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# Patient-reported Outcomes and Adult Patients' Disease Experience in the Idiopathic Inflammatory Myopathies. Report from the OMERACT 11 Myositis Special Interest Group

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**ABSTRACT.** The newly formed Outcome Measures in Rheumatology (OMERACT) Myositis Special Interest Group (SIG) was established to examine patient-reported outcome measures (PROM) in myositis. At OMERACT 11, a literature review of PROM used in the idiopathic inflammatory myopathies (IIM) and other neuromuscular conditions was presented. The group examined in more detail 2 PROM more extensively evaluated in patients with IIM, the Myositis Activities Profile, and the McMaster-Toronto Arthritis Patient Preference Disability Questionnaire, through the OMERACT filter of truth, discrimination, and feasibility. Preliminary results from a qualitative study of patients with myositis regarding their symptoms were discussed that emphasized the range of symptoms experienced: pain, physical tightness/stiffness, fatigue, disease effect on emotional life and relationships, and treatment-related side effects. Following discussion of these results and following additional discussions since OMERACT 11, a research agenda was developed. The next step in evaluating PROM in IIM will require additional focus groups with a spectrum of patients with different myositis disease phenotypes and manifestations across a range of disease activity, and from multiple international settings. The group will initially focus on dermatomyositis and polymyositis in adults. Qualitative analysis will facilitate the identification of commonalities and divergent patient-relevant aspects of disease, insights that are critical given the heterogeneous manifestations of these diseases. Based on these qualitative studies, existing myositis PROM can be examined to more thoroughly assess content validity, and will be important to identify gaps in domain measurement that will be required to develop a preliminary core set of patient-relevant domains for IIM. (First Release Jan 15 2014; J Rheumatol 2014;41:581-92; doi:10.3899/jrheum.131247)

## Key Indexing Terms:

MYOSITIS PATIENT-REPORTED OUTCOMES OUTCOME AND PROCESS ASSESSMENT

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The idiopathic inflammatory myopathies (IIM) are a heterogeneous group of diseases, but commonalities among them include proximal muscle weakness, elevated muscle enzymes, electromyogram (EMG) abnormalities including irritability, and muscle biopsies usually characterized by lymphocytic inflammation<sup>1</sup>. Evaluating people affected by IIM, which include dermatomyositis (DM), polymyositis (PM), inclusion body myositis (IBM), and immune-mediated necrotizing myopathy, is further complicated by extramuscular manifestations including interstitial lung disease (ILD), arthritis, Raynaud phenomenon, and other autoimmune features<sup>2</sup>. The cardinal clinical feature traditionally associated with IIM has been described as painless muscle weakness with limitations in activities of daily living (ADL) and quality of life (QOL)<sup>3,4</sup>, but few data are available concerning patients' experience of the disease with detailed characterization of important symptoms and disease burden.

The International Myositis Assessment and Clinical Studies Group (IMACS) is a group of healthcare providers and researchers with experience and interest in the myositis syndromes. Represented by diverse subspecialties including rheumatology, neurology, dermatology, and physical medicine and rehabilitation, the goal of IMACS is research and discovery that improves the lives of those living with myositis. To date, through international collaborative efforts, IMACS members have developed consensus standards on the conduct and reporting of adult and juvenile myositis studies. The preliminary core set of measures of disease activity for myositis therapeutic trials developed by IMACS includes a physician global assessment of disease activity, muscle strength testing (e.g., strength, endurance), physical function, laboratory assessments [e.g., muscle enzymes such as creatine phosphokinase (CPK), imaging, biomarkers], and scoring of extramuscular disease activity<sup>5</sup>. This core set also includes several patient-reported outcome measures (PROM) such as the patient/parent report of disease activity, a measure of physical function/ADL. IMACS also recommends including a measure of health-related QOL (HRQOL), e.g., the generic Medical Outcome Study Short Form-36 survey (SF-36) in clinical studies<sup>5,6</sup>. While disease activity and damage core sets of measures have been derived and validated, no specific PROM have been developed under IMACS initiatives, although the group is undertaking an initiative to further assess fatigue in these diseases. Outcome Measures in Rheumatology (OMERACT) provides a complementary, non-overlapping approach to the IMACS work to date, uniquely bringing healthcare providers, patients, and other stakeholders together to facilitate research to evaluate, develop, and validate PROM under a well-established framework. Increasingly it has been emphasized that clinical trials and observational studies should include an assessment of the outcomes that matter most to patients. OMERACT has contributed substantially to this effort over

