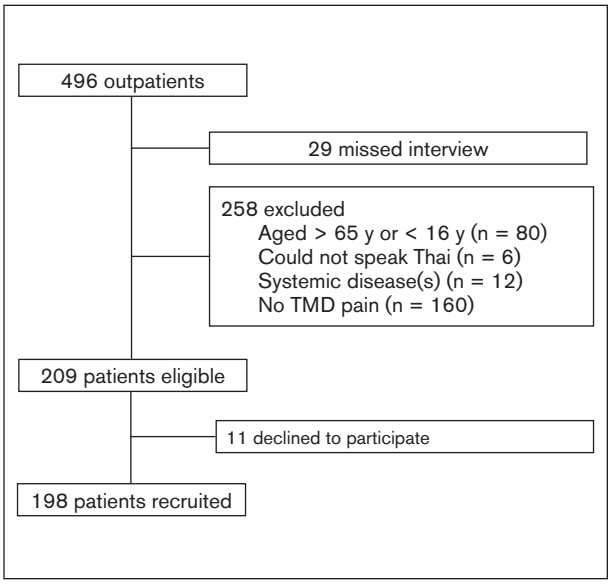

Fig 1 Flowchart of participants.

Table 1 Demographic Characteristics and Distribution by Pain Type of the Participants

	Chronic TMD pain (≥ 3 mo) (n = 88)	Acute TMD pain (< 3 mo) (n = 110)	Total (N = 198)
Age (y), mean ± SD	34.6 ± 12.6	33 ± 11.9	33.8 ± 12.2
Gender, n (%)			
Female	72 (81.8)	79 (71.8)	151 (76.3)
Male	16 (18.2)	31 (28.2)	47 (23.7)
Pain parameters			
Pain duration, mo	31.4 ± 49.2	0.75 ± 0.74	14.4 ± 5.6
Pain intensity, mean 0–10 NRS score	5.9 ± 1.9	5.4 ± 1.9	5.6 ± 0.7
Pain frequency, % of pain duration	68.5 ± 34.8	77.6 ± 36.8	70.3 ± 36.1
Diagnosis			
Myalgia	52 (59.1)	67 (60.9)	119 (60.1)
Arthralgia	8 (9.1)	19 (17.3)	27 (13.6)
Combined	28 (31.8)	24 (21.8)	52 (26.3)

SD = standard deviation; NRS = numeric rating scale.

Table 2 Prevalence of the Presence of Comorbidities and Coexisting Pain in Acute and Chronic TMD Pain Patients

	Acute TMD pain	Chronic TMD pain	Total
Presence of coexisting pain beyond orofacial area, n (%)			
Yes	44 (40)	64 (72.7)	108 (54)
No	66 (60)	24 (27.3)	90 (46)
Presence of comorbidities, n (%)			
Yes	–	66 (82.5)	66 (33.3)
No	–	22 (17.5)	132 (67.7)

Table 3 Correlations Between Widespread Pain Index, Pain Parameters, and Potential Confounders in all TMD Pain Patients

	Pain duration	Pain intensity	Pain frequency	Age	Gender
Bivariate correlation analysis					
r	0.48	0.2	−0.09	0.25	−0.1
P	.00*	.00*	.22	.00*	.16*
Multiple linear regression					
R	0.05	0.25	–	0.04	0.28
P	.00*	.01*	–	.02*	.5

*Significant values.

Table 4 Results of Logistic Regression for Odds of Having Pain Beyond the Orofacial Area in TMD Pain Patients

	Odds ratio	95% confidence interval	*P*	*P* of model
Duration	1.045	1.024–1.066	.001	.000
Intensity	1.206	1.068–1.344	.026	
Age	1.033	1.012–1.054	.014	

mean pain intensity of all patients was 5.6 ± 0.7, and the mean pain frequency was 70.3% (± 36.1%).

Pain Parameters and WPI

The number of pain sites is illustrated as WPI (excluding the two facial sides). Among the 198 patients with TMD pain, 108 (54.5%) reported pain in other areas of the body (Table 2).

The Spearman rank bivariate correlation analysis showed that the predictors in linear regression were pain duration and pain intensity, and the confounders were age and gender. The multiple linear regression analysis with WPI as the dependent variable showed significant positive correlations with pain intensity ($P = .01$), pain duration ($P < .001$), and age ($P = .02$); gender was no longer associated with the WPI (Table 3). Multivariate binary logistic regression analysis was performed to determine the odds ratio (OR) for patients with and without the presence of pain beyond the orofacial area. Pain duration, pain intensity, and age were incorporated into the model, and the analysis showed that all three were associated with the presence of pain beyond the orofacial area. The analysis suggested that when pain duration reached 1 month, patients had a 1.045-times higher probability of pain presence beyond the orofacial area. For an increase of 1 score on the NRS, this probability increased by 1.206 times, and for an increase of 1 year of age, by 1.033 times (Table 4).

