

# Identifying the Clinical Domains of Fibromyalgia: Contributions From Clinician and Patient Delphi Exercises

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**Objective.** In evaluating the effectiveness of fibromyalgia (FM) therapies, it is important to assess the impact of those therapies on the full array of domains considered important by both clinicians and patients. The objective of this research was to identify and prioritize the key clinically relevant and important domains impacted by FM that should be evaluated by outcome assessment instruments used in FM clinical trials, and to approach consensus among clinicians and patients on the priority of those domains to be assessed in clinical care and research.

**Methods.** Group consensus was achieved using the Delphi method, a structured process of consensus building via questionnaires together with systematic and controlled opinion feedback. The Delphi exercises involved 23 clinicians with expertise in FM and 100 patients with FM as defined by American College of Rheumatology criteria.

**Results.** The Delphi exercise revealed that the domains ranked most highly by patients were similar to the domain rankings by clinicians. Pain was consistently ranked highest by both panels. Fatigue, impact on sleep, health-related quality of life, comorbid depression, and cognitive difficulty were also ranked highly. Stiffness was ranked highly by patients but not clinicians. In contrast, side effects was important to clinicians but was not identified as important in the patient Delphi exercise.

**Conclusion.** The clinician and patient Delphi exercises identified and ranked key domains that need to be assessed in FM research. Based on these results, a conceptual framework for measuring patient-reported outcomes is proposed.

## INTRODUCTION

Fibromyalgia (FM) is a chronic disorder characterized by persistent, widespread pain and tenderness (1). FM is estimated to occur in 2% of the US general population, affecting more women than men (2). Symptoms frequently associated with FM include fatigue, sleep disruption, headache, memory or concentration problems, mood dis-

turbances, and irritable bowel symptoms (1,2). FM has a substantial impact on daily life, limiting patients' functioning and negatively affecting emotional well-being (3,4).

Recently, a number of large controlled trials have evaluated newly developed FM therapies that have effectively distinguished placebo and treatment response in domains

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such as pain, fatigue, sleep, and function (5,6). However, consensus has not yet been reached regarding the core domains that should be assessed in all clinical trials of FM. Achievement of consensus regarding core domains is important in the process of developing reliable and meaningful outcome measures.

Consensus building takes time, and in order to facilitate such a goal with regard to the core domains for FM, the Delphi technique was used in the present study. The Delphi method, developed by the RAND Corporation (7), is a structured process of consensus finding by means of a distribution of questionnaires combined with systematic and controlled opinion feedback (8–11). Historically, applications of the Delphi technique have sought opinions from experts in their fields (12–14), with the use of nonexperts being less common (15). However, studies using nonexperts have been conducted, showing good agreement and demonstrating that the Delphi technique may be applied among individuals who may not traditionally be considered sufficiently knowledgeable for participation as a Delphi panel member (15).

The Delphi method provides a unique insight for the treatment of patients with FM because it can elicit and account for both expert and nonexpert perspectives. It could be argued that the most knowledgeable “expert” impacted by a disease or condition is the patient living with the disease and experiencing its effect daily. Clinical experts, who see patients at a given point in time, must rely on patients’ reports of their experiences over time to make the most accurate clinical judgments. Together, the clinician and patient could be the “expert” when deciding which domains are clinically relevant and important to the patient.

The results of the expert clinician Delphi exercise that identified key clinical domains of FM were recently published (16). However, it cannot be assumed that the same domains will be considered equally important and relevant by patients in comparison with clinicians. The Food and Drug Administration’s guidance to industry on the use of patient-reported outcome (PRO) measures highlights the importance of including the patient perspective (17). It states that many treatment effects are only known to the patient and that formal PRO instruments are more reliable than the clinician’s assessment of an informal interview.

The objective of the present study was to identify and prioritize the key domains impacted by FM from a patient’s perspective using the Delphi method. These results were compared with the previously completed expert clinician Delphi (16). The goal was to approach consensus on the priority of domains to be assessed in clinical care and research among clinicians and patients.