the last decade, with the identification by patients of fatigue as a recommended core set measure in rheumatoid arthritis (RA) and the development of recommendations for a process of patient-reported outcome (PRO) domain selection<sup>7,8,9</sup>. Additional recommendations through the World Health Organization, regulatory agencies including the European Medicines Agency, and the US Food and Drug Administration through the critical pathway initiative, and the newly established patient-centered outcomes research institute in the USA have also emphasized the importance of PROM inclusion<sup>10,11,12,13</sup>. Most outcome measures in IIM to date, however, have focused on the pathophysiologic manifestations of these diseases (e.g., physical strength testing, EMG, CPK). Although PROM are widely used and applied in different disease areas in rheumatology and neurology, they have not been extensively studied in patients with IIM. While IMACS has recommended inclusion of certain PROM as part of their core set (patient global assessment, physical function), the extent to which these include the aspects of the disease most important to patients has not been well studied. In a Swedish study of 28 patients with myositis using the McMaster-Toronto Arthritis Patient Preference Disability Questionnaire (MACTAR) semistructured interview, several areas of health that were prioritized by patients, including sexual activity, social activities, and sleep, were not covered by items in standard assessments of physical function<sup>14</sup> used most in myositis studies to date: the Health Assessment Questionnaire (HAQ)<sup>15</sup>, and the Myositis Activities Profile (MAP)<sup>16</sup>. OMERACT groups working in other diseases have demonstrated that patients and healthcare providers weigh domains differently in terms of perceived importance<sup>17,18,19</sup>.

The purpose of the Myositis Special Interest Group (SIG) is to evaluate existing PRO assessments used in IIM and to better understand the patient-valued aspects of the disease that will allow the delineation of domains that reflect important disease features. This will help inform subsequent PROM identification, development, and validation for IIM, which can then provide a more comprehensive assessment of IIM disease activity and burden.

## METHODS

*Overview of the OMERACT Myositis SIG.* An organizing OMERACT Myositis SIG group meeting was held at the American College of Rheumatology (ACR) annual meeting in Chicago in 2011. Twenty-five attendees representing 8 countries were present. A 90-min SIG meeting was held at the OMERACT 11 conference in Pinehurst, North Carolina, USA, in May 2012 and was attended by 20 participants representing 5 countries (USA, Canada, Sweden, UK, and Japan), including 1 patient with myositis. The group met again at the European League Against Rheumatism (EULAR) June 2012 meeting in Berlin, Germany, with an expanded discussion on ensuring international representation of the group and further developing a research agenda. Individuals from 4 countries and 3 continents were represented. At the ACR meeting in Washington, DC, USA, the group met again to discuss how to move forward with a standardized focus group discussion guide that could be used across different nationalities.

*Literature review of PRO used in IIM.* We searched MEDLINE and trial

registries from inception until June 2012. The search terms included “patient related outcome,” “patient reported outcome,” “patient centered outcome,” “assessment,” AND “dermatomyositis,” “juvenile dermatomyositis,” “polymyositis,” “immune-mediated necrotizing myopathy,” “inclusion body myositis,” and “idiopathic inflammatory myopathies.” Given the paucity of IIM-related PROM, we then broadened the search to additional neuromuscular diseases: “centronuclear myopathy,” “progressive muscular atrophy,” “spinal muscular atrophy,” “sarcopenia,” “Charcot-Marie-Tooth disease,” “muscular dystrophy,” “Duchenne muscular dystrophy,” “multiple sclerosis,” and “myasthenia gravis.” Articles that included only non-patient-centered outcomes were excluded. This approach was reviewed and agreed upon by the OMERACT Myositis SIG members at the ACR Annual Meeting, in November 2011 in Chicago. Additional articles known to the investigators and from the references in a review on outcome measures in myositis<sup>20</sup> supplemented the above search. All retrieved data were summarized into a tabulated format according to the OMERACT criteria of truth, discrimination, and feasibility in the setting of myositis<sup>21</sup>.

**Focus group.** A 90-min focus group discussion was conducted with 7 patients with IIM seen at the Johns Hopkins Myositis Center. This study was conducted under the auspices of the Johns Hopkins Institutional Review Board, and all patients signed informed consent prior to any questionnaire completion or discussions. Patients completed a short questionnaire before the focus group that included demographics, disease duration, global assessment, pain, stiffness, fatigue, and the HAQ. The focus group was led by a qualitative researcher and a rheumatologist not involved with the care of the patients. Initial questions were non-directive, encouraging patients to discuss freely the way the disease affected their lives. Topics of great interest for multiple participants in the focus group were then prioritized. The focus group was recorded and transcribed, and all patient identifiers were removed to maintain anonymity. Data analysis was largely inductive and exploratory, with a goal of identifying and reporting on major thematic elements pertaining to patients’ experience of living with and being treated for myositis. The analytic process included use of qualitative software Atlas.ti. for data management as well as to facilitate an iterative consensus process among a team of clinical and behavioral scientists to identify common themes and consider their potential importance for understanding and improving patient experiences<sup>22</sup>.