Pain Parameters and Comorbidities

Among the 88 patients with chronic TMD pain, presence of comorbidities was reported by 66 (82.5%),

including 55 women and 11 men (Table 2). The prevalence of the seven comorbidities is shown in Fig 2. The group of symptoms (frequent headache, chronic pelvic pain, chronic low back pain, and chronic fatigue syndrome) were more common than the group of comorbid diseases (fibromyalgia, irritable bowel syndrome, and interstitial cystitis). The symptoms chronic fatigue syndrome, chronic pelvic pain, and chronic low back pain had a prevalence of greater than 30%. Frequent headache was the most common comorbidity (46.6%), while interstitial cystitis was the least common (2.3%).

In the bivariate analysis, only pain duration and age were significantly correlated with the number of comorbidities (Table 5) and were put into the multiple linear regression model. In the regression analysis, age was no longer associated with the number of comorbidities (P = 0.18). Finally, pain duration was the unique independent variable in logistic analysis for determining the OR for patients with and without the presence of comorbidities. The logistic regression model showed that with a 1-month extension of pain duration, patients had a 1.028-times higher probability of having comorbidities (OR = 1.028; 95% CI = 1.005 to 1.05; P = .008).

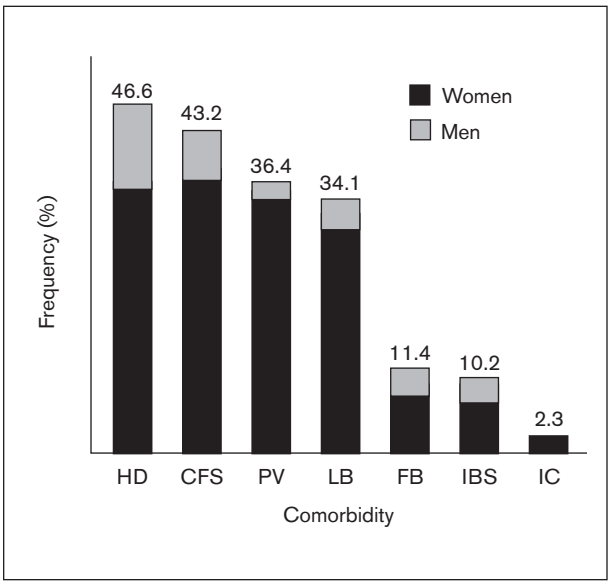

Fig 2 Prevalence of comorbidities in the chronic TMD pain group. HD = frequent headache; CFS = chronic fatigue syndrome; PV = chronic pelvic pain; LB = chronic low back pain; FB = fibromyalgia; IBS = irritable bowel syndrome; IC = interstitial cystitis.

Table 5 Correlations Between Number of Comorbidities, Pain Parameters, and Potential Confounders in the Chronic TMD Pain Group

	Pain duration	Pain intensity	Pain frequency	Age	Gender
Bivariate correlation analysis					
r	0.22	0.00	0.08	0.25	0.06
P	.04*	.99	.46	.02*	0.61
Multiple linear regression model					
R	0.01	–	–	0.02	–
P	.05*	–	–	.18	–

*Significant values.

Discussion

In the present study, 82.5% of patients with chronic TMD pain reported at least one comorbidity, which is similar to Western studies, in which the presence of comorbidities ranges from 62.2% to 83.3%.[5,10,11] Except for irritable bowel syndrome and chronic pelvic pain, the prevalence of other comorbidities corresponded with previous studies.[3,11,43] The differences in the prevalence of irritable bowel syndrome and chronic pelvic pain may be because the prevalence of these conditions in the general population in the United States is greater than 20% and from 10% to 20%, respectively, whereas in Thailand, they are less than 10% and greater than 30%, respectively.[44,45]

According to the regression analyses, the risk of having comorbidities and coexisting pain, as well as the number of pain sites and comorbidities, increases when pain duration increases. This finding is consistent with previous reports in which the number of pain sites and the number of comorbidities were significantly higher in patients with longer pain duration.[11,13,15] This finding is also supported by the biologic mechanism of central sensitization, which progresses with time.[22,23]