## PARTICIPANTS AND METHODS

**Clinician Delphi methods.** Full details of the clinician Delphi panel have been previously presented by Mease et al (16). Briefly, a list of 40 potential domains was prepared through a literature review and discussion among the authors (PJM, LMA, and LJC). Potential participants for the clinician Delphi panel exercise were selected as having a

major interest in FM. The selected domains were distributed to all clinicians, who were asked to determine the relative importance of each domain by distributing 100 points among the 40 domains. Clinicians were free to assign points to as many or as few domains as they wished. The number of points assigned to any particular domain reflected its relative importance, with more points being assigned to more important domains. In subsequent rounds, clinicians were given their own response and the group opinion for each domain (median, interquartile range, and total range) from the previous round. They were able to submit new scores or leave their scores unchanged. In total, 3 rounds were conducted.

**Patient Delphi methods.** *Overview.* Patients were recruited from the following sites: Seattle, Washington; Cincinnati, Ohio; Ann Arbor, Michigan; and San Antonio, Texas. The Delphi exercises were conducted between September 2005 and May 2006. The institutional review boards at each of the 4 sites approved the protocol, and all patients provided written informed consent after the study was explained and their questions were answered and before study procedures were initiated. The patients were identified by the investigators (LMA, LJC, PJM, and IJR) from outpatient clinics or from registries of patients with FM at each of these sites.

*Entry criteria.* Patients were eligible to participate in the research if they were at least 18 years of age and met the American College of Rheumatology 1990 criteria for FM (1). Patients could not participate in the study if they had a life-threatening health condition or an uncontrolled psychiatric condition.

*Patient Delphi exercise.* A list of possible domains was identified by patient focus groups (data available upon request). Because this list was too extensive for inclusion in the patient Delphi exercise, the patient Delphi exercise started with a pretest round in which patients scored the importance of each domain using a numeric rating scale ranging from 0 (not at all important) to 10 (extremely important). The aim of the pretest round was to narrow the focus and reduce the number of domains generated during the patient focus groups to be used in the subsequent rounds of the Delphi exercise.

Based on the patients’ ratings of importance, 40 domains from the pretest round were used in the Delphi exercise. The language used over the course of the Delphi exercise was carefully written and reviewed to ensure that the instructions were clear to patients and that each domain was understandable in terms of the FM experience or referred symptom.

In rounds 1 and 2 of the patient Delphi exercise, participants were asked to rank each domain as it applied to them and impacted their life. Participants were instructed to distribute 100 points among the 40 domains, giving more points to the domains considered to be more applicable and having more of an impact. In round 2, participants were presented with their score on each domain from the previous round and the domain ranking results from round 1 for all patients, which were revealed as the mean and total range.

The goal of the Delphi exercise was to come to a consensus on prioritizing the domains that are important to patients with FM. To achieve this goal, participants had an opportunity to reflect on their response from round 1 in the context of the responses from all other participants, which were presented in an anonymous manner. Participants then repeated the exercise (round 2) with the opportunity to change their previous responses if desired.

For each of the 40 domains in the Delphi rounds, mean and median values were calculated according to the points allocated in each round and the overall exercise. The percentage of patients who endorsed the domain (i.e., allocating  $\geq 1$  point to the domain) was also calculated.

## RESULTS

**Clinician Delphi results.** As reviewed by Mease et al (16), 51 FM experts were approached to participate in the clinician Delphi panel exercise and 23 completed all 3 rounds. Clinicians were asked to rate the importance of the domains for assessment in a context called symptom modifying. The results of the Delphi exercise were presented to the 2004 Outcome Measures in Rheumatology Clinical Trials VII (OMERACT VII) FM workshop attendees. OMERACT is an international consortium of clinical investigators and representatives of regulatory and scientific agencies and biopharmaceutical companies who meet every other year to determine relevant domains for assessment in the rheumatic diseases and to develop and evaluate outcome measures for these domains. The findings of the clinician Delphi were presented to workshop attendees who then voted on the prioritization of domains in terms of their potential inclusion in a core set of domains to be assessed in FM research.