**Patient inclusion.** One patient with DM and ILD participated in the Baltimore focus group and attended the OMERACT 11 Meeting in Pinehurst as a patient research partner (PRP). During the Myositis SIG meeting, she shared her detailed experience of living with inflammatory myopathy and the effect of the disease on her life, as well as her experience as a participant in the focus group and as a PRP at OMERACT 11.

## RESULTS

**Literature review.** We reviewed the literature concerning PROM in IIM with regard to use and validation. In our initial analysis we found that the spectrum of PRO domains studied in patients with IIM was limited to patient/parent global assessment, physical function, HRQOL, pain, and fatigue. When the search was expanded to other neuromuscular conditions, we found that many additional domains had been studied. These included psychological function (mood, including depression) and the effect of IIM on pain interference, sleep, coping, cognitive functioning, occupational and leisure activities, satisfaction with life roles and activities, social supports, health utilities (European Quality of Life), and a number of disease-specific QOL and functional status measures (data not shown). Several short forms reflecting domains within the Patient Reported

Outcome Measurement Information System framework including pain interference, sleep, fatigue, depression, and satisfaction with social roles have been evaluated in multiple sclerosis and muscular dystrophy<sup>23</sup>. Table 1 outlines the domains that have been used in IIM and evaluates instruments in the context of the OMERACT Filter 1.0. Most of the instruments that have been evaluated in IIM were generic instruments or were adopted from use in other rheumatic or neuromuscular diseases. We identified only 1 instrument, the MAP, that was created specifically for adult PM and DM<sup>16</sup> and 1, the MACTAR<sup>14</sup>, that was adapted for these 2 diagnoses. In addition, the IBM Functional Rating Scale (IBMFRS) was created and validated for patients with IBM while the QOL scores Individualized Neuromuscular Quality of Life Questionnaire and Childhood Health Questionnaire (CHQ), and activity limitation scales such as Child Health Assessment Questionnaire (CHAQ) and parent’s global assessment, were validated for juvenile myositis<sup>24,25,26,27</sup>. Other scores that have been used in these disorders include the Neuromuscular Symptom and Disability Functional Score, the Amyotrophic Lateral Sclerosis Functional Rating Scale, and the Barthel’s ADL Index<sup>28,29,30</sup>.

The OMERACT Filter 1.0 was created to set a standard for the validation process and applicability of PROM and can be summarized as truth, discrimination, and feasibility<sup>21</sup>. The 22 PROM that were identified and used in juvenile or adult myositis are outlined in Table 1 according to the OMERACT Filter components in myositis with definitions of “low,” “moderate,” or “high” validity or reliability. High content validity reflects patient involvement from qualitative research, moderate as patients being partly involved, and low with no patient input. Spearman correlation coefficients for analysis of construct or criterion validity were defined as rs 0–0.25 (no or very low correlation), 0.26–0.49 (low), 0.50–0.69 (moderate), 0.70–0.89 (good), and 0.90–1.00 (very high correlation)<sup>31</sup>. For analysis of item fit within their subscale, Cronbach’s alpha coefficients < 0.70 were defined as inadequate<sup>32</sup>. Test-retest reliability was defined as weighted kappa coefficients of 0–0.20 (no or low agreement), 0.21–0.40 (fair), 0.41–0.60 (moderate), 0.61–0.80 (substantial), and 0.81–1.00 (almost perfect agreement)<sup>33</sup>. We defined high sensitivity to change as demonstrating clinically relevant and statistically significant changes, moderate sensitivity showing only statistically significant changes, and low sensitivity to change as no significant changes. We defined examiner burden as low when scores can be calculated by hand in a short time and high when a software program is not available to score complicated scores. Examiner burden also involved costs of requiring measures or software limiting feasibility. High respondent burden was defined as more than 10 min to complete. We indicated only the languages in which the outcome was used in myositis.

Table 1. Patient-reported outcomes used in idiopathic inflammatory myopathies outlined according to the OMERACT Filter 1.0 (numerals in parentheses are references).