In this study, the risk of having coexisting pain and an increased number of pain sites increased with pain intensity; however, pain intensity was not found to be associated with the risk of having comorbidities or with the number of comorbidities. The relationship between pain intensity and the degree of spreading pain and comorbidities is controversial. Higher pain intensity was reported to be associated with a higher number of comorbidities[11] and a wider spreading of pain in several studies[12,15]; conversely, other studies showed that pain intensity was more likely to be related to patients' reasons for treatment than to the degree of spreading pain.[13,46,47] This controversy may be related to pain duration, in that the pain did not last long enough to induce central sensitization.[16,22] In addition, pain intensity is strongly affected by recall bias, which is positively related to pain duration[48] and the repeated experience of pain.[49] Furthermore, pain intensity is also related to the response pattern of patients: Specifically, those with a fear-avoidance–response pattern or endurance-response pattern tended to report higher pain intensity than those with an adaptation-response pattern.[50,51]

Pain frequency in the present study was not related to WPI nor to the number of comorbidities. This may be due to the quantitative pain frequency measurement used, which was used to reduce the survey bias of qualitative scales. However, the drawback of this measurement is that it conflicts with the role of pain duration; for example, the pain frequency of patients with 1-day pain and patients with 1-year pain will be the same if both reported that they have pain every day. To overcome this shortcoming, cases with pain duration of 1 month (the most common pain duration value in this study) were selected for the bivariate correlation between pain frequency and WPI. The result was a positive correlation ($P = .007$). This finding indicates that to analyze the correlation between pain frequency and the number of pain sites or comorbidities, the effect of pain duration should be eliminated first.

No association was found between gender and the risk of having coexisting pain or comorbidities, which is in disagreement with previous findings.[5,11] For the presence of comorbidity, gender was shown to have an insignificant difference in the prevalence of chronic low back pain,[8] which was one of the common comorbidities in the present study. For the WPI, this finding may be due to the domination of pain intensity over gender in the regression model. Similarly, although age was reported to be related to exhibiting both multiple pain sites[52] and comorbidities,[53] the domination of pain duration could eliminate the effect of age on the number or presence of comorbidities in the regression analyses.

The logistic regression analysis showed that for the addition of 1 month of pain, the odds of having coexisting pain beyond the orofacial area increased by 4.5%, and the odds of having comorbidities increased by 2.8%. For an addition of 1 score on the NRS, the odds of having coexisting pain increased by 20.6%. For an increase of 1 year of age, the odds of having coexisting pain were higher by 3.3%. The probability of having coexisting pain and comorbidities can be estimated using odds generated in a logistic regression model. For example, for a patient of 40 years of age with a pain duration of 2 years and a pain intensity of 5, the probability of having comorbidities is 80% and of having coexisting pain is 72.3%. However, because each clinical setting has different patient data, future studies can generate different models that are suitable for their particular population.

This study was a cross-sectional design, which cannot explore the causal effect between TMD pain and comorbidities nor coexisting pain outside the orofacial area. The cohort studies in 2013[18,54,55] have demonstrated that patients with chronic pelvic pain, low back pain, and frequent headache have a significantly higher incidence of TMD pain. These findings mean that TMD pain can develop before or after comorbidities. To explore the causal effect, cohort studies are required that follow TMD pain patients who do not have any other pain disease and who are not provided with any treatment for TMD. However, this design is in conflict with medical research ethics. Another weakness of the present study was that using only a quantitative frequency scale could not reflect how much the TMD pain influenced the daily life of patients. Pain frequency in future studies could be evaluated using a combination of quantitative and qualitative measurements, accompanied by elimination of the effect of pain duration. The relations found in this study may also be underpowered, since the sample size was small (88 chronic pain patients; 198 in total), the number of patients with TMJ pain was also small (8 in chronic pain group; 27 in total), and there was a large difference between the number of female and male patients.

Conclusions

Despite the aforementioned limitations, this study provides several benefits. It is the first to report the distribution of comorbidities in chronic TMD patients in an Asian sample, and these results confirm the hypothesis that there is a relationship between coexisting pain conditions and/or comorbidities and TMD pain parameters: High pain intensity and long pain duration increase the probability of having co-existing pain and comorbidities in TMD patients.

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*Rome questionnaires are diagnostic questionnaires designed by the Rome Foundation, an independent not-for-profit organization. The Rome Foundation provides support for specific activities to create scientific data and educational information to assist in the diagnosis and treatment of functional gastrointestinal disorders.

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