In general, there was a high level of agreement between the Delphi clinicians' median scores and the voting by the OMERACT group (see Mease et al [16] for details). In summary, pain was the key domain for clinicians, followed by fatigue, patient global assessment, sleep quality, health-related quality of life, physical function, treatment side effects, depression, tender point, cognitive impairment, anxiety, and clinician global assessment. The OMERACT participants agreed that pain, fatigue, and patient global assessment ranked the highest among the domains of assessment for clinical trials. The OMERACT participants also recommended that health-related quality of life be ranked as highly important, with an emphasis on assessing multidimensional aspects of function rather than simply physical function (16).

**Patient Delphi results.** In the patient Delphi panel, 100 patients with a physician-confirmed FM diagnosis participated in the importance-rating task conducted in the pretest round. Of 100 patients (95% women) who completed the pretest, 73 patients responded to round 1 of the Delphi exercise and 84 patients responded to round 2.

Ages ranged from 23 to 74 years (mean age 49 years). Other patient characteristics are reported in Table 1. The majority of patients (52%) had been diagnosed with FM between 1 and 4 years before this study took place. How-

**Table 1. Patient characteristics\***

Patient characteristic	Sample (n = 100)
Women	95 (95)
Age, mean $\pm$ SD	49 $\pm$ 11
Race	
White	66 (66)
Hispanic	25 (25)
African American	5 (5)
American Indian, Hawaiian, or Pacific Islander	3 (3)
Education level	
High school diploma or less	21 (21)
Some college or certificate program	39 (39)
College/university degree or professional degree	39 (39)
Work status	
Full or part time	33 (33)
Part time due to FM	10 (10)
Not working due to FM or applied for or receiving disability	33 (33)
Looking for work	3 (3)
Full-time homemaker	7 (7)
Student	1 (1)
Retired	9 (9)
Other	2 (2)
Relationship status	
Single	16 (16)
Divorced or widowed	18 (18)
Significant partner or married	63 (63)
Self-reported severity of FM symptoms	
Extremely severe/severe	43 (43)
Moderately severe	49 (49)
Mild/very mild	7 (7)
Comorbidities	
Depression	57 (57)
Chronic fatigue syndrome	55 (55)
Migraine or tension headaches	52 (52)
Irritable bowel syndrome	51 (51)
Anxiety	49 (49)

\* Values are the number (percentage) unless otherwise indicated.  
FM = fibromyalgia.

ever, 67% of patients reported that they had experienced FM symptoms for  $>5$  years. Thirty-three percent were not working due to FM. Forty-two percent of patients labeled their health as poor or fair. Comorbidities were similar to previous reports (18,19); depressive and chronic fatigue syndrome symptomatology were identified in 57% and 55% of patients, respectively.

Patients were initially given a list of 104 domains (generated from patient focus groups, the results of which are presented elsewhere [20]) organized according to 3 concepts: FM symptoms (39 domains, e.g., abdominal pain, dizziness, and weight gain), impact of FM on daily life (41 domains, e.g., difficulty cooking, lack of vitality, and loss of job), and impact of FM on emotional well-being (24 domains, e.g., anger, feeling unmotivated, and irritability). After the importance-rating task/pretest round, investiga-

**Table 2. Delphi domains according to concept and their relevant score(s) from the importance-rating pretest round: fibromyalgia symptoms\***