Domain	Outcome Measure	Truth Validity	Discrimination		OMERACT Filter 1.0			Studies using Outcome Measure
			Reliability	Ability to Detect Change	Language of Scale as Adopted and Used in Myositis	Feasibility Respondent Burden	Administrative Burden	
HRQOL	SF-36 (6)	High construct and criterion validity (3, 52–54); generic — population-based			English, Swedish Hungarian	Low; 36 items, self-administration, telephone administration or administration during personal interview	Low with software; available on payment	(3, 49–53)
	CHQ (26, 53) NHP (56)				English	50 items High; 38 items; about 12 min; administration during a personal interview or self-administration	Low with software; about 12 min	(54, 55) (57)
	PedsQL (58)			Fatigue scale has high responsiveness in JDM (59)	English	NA; self-administration	NA	(59)
	INQoL (IBM) (25)	High content and construct validity (25, 60, 61)	High test-retest reliability	Low responsiveness	English, Italian	NA	NA	(62)
	PGA (patient/parents)	Good construct validity in JDM (63)		Excellent responsiveness $\geq 20\%$ improvement is consensus of clinically meaningful change (68)		Language is not important: scale is numerical	High; self-administration or by interview, < 1 min	High; < 1 min
Physical function	HAQ-DI (15)	Fair construct validity (3, 64, 67); validated in JDM, not adult			English	High; 20 items, available online	High; available online	(45, 65, 67–72)
	CHAQ (27)	High construct validity in JDM (73, 74)	Moderate test-retest reliability, internal consistency only available for JM (84)	High responsiveness	English	Low; 10 min to compile, available free online	Low; 10 min to compile, available free online	(55, 66, 71, 75–77)
	Hap (78, 79)	High; no data on content validity. Low correlation to VO2-max in PM			English	NA; 94 listed activities	NA	(80)
	MAP (16, 34)	Moderate content validity; correlates highly to HAQ, moderately to FI (muscle function), low or no correlation to VAS effect on well-being, CPK levels (16)	Moderate test-retest reliability, moderate to strong internal consistency (16)	Poor responsiveness in 1 short-term exercise study (45); moderate responsiveness in a 12-wk endurance exercise study (39)	English, Swedish	Low; 32 items (English); 31 items (Swedish)	Low	(39, 45)
	MACTAR semi structured interview (14)	High construct validity (14)		No data in myositis	Swedish, Dutch	High; administered only by interviewer	High	(39)

Table 1. Continued.

Domain	Outcome Measure	Truth Validity	OMERACT Filter 1.0					
			Discrimination Reliability	Ability to Detect Change	Language of Scale as Adopted and Used in Myositis	Feasibility Respondent Burden	Administrative Burden	Studies using Outcome Measure
	NSS (IBM) 28			High responsiveness (validated in 1 study) 81	English	NA; 20 items	NA	(28, 81–84)
	ALSFRS (IBM) (29)			Limited data of responsiveness	English	NA; 11 items	NA	(62)
	IBMFRS (24)	Moderate construct validity		Very responsive in 1 therapeutic trial (84)	English	NA; 10 items	NA	(84)
	Convery Assessment Scale (85)			Low responsiveness based on 2 studies (103, 104)	English	NA	NA	(86–87)
	ADL Barthel Index (30)			High responsiveness based on 1 study (34, 37)	English	NA	NA	(88)
Pain	VAS 10 [visual (66) and numeric (65)]			Low responsiveness based on 2 studies	Language not important	High; easy to use; minimal time commitment	High; minimal time commitment	(72, 83)
	Short form McGill Pain Questionnaire (89)			High responsiveness	English	NA; 16 items	NA	
Fatigue	Chalder Fatigue Score (90)			High responsiveness	English	NA	NA	
	MAF (91)			Low responsiveness	English	NA; 16 items	NA	(80)
	POMS-F (92)			Low responsiveness	English	NA; 7 items	NA	(80)

Medical Outcome Study Short Form-36 health survey questionnaire (SF-36); Child Health Questionnaire (CHQ); Nottingham Health Profile (NHP); Pediatric Quality of Life Inventory (PedsQL); Individual Neuromuscular Quality of Life Questionnaire (INQoL); HAQ-DI (Health Assessment Questionnaire-Disability Index); CHAQ (Child Health Assessment Questionnaire); HAP (Human Activity Profile); MAP: Myositis Activities Profile; MACTAR (McMaster Toronto Arthritis Patients Preference Questionnaire); Neuromuscular Symptom and Disability Functional Score (NSS); ALSFRS (Amyotrophic Lateral Sclerosis Functional Rating Scale); IBM Functional Rating Scale (IBMFRS); MAF (Multidimensional Assessment of Fatigue); POMS-F (Profile of Mood States-Fatigue scale); JDM: Juvenile dermatomyositis; VAS: visual analog scale; PGA: patient/parent global assessment; IBM: inclusion body myositis; NA: not available; CPK: creatine phosphokinase; ADL: activities of daily living; PM: polymyositis; FI: functional index.

The PROM used in juvenile myositis (e.g., CHAQ and CHQ) have been more extensively validated than those for adult IIM. The SF-36 and HAQ-DI were not validated in IIM; however, the SF-36 has good construct and criterion validity, according to our definition, and good feasibility, but discrimination is not defined<sup>20</sup>. HAQ-DI has only good feasibility and fair construct validity. Only 1 PROM used in myositis was specifically developed for adult PM or DM (MAP)<sup>16</sup>, and 1 was validated for adult PM and DM (MACTAR semistructured interview)<sup>14</sup>.

*Truth, discrimination, and feasibility of PRO in myositis. OMERACT Filter 1.0: MAP and MACTAR.* Only 2 nongeneric, validated PRO have been validated in adult PM and DM, the MAP<sup>16</sup>; and the MACTAR<sup>14</sup>, according to the OMERACT Filter<sup>21</sup>. Alexanderson, *et al* created the disease-specific MAP questionnaire to assess limitations, difficulty, and importance in daily activities of PM and DM in adult patients in Sweden<sup>16</sup>. The MAP consists of 31 items divided into 4 subscales (movement, moving around, personal hygiene, domestic) and 4 single items (social activities, avoiding overexertion, work/school, leisure activities).

Each subscale is scored separately. The MAP has been translated into English and studied in US patients with PM and DM<sup>34</sup>.

The MACTAR was originally developed for patients with RA as a self-administered questionnaire<sup>35</sup>. A French version was also used in systemic sclerosis<sup>36</sup>. The MACTAR was later adapted into a semistructured interview format that requires administration by a trained interviewer. Its validity and responsiveness was demonstrated in a multicenter randomized trial of RA<sup>37</sup>. The MACTAR interview consists of 1 patient-preference part, in which patients are asked to identify disabilities in relation to their rheumatic condition that they deem important to improve, and a second part with predefined items relating to global health, QOL, physical function, social function, and emotional function<sup>14,37</sup>. In contrast to traditional fixed-item questionnaires, the ability to rank items by importance is felt by some to provide a more individualized assessment of function. The MACTAR was translated into Swedish and adapted to the Swedish context<sup>14</sup> according to the process described by Guillemin<sup>38</sup> and was recently found to be

responsive in detecting improvements in patient preference following intensive endurance exercise in established PM and DM<sup>39</sup>.

**Truth:** The first draft of the MAP included 81 activities from the International Classification of Functioning Disability and Handicap<sup>40</sup>. These activities were selected by healthcare providers involved in the clinical care of patients with myositis as being the most relevant for individuals living in the Western world and affected with these conditions. Ten patients, selected to represent men and women and various disease duration, disease activity, and life situations, rated their difficulty with each activity and the importance of being able to perform each in daily life; as well, they were encouraged to add any important activities. Separate visual analog scales (VAS) for difficulty and importance were combined to a median value ranging from 0–10, with 10 as severe difficulty/very high importance. Thirty-seven items met or exceeded a cutoff of  $\geq 6$ , and were taken forward to a second draft. Altogether, 6 activities were omitted because of internal redundancy or poor internal consistency, resulting in a third draft containing 31 items, which was tested in 32 consecutive patients with PM or DM with other referent physical function questionnaires. The MAP correlated best with HAQ and Arthritis Impact Measurement Scales Health Status Questionnaire<sup>41</sup>, with Spearman correlation coefficients ranging from 0.51–0.70. Lower correlations were observed for measures of muscle impairment<sup>42</sup>, disease effect on well-being (assessed on a 100 mm VAS), and serum CPK. The MAP was translated into English and evaluated in 64 US patients with PM and DM and validated according to the same process as the original Swedish MAP, with the only difference that patients rated difficulty and importance of all the 31 included items, while also adding any activity of choice in an open question at the end of the questionnaire. This process revealed a slightly lower cutoff for combined difficulty and importance of activities of  $> 5$  for inclusion in the second draft of the MAP, which was found valid and reliable<sup>34</sup>.

The MACTAR interview has not been presented to patients with myositis for evaluation of content validity, and no analyses of internal redundancy or internal consistency have been performed<sup>14</sup>. Twenty-eight patients with established, stable PM and DM performed the MACTAR interview; Spearman correlation analysis revealed moderate to high correlation to SF-36 domains: mental health, social functioning, and role-emotional (0.67–0.73), with lower correlations to measures of ADL (the HAQ and MAP), muscle impairment by manual muscle testing, a strength test of 8 muscle groups<sup>43</sup>, Functional Index-2<sup>44</sup>, and disease activity (6-item core set)<sup>5</sup>.