Domains as presented in the Delphi exercise	Domains from the pretest round (pretest mean score)
Pain or physical discomfort	Pain (9.05)
Lack of energy or fatigue	Physical discomfort (8.30)
Stiffness	Fatigue or tiredness (8.66)
Joints aching or pain	Lack of energy (8.19)
Feeling tender where touched	Stiffness (8.33)
Problems with attention or concentration (e.g., difficulty concentrating on things, difficulty thinking, "fibro-fog")	Aching or painful joints (8.14)
Difficulty moving, walking, or exercising	Feeling tender where touched (7.65)
Memory problems	Difficulty concentrating (7.57)
Weight gain	Difficulty thinking or "fibro-fog" (7.04)
Depression (e.g., disappointed, sad, resigned, or unmotivated)	Difficulty moving (7.21)
Disorganized thinking (e.g., difficulty in expressing yourself, difficulty in answering questions quickly, or difficulty making plans)	Inability to exercise (7.16)
Numbness or tingling in your fingers or toes	Difficulty walking (5.98)
Headache or migraine	Difficulty remembering things (7.15)
Being sensitive to outside factors (e.g., smells, sounds, temperature changes, light, or touch)	Memory loss (6.13)
Cold hands	Weight gain (6.08)
Susceptibility to colds or other infections	Depression (6.44)
Involuntary movements	Sadness (6.31)
Dizziness	Feeling unmotivated (6.08)
Stomach/intestinal symptoms (e.g., abdominal pain or discomfort, nausea, or upset stomach)	Disappointed (5.80)
	Resigned (4.42)
	Difficulty in answering a question quickly (5.90)
	Difficulty in expressing yourself (4.79)
	Numbness or tingling in your fingers or toes (5.35)
	Headache (5.61)
	Migraines (4.37)
	Being sensitive to temperature or temperature changes (6.70)
	Skin sensitivity (5.33)
	Being sensitive to sounds (4.20)
	Being sensitive to odors (4.14)
	Being sensitive to light (3.88)
	Cold hands (4.62)
	Susceptibility to colds or other infections (4.45)
	Involuntary movements (3.85)
	Dizziness (3.63)
	Upset stomach (3.93)
	Abdominal pain or discomfort (3.80)
	Nausea (3.10)

\* Score range 0–10.

tors evaluated the importance of each domain to patients, and important domains were condensed to finalize the 40 domains used in the Delphi exercise. The manner in which the pretest domains were condensed to the final list of 40 domains for the Delphi exercise is summarized in Tables 2, 3, and 4. More than two-thirds (67.5%) of the Delphi domains consisted of  $\geq 2$  items from the importance-rating task. For example, the Delphi domain problems with attention or concentration was based on 2 pretest items: difficulty concentrating and difficulty thinking or "fibro-fog." By combining conceptually related domains identified as important at the pretest stage, it was possible to ask patients about a broader range of symptoms with fewer items. Of the 104 domains originally included at the pretest stage, 92 were captured by the 40 Delphi domains, but 12 were not included because they were not ranked as important by most patients.

In the Delphi rounds, consistency was observed between

patients in terms of the hierarchy of domains with the highest to lowest mean values. In round 1, all of the top 15 domains listed in Table 5 were allocated  $\geq 1$  point by at least 68% of the patients (range 68–96%). In round 2, the same domains were identified by at least 71% of participants (range 71–96%).

There were 7 domains with a median value of 0 (more than half of all participants did not allocate any points) in both rounds of the Delphi exercise: feeling alone, shame, involuntary movements, changes in diet to help relieve symptoms, cold hands, loss of job or career, and susceptibility to colds or other infections. The results suggest that these domains are seldom experienced by patients or may not have a significant impact on patients' lives relative to the other domains listed.

Thirty-seven patients (53%) allocated more points to the 15 top-ranked domains in the second round than they had in the first round (range 1–14 points). In other words,

**Table 3. Delphi domains according to concept and their relevant score(s) from the importance-rating pretest round: impact of fibromyalgia on daily life\***