**Discrimination:** Seventeen of the 31 patients with stable myositis disease activity completed the third draft of the

MAP twice within 1 week for test-retest evaluation of reliability. Weighted kappa coefficients ranged between 0.56–0.77 for subscales and single items without systematic variations. MAP was used in 1 small 7-week resistance training study in patients with PM and DM leading to improved muscle function and reduced disease activity<sup>45</sup>, but no statistically significant change was obtained on a group level compared to baseline. However, 2 patients were responders according to criteria defined as improvement in at least 2 scale steps in at least 1 subscale or single item<sup>45</sup>. There are no data on specificity, error of measurement, or cutoff scores of the MAP. The weighted kappa coefficient of the Swedish MACTAR interview total score was 0.68 without systematic variation, and the intraclass correlation coefficient was 0.83, revealing a measurement error of 3.28 in PM and DM. There are to date no data published on responsiveness of the MACTAR in myositis.

**Feasibility:** The MAP has low patient and observer burden; it only takes about 5 min to complete and about 5 min to calculate by hand. The MAP is available free of charge, but so far only in Swedish and American English. It has been validated as to content and construct validity, and test-retest reliability for a US context, also demonstrating good item fit according to Cronbach's alpha analysis<sup>34</sup>. The MACTAR interview takes about 15 min to complete; however, the need for a trained interviewer and a complicated scoring system hamper its feasibility<sup>14</sup>.

The relative strengths and weaknesses of the MAP and the MACTAR were discussed during the SIG session at OMERACT 11. One advantage of the MAP is that patients were involved in the development process; however, the originating list of items presented to patients came from experts selecting items from the International Classification of Functioning, Disability and Health framework, although patients were encouraged to add any activities of choice in an open question. It is possible that qualitative studies may have been useful for revealing additional important areas. Presenting the questionnaire to patients again would further strengthen the validity of the MAP. Further, CPK was used as a surrogate marker for myositis disease activity; the relevance of CPK as an anchor can be questioned.

When the Swedish MAP was developed, the IMACS consensus 6-item core sets for disease activity measures<sup>20</sup> were not yet available. However, the American MAP was validated using the IMACS 6-item core set. The MAP was considered an easy-to-use measure, but feasibility is hampered to date because it has not yet been adapted to several languages and cultures. A limitation of the MACTAR is that patients were not involved in the development process, neither in the original nor the Swedish version. This measure also needs to be presented to patients for evaluation of relevance. It is important to note that each of these measures is primarily focused on activities and

physical function, although the MAP includes additional areas.

*Myositis patients' perspectives of symptoms.* While it is imperative to derive the PRO-related information directly from patients, the majority of PRO are created by physicians and based on their point of view, including physicians' understanding of their patients' experiences.

*Patient research partner perspective.* A PRP who participated in the focus group conducted at Johns Hopkins and who attended the OMERACT 11 meeting in May 2012 shared with the OMERACT attendees her experience of living with myositis over 4 years. She discussed the effect of initial uncertainties in diagnosis, 47 days of hospitalizations and intensive care unit requirements, challenges in identifying medications to control her symptoms, and specific symptoms and changes in her life as a result of her condition. Her comments were directly transcribed.

With my muscle issues, the hardest thing has been dealing with how my life has changed, seemingly overnight, and adjusting to the fact that I have to have an oxygen bottle with me wherever I go and the slowness of my movement and the fatigue. It's been hard to deal with my loss of my vitality.

She also poignantly discussed the effects of her illness on her family and social network: "I don't think I could've survived or be as well as I am now, if I did not have their [my family's] help and support." She emphasized the shared experience of patients with myositis in the focus group she attended.

I found it to be very liberating to sit and talk with people that know what it's like to have this disease and deal with it. The things we discussed [in the focus group included] pain, fatigue, shortness of breath, personal outlooks, and again the loss of vitality that each one of us share in such a personal way.

She said she was at times overwhelmed by her experience as a new OMERACT attendee, but that she had improved her understanding of the research process and nomenclature: "I think that the objectives of the doctors are very sound and a lot of goodwill comes from their research."

*Focus group results.* The initial focus group of patients with myositis comprised 6 women and 1 man ranging in age from 33 to 69 years (mean 45 yrs). Six patients were white and 1 was Asian; disease duration ranged from 2 to 24 years. Patient global assessment, pain, fatigue, and stiffness were recorded on a 100 mm VAS. The mean scores were 35.7 for patient global assessment, 15.4 for pain, 54.6 for fatigue, and 40.9 for stiffness; the mean HAQ score for the group was 0.61 (range 0–1.5). In this initial focus group, high-level themes identified included pain, physical tightness/stiffness and flexibility, fatigue, emotional consequence of the illness, the effect of the disease on relationships, and treatment-related side effects. It is notable that with the exception of fatigue, and to some extent the social

effects as measured in the MAP, these domains have not been previously evaluated in patients with IIM.

As noted, healthcare providers are traditionally taught that "typical" symptoms in IIM are painless weakness. However, there was widespread acknowledgment by the patients with myositis in the focus groups and from our PRP that pain was an important component of many patients' disease experiences. Quotes illustrative of the identified theme of pain: "There is plenty of pain." "But it's a pain; it's a better way to say it. It's not stiffness; it's...a bone thing. It's like tightening up..." "...the pain is one my body would feel like someone just either scalded you with red-hot water, just constant burning..." "Another feeling in a different area, depending where I was complaining about, felt like someone just had a thousand straight pins and just stuck it, just brutal pain." "And I always think of...a board with a million needles on it and someone's just like pressing on my legs or...because when your leg falls asleep you think of pins and needles, but it's not that pins and needles of being asleep."

Pain is the most prominent symptom in most musculoskeletal diseases, but there has been limited evaluation of this symptom in patients with myositis. These dramatic descriptions of pain from this first focus group suggest that this is a manifestation that requires further study. It highlights that domains identified as important by healthcare providers to assess in myositis do not necessarily reflect areas that are most important to patients. While these are preliminary data derived from a single focus group, additional focus groups are currently under way internationally, and analyses will be conducted to better describe and understand the range and nature of patient perspectives.

In moving toward a comprehensive PRO assessment in myositis, foundational qualitative studies are needed to develop a conceptual framework for the patient's experience. Adding to the complexity of myositis is the greater heterogeneity in terms of extramuscular manifestations of disease that may also affect various aspects of HRQOL.

*Discussion and voting.* At the Myositis SIG meeting, there was consensus that the MAP does not meet the OMERACT Filter 1.0 because of the absence of direct patient input on item selection, and that the MAP will need to be presented to patients at a future SIG meeting to strengthen content validity. There was overwhelming support that the Myositis SIG was worthwhile to continue, but that voting on specific PROM at this preliminary stage was premature.

It was decided that we should begin by including only PM and DM and to have focus groups that have representations from both rather than separate the groups by disease phenotype. Because IBM differs clinically and is likely to yield a different set of PRO (e.g., distal muscle weakness), it was decided that IBM would be studied after PRO were defined for PM and DM. It was also decided that children



would not be included at this time, given the additional expertise and resources required for PROM development and validation in children, but that this would remain a future consideration. Further discussion at the 2012 annual meeting of the EULAR suggested that future focus groups should be constructed to include male participants, disease presence for at least 1 year, varied employment and educational status, and varied levels of education when possible. As DM and PM often coexist with ILD<sup>2</sup>, it was felt that patients with severe ILD with oxygen dependence should not be initially included given the difficulty in distinguishing outcomes related to ILD and those related to the underlying myositis (e.g., fatigue). Thus, this important comorbidity will be addressed specifically by the connective tissue disease (CTD)-ILD group. It was suggested that groups should last about 1.5 to 2 h with an anticipation of 90 min of active discussion. While free discussion was encouraged, the group intends to provide all focus group leaders with a set of potential questions to prompt discussion.

## DISCUSSION

Most studies and PROM have focused on physical function measures largely generated by healthcare providers in the absence of patients. Recently, an extensive review on outcome measures in IIM outlined the measurement properties of a large number of clinical outcome measures used in myositis, of which 6 were PROM, confirming that there are very limited data on measurement properties of the often-used HAQ and SF-36 in adult myositis, but that the CHAQ has been extensively studied in juvenile dermatomyositis<sup>20</sup>. Our preliminary results from 1 focus group suggest that while not usually considered as a symptom in reference to myositis, pain is frequently reported by patients. Other important themes included the identification of fatigue as a central issue that affects the ability to perform activities and to participate in social roles. Preliminary descriptive statistics from studies in myositis have reported that fatigue is frequently encountered in patients with PM and DM<sup>46,47,48</sup>.

*Symptoms in myositis.* There was consensus among SIG meeting participants that extensive qualitative work is needed, specifically additional focus groups to understand the patient perspective on myositis and define core domains for myositis. These focus groups are planned at multiple centers in the United States and in countries in Europe and Asia. The results will be discussed at future group meetings. These investigations will guide the development or use of clinical outcome measures in myositis and will likely reveal symptoms previously unappreciated by providers.