Domains as presented in the Delphi exercise	Domains from the pretest round (pretest mean score)
Unpredictability of the symptoms	Unpredictability of the symptoms (8.00)
Having to push yourself to do things	Having to push yourself to do things (7.93)
Impact on sleep (e.g., difficulty falling asleep, staying asleep, or getting up in the morning)	Impact on sleep (8.46) Difficulty staying asleep (7.53) Difficulty in getting up in the morning (7.43) Difficulty falling asleep (7.41)
Impacted/limited in doing normal daily life and household activities	Impact on daily activities (7.63)
Impact on ability to make plans, accomplish goals, or complete tasks	Limited in doing other day-to-day activities (7.37) Interference with your ability to accomplish daily tasks (7.34) Hesitant to make plans (6.15) Unable to make plans (5.71)
Social life impact (e.g., limited in doing your favorite hobby or pastime or inability to travel)	Limited in doing your favorite hobby or pastime (7.08) Social life impact (6.47) Inability to travel (5.28)
Problems with medication (e.g., medication side effects or reliance on medications)	Reliance on medication (6.79) Treatment side effects (4.95)
Impact on family (i.e., relationship with your spouse or partner and/or children)	Impact on your family (6.35) Strain on your relationship with your spouse (3.95)
Impacted/limited in your ability to work, go to school or college	Impact on work/school (6.85) Interference with ability to accomplish tasks on the job (5.47) Interference in going to school or college (2.69)
Impact on intimacy and sexual relationships with spouse or partner	Lack of libido or sex drive (5.01) Sexual activity limitations (4.81) Difficulty being sexually intimate with spouse or partner (4.50) Being unable to have sexual intercourse with spouse or partner (4.50)
Changes in diet to help relieve symptoms	Changes in diet to help relieve symptoms (4.60)
Loss of job or career	Losing your job (4.32) Loss of career (4.27)
Financial impact due to medical costs and health insurance	Financial impact (5.63) Medical costs (5.01) Loss of health insurance (2.06)
Impact on driving (e.g., due to pain or fatigue or due to memory problems)	Driving limitations (3.45) Difficulty driving due to memory problems (3.19)

\* Score range 0–10.

having received the feedback of the group's results from round 1, more than half of the patients changed their distribution of points to be more in line with the feedback. Twenty-two patients (31%) did the opposite and allocated fewer points to the top-ranked domains in the second round, changing their distribution of points to be less in line with round 1 feedback (range 1–44 points). Eleven patients (16%) did not differ in the number of points they assigned to the top-ranked domains between round 1 and round 2.

The scores of the 15 domains ranked highest overall and in each round of the Delphi exercise are shown in Table 5 and are compared with the scores from the importance-rating pretest round. In the importance-rating pretest round, patients ranked domains from the FM symptoms concept as the most important; this was reflected in the Delphi exercise in which 11 of the top 15 Delphi domains also came from FM symptoms. The remaining 4 domains fell under the impact on daily life concept and corre-

sponded well to those ranked most important within this group, with the exception of unpredictability of the symptoms, which was ranked as important in the importance-rating task (mean 8.00) but as not important for assessment during the Delphi exercise (mean 1.8).

**Comparison of clinician and patient Delphi panel results.** Overall, the domains ranked highest by patients were similar to the domain rankings by the clinician Delphi panel. Pain was consistently ranked highest by both panels. Fatigue, impact on sleep, health-related quality of life, depression as a comorbid problem, and cognitive difficulty were also ranked highly, supporting the notion that these domains are considered to be important for assessment for both clinicians and patients. One domain ranked highly by patients but not by clinicians/investigators was stiffness.

Although patients did not directly refer to domains as "patient global" or "health-related quality of life" as clini-

**Table 4. Delphi domains according to concept and their relevant score(s) from the importance-rating pretest round: impact of fibromyalgia on emotional well-being\***