*Disease-specific and validated PRO for myositis.* The MAP had been available only in Swedish, but the American adaptation has been published<sup>34</sup>. To meet the Filter 1.0, the Swedish and American MAP should be again presented to

patients to ensure content validity. To further validate responsiveness, the Swedish MAP is currently used as a complement to the HAQ in standard clinical care and research in Sweden and for the same purpose the American MAP should also be included in US-led clinical trials. To broaden the availability of the MAP, translation to other languages and adaptation to other cultures is needed. Otherwise, to date, myositis-specific indices are limited to IBM in the form of the IBMFRS<sup>24</sup>. A similar effort to translate the IBMFRS and adapt it for other cultures, followed by inclusion in trials where possible, should be a research priority, given that IBM is expected to be added later as a separate group.

Finally, as stated, ILD can coexist with myositis, as in the case of our PRP. Because there is ongoing OMERACT work in CTD-ILD in which patients with myositis have participated, it is reasonable to consider reviewing those transcripts specifically to determine whether other themes regarding myositis may have emerged. The presentations at OMERACT and subsequent discussions have allowed the group to develop an active research agenda (Table 2).

The Filter 1.0 framework provided a useful construct in which to evaluate the extant PRO that have been used in myositis and related neuromuscular disorders, with only 2 instruments ever validated specifically in inflammatory muscle disease. The expanded Filter 2.0 framework provides a more overarching approach to development of core sets of outcome measures. The work of this SIG has been concentrated under the conceptual area of effect of health conditions, more specifically within the core area of life effect measures to better understand how (and what) to measure from the patient's perspective of living with myositis and its comorbidities. The group elected to first focus on 2 key diseases, DM and PM. Although our work was initiated before development of the OMERACT Filter 2, we followed the outline that has subsequently been delineated toward the development of core domain sets, in our case a core domain set of PROM. We initiated our studies with a review of current domains and instruments used to evaluate HRQOL in myositis. Because we focused on patient perspective, there was obligatory inclusion of patients in the initial identification of relevant domains, which we have begun to obtain through our qualitative studies. The next steps toward the development of a draft core domain set will require additional studies in patients with IIM that are representative of different aspects of the disease (e.g., with and without lung disease, level of disability, disease duration) in order to ensure that all potentially relevant domains are identified. The IMACS group has separately engaged healthcare providers in the identification of important areas.

Our preliminary qualitative studies have identified a number of relevant contextual factors that will be important to address in future studies, including the influence of

Table 2. Research agenda.

Qualitative studies to include the range of patient experiences and perspectives in adult patients with polymyositis and dermatomyositis.

Identification of additional myositis investigators and patient research partners  
Collaboration with IMACS activities regarding fatigue and pain assessment in myositis  
Analysis of SF-36 data collected in previous myositis studies and clinical trials  
Review of other PRO instruments related to muscle function from neurology literature  
Identification of settings for use (e.g., clinical trials, longitudinal observational studies) and relevant contextual factors (e.g., extramuscular manifestations) that may influence interpretation of PRO so that the new OMERACT Filter 2.0 can be addressed  
Defining referent “gold standards” and study designs that are needed to conduct validation studies of myositis PRO

IMACS: International Myositis Assessment and Clinical Studies Group; PRO: patient reported outcomes; SF-36: Medical Outcome Study Short Form-36 Survey.

disease-related and individual contextual factors (e.g., the coexistence of ILD, disease duration, social support, and coping strategies). As the work of this SIG moves forward, the development of a conceptual framework of the patient’s experience of myositis will be important to determine the optimal domains and instruments to measure relevant aspects.

With this framework in mind, we plan to start at the level of the patient to identify the most important domains and develop psychometrically grounded items and anchors based on cognitively debriefing.

Because we have highlighted the problems with a generic HRQOL instrument (e.g., determining which subscores of the SF-36 are most applicable), we will move toward appreciation of participation and disease effect<sup>17,18</sup>. Patient ranking and appreciation of patient relevant versus healthcare-provider rated are highly valued; however, they will be examined through an iterative Delphi process, to achieve consensus between proportional groups (e.g., physician and PRP). It is hoped that the work of this OMERACT SIG will distill those aspects of health that are most important to patients with myositis. This may then help to inform a conceptual framework for IIM, within which patient-relevant domains can be identified, instruments developed/tested, and measures validated in randomized controlled trials and longitudinal observational study settings. This information will provide a much needed and richer understanding of these complex illnesses from the patient’s perspective.

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