Domains as presented in the Delphi exercise	Domains from the pretest round (pretest mean score)
Feeling like you've lost who you are Anger or irritability	Feeling like you've lost who you are (5.90) Irritability (6.37) Anger (4.85)
Frustrated (e.g., frustrated by limitations; frustrated by encounters with family, friends, or physicians)	Frustrated about not being able to accomplish goals (7.38) Frustrated about not being able to complete tasks (7.15) Frustrated by encounters with your physicians (4.72) Frustrated by encounters with family (4.39) Frustrated by encounters with your peers (4.10)
Feeling like you are no longer valued by others (e.g., feeling as if people thought you were lazy, feeling that you are a burden to your family, feeling like the pace of your life is slower than most other people, or feeling unreliable)	Feeling like pace of life is slower than most other people (6.31) Feeling as if people thought you were "lazy" (5.87) Feeling unreliable (4.94)
Anxiety (e.g., nervousness or having panic attacks)	Feeling that you are a burden to your family (4.86) Feeling like you are no longer valued by others (4.20) Anxiety (5.23) Nervousness (5.14) Panic attacks (3.26)
Feeling alone (e.g., feeling like you are the only person who has fibromyalgia or feeling isolated)	Feeling isolated (5.25) Feeling alone (5.22) Feeling like you are the only person who has fibromyalgia (2.86)
Shame (e.g., guilt or embarrassment)	Guilt (4.17) Embarrassment (3.71) Ashamed (3.32)

\* Score range 0–10.

cians did, the impact of FM on functioning was captured by several of the domains identified by patients. These domains included the impact on ability to make plans, accomplish goals, and complete tasks, and impact on daily life. Although side effects was included in the 40 domains shown to patients during the Delphi exercises and was ranked as important in the importance-rating task exercise, it was not identified as an important domain for assessment in the patient Delphi exercise, nor did patients refer

to or use a different domain name that may be related to treatment or medication side effects (the overall mean for the treatment side effects domain was 1.65).

**DISCUSSION**

The clinician and patient Delphi exercises described in this report represent important and novel approaches to

**Table 5. Comparison between the top 15 domains in each round of the patient Delphi exercise according to mean score, domain pretest score, and percentage of patients who endorsed the domain (n = 100)**

Domain	Delphi mean score		Overall patients endorsing domain, no. (%)*	Pretest mean score†
	Round 1 (n = 73)	Round 2 (n = 84)		
Pain or physical discomfort	6.75	7.01	95 (95)	8.68
Joints aching or pain	5.78	5.58	90 (90)	8.14
Lack of energy or fatigue	5.53	5.48	96 (96)	8.43
Impact on sleep	5.22	5.45	92 (92)	7.71
Problems with attention or concentration	4.62	4.72	91 (91)	7.31
Stiffness	3.89	4.49	90 (90)	8.33
Disorganized thinking	3.62	3.61	85 (85)	5.35
Difficulty moving, walking, or exercising	3.54	3.52	86 (86)	6.78
Having to push yourself to do things	3.10	3.16	83 (83)	7.93
Depression	2.95	2.97	73 (73)	5.81
Feeling tender where touched	3.04	2.89	77 (77)	7.65
Impact on ability to make plans, accomplish goals, or complete tasks	2.79	3.12	78 (78)	6.40
Impacted/limited in doing normal daily life and household activities	2.95	2.65	82 (82)	7.50
Memory problems	2.51	2.68	80 (80)	6.64
Being sensitive to outside factors	2.75	2.46	70 (70)	4.85

\* Percentage of patients who allocated at least 1 point to the domain during both Delphi exercises.  
 † Calculated from the mean scores of the individual pretest domains in Tables 2, 3, and 4.

Patient domains		PRO concept		Clinician domains
<ul style="list-style-type: none"> <li>• Pain or physical discomfort</li> <li>• Joints aching or pain</li> <li>• Stiffness</li> <li>• Feeling tender where touched</li> </ul>	→	PAIN	←	<ul style="list-style-type: none"> <li>• Pain</li> <li>• Patient global status</li> <li>• Clinical global status</li> <li>• Tender point intensity</li> </ul>
<ul style="list-style-type: none"> <li>• Problems with medication (e.g., medication side effects or reliance on medications)*</li> </ul>	→	TREATMENT SIDE EFFECTS	←	<ul style="list-style-type: none"> <li>• Side effects</li> </ul>
<ul style="list-style-type: none"> <li>• Difficulty moving, walking, or exercising</li> </ul>	→	MOBILITY	←	<ul style="list-style-type: none"> <li>• Physical function</li> <li>• Health-related quality of life</li> </ul>
<ul style="list-style-type: none"> <li>• Problems with attention or concentration</li> <li>• Disorganized thinking</li> <li>• Memory problems</li> </ul>	→	COGNITION	←	<ul style="list-style-type: none"> <li>• Dyscognition</li> <li>• Health-related quality of life</li> </ul>
<ul style="list-style-type: none"> <li>• Lack of energy or fatigue</li> <li>• Having to push yourself to do things</li> </ul>	→	ENERGY	←	<ul style="list-style-type: none"> <li>• Fatigue</li> <li>• Health-related quality of life</li> </ul>
<ul style="list-style-type: none"> <li>• Limited in doing normal daily life and household activities</li> <li>• Ability to make plans, accomplish goals, or complete tasks</li> <li>• Being sensitive to outside factors</li> <li>• Unpredictability of symptoms*</li> </ul>	→	IMPACT ON DAILY LIVING	←	<ul style="list-style-type: none"> <li>• Health-related quality of life</li> </ul>
<ul style="list-style-type: none"> <li>• Depression</li> <li>• Having to push yourself to do things</li> <li>• Frustration*</li> <li>• Irritability*</li> </ul>	→	EMOTIONAL WELL-BEING	←	<ul style="list-style-type: none"> <li>• Depression</li> <li>• Anxiety</li> <li>• Health-related quality of life</li> </ul>
<ul style="list-style-type: none"> <li>• Impact on sleep (e.g., difficulty falling asleep, staying asleep, or getting up in the morning)</li> </ul>	→	SLEEP	←	<ul style="list-style-type: none"> <li>• Sleep quality</li> <li>• Health-related quality of life</li> </ul>

**Figure 1.** Possible conceptual framework for fibromyalgia assessment. \* Included based on scores from importance-rating pretest round. PRO = patient-reported outcomes.

identification and prioritization of key domains of FM that impact patients. The results of these exercises will be used to construct a core set of domains for FM assessment in research studies and clinical practice. Whereas clinician/investigator Delphi exercises have been used in similar processes in other disease states, we are not aware of this technique being used in a large group of patients to provide a patient perspective on what domains are considered important. The Delphi method is considered an ideal way to gain understanding because it is conducted anonymously, minimizing the chance that a dominant person will unduly influence all participants. By providing feedback on aggregate opinion, with allowance for subsequent change of numeric prioritization, the exercise provides an opportunity for consensus in areas where consensus is lacking.

Despite uncertainties in the classification and etiology of FM, there is increasing understanding and acceptance of

FM due to an increase in research of the pathophysiologic processes that may be involved in the development of FM. Furthermore, clinical trials have demonstrated meaningful improvement in some symptoms of FM using a variety of nonpharmacologic and pharmacologic therapies (5). By ascertaining the key domains of FM when taking into account the patient perspective, this study and the previous clinician Delphi study (16) provide guidance concerning the key domains that should be assessed in the treatment of patients with FM. The results demonstrate consensus both within and between these constituencies on the following domains: pain, fatigue, sleep disturbance, multidimensional function, cognitive dysfunction, mood disturbance, and the experience of stiffness. The results of this study support the validity of focusing on these domains in FM assessment and provide reassurance that the domains are important to both clinicians and patients.

Despite the overall congruence of domain prioritization

between clinicians and patients, some discrepancies existed. Clinicians rated treatment adverse effects as important to assess. Patients did not rate this domain as highly in the Delphi exercise but ranked it as important in the importance-ranking pretest. Research clinicians recognize that for a treatment to be worthwhile, the balance of efficacy and safety/tolerability must be acceptable, making safety assessment absolutely necessary. Patients appreciate the need for a treatment to be safe and tolerable, but perhaps tend to focus on the impact of the disease on their day-to-day experience. Any change in this experience as a result of therapy effectiveness may be attributed to side effects of FM rather than to treatment.

It is also possible that clinicians included side effects as an important domain because they realized that this study was part of a trial design strategy, whereas patients were not aware of this fact and therefore placed this domain in a lower priority. However, the exercise directions stated, "Information gained from this study may help develop new outcome assessments for fibromyalgia studies in the future, which could potentially help in the development of new treatments for fibromyalgia." Given that patients were required to read these instructions, patients should have been aware that the results of this study would be used to develop assessments for use in clinical trials. However, it is possible that the patients did not completely understand the instruction.

Additionally, patients considered stiffness to be a highly important symptom domain. Clinicians might associate the phenomenon of stiffness with conditions such as inflammatory arthritis and may not appreciate how stiffness might occur in FM, thus failing to consistently address it in discussions with patients.

Patients described problems with attention or concentration, disorganized thinking, and memory problems as 3 different items within the top 15 domains. In the previous study of the clinician Delphi (16), clinicians ranked dyscognition as the 10th priority, demonstrating their recognition of its importance. However, dyscognition may not be as well understood by clinicians, partly because of a relative lack of research on this domain in FM, the absence of effective measures or treatment for dyscognition in clinical trials or practice, and possibly the difficulty patients have in reporting it.

It was hypothesized that there may be greater variability and range among patients when identifying 40 important domains for FM, thus different approaches were used to develop the domain list for the clinician Delphi and patient Delphi exercises. This difference needs to be considered because it may have impacted the results of the Delphi method. The list of 40 domains generated for the patient Delphi was the result of the importance-rating task in which 104 domains identified in patient focus group research were reduced to 40 based on patients' ranking of importance and the combining of conceptually related items. For the clinician Delphi panel, the list of 40 domains was created through literature review and discussion among the authors. It may have been informative to have conducted a pretest item reduction process, similar to that used among patients (i.e., the importance-rating task), to allow clinicians the opportunity to select which

domains were most important from a larger pool. This may have allowed some domains, such as dyscognition, global status, and health-related quality of life, to have been described more specifically than these broader terms. However, the methods used followed standard and accepted Delphi techniques (7).

A comparison between the proposed conceptual framework (Figure 1) and a review of the existing FM outcome instruments indicates that there may be gaps between what patients and clinicians say is important and what currently available instruments are measuring. Given the number of important FM concepts outlined in the conceptual framework, it is not necessarily the case that all concepts will need to be assessed in clinical trials at any one time. In fact, what is important is that the concept(s) (e.g., impact of FM on daily living or FM mobility) that is targeted is measured and evaluated comprehensively by an instrument(s) that includes all relevant items required for a full assessment of that concept(s). If the full spectrum of FM concepts were to be measured, it is likely that a battery of instruments would be required for adequate and comprehensive measurement (21).

FM impacts many aspects of physical and mental health, function, and participation in life activities. In evaluating the effectiveness of therapies, it is important to assess the impact of these therapies on the full array of domains considered important by both clinicians and patients as a core set of domains.

## AUTHOR CONTRIBUTIONS

Dr. Mease had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

**Study design.** Mease, Arnold, Crofford, Williams, Russell, Abetz, Martin.

**Acquisition of data.** Mease, Arnold, Crofford, Williams, Russell.

**Analysis and interpretation of data.** Mease, Arnold, Crofford, Williams, Russell, Humphrey, Abetz, Martin.

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**Statistical analysis.** Mease, Humphrey, Abetz.

## ROLE OF THE STUDY SPONSOR

The manuscript was written by the authors with the assistance of Louise Humphrey, Linda Abetz, and Gregory Bezkorovainy (nonauthor), who were paid consultants to Pfizer in connection with the development of this manuscript. All authors reviewed and contributed to the manuscript during its development, agreed to submit the manuscript, and approved the content of the submitted manuscript.

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