Outcome Domains for Studies of Acute and Chronic Gout

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ABSTRACT. Discussion and voting at OMERACT 9 confirmed 5 essential domains for outcomes of acute gout: pain, joint swelling, joint tenderness, patient global assessment and activity limitations. For studies in chronic gout 7 essential domains are: serum urate, acute gout attacks, tophus burden, health-related quality of life, activity limitations, pain, and patient global assessment. Implications of patient perspectives, discretionary domains for specific studies, measurement instruments and a possible responder index are under study. (J Rheumatol 2009;36:2342–5; doi:10.3899/jrheum.090370)

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There has been increased interest and attention paid to gout, motivated in part by improved understanding of the pathogenesis of gouty inflammation[1], new insights into the genetics of hyperuricemia[2,3] and the introduction and investigation of potentially important new interventions[4,5]. Previous meetings of investigators in the OMERACT gout group[6] have highlighted the paucity of validated outcome measures for evaluation of either acute gout or the longterm management of chronic gout in clinical trials. As an important first step, it was necessary to define the relevant domains for outcome measurement in both of these contexts. At the second meeting of a special interest group (SIG) at OMERACT 8 in 2006 a preliminary list of proposed domains was developed and published[7].

Taylor, *et al*[8] followed this with a modified Delphi exercise to assess the importance of the domains proposed by the SIG. During 3 iterations, 30 rheumatologists and 3 industry representatives rated the domains for both acute and chronic gout. Consensus was defined as a UCLA RAND disagreement index of less than 1. Outcome domains considered essential for acute gout were pain, patient global, physician global, joint swelling, joint tenderness, and functional disability. Essential domains for chronic gout were listed as serum urate, flares, tophus regression, health related quality of life, functional disability, pain, patient global, physician global, work disability, and joint inflammation.

Methods. A two-and-half hour workshop at OMERACT 9 addressed domains for both acute and chronic gout and some initial evaluation of measures. A 15-minute presentation reviewed the current state of the proposed domains. Two separate, hour-long breakout groups discussed the acute and chronic domains and then reported back to the assembled workshop composed of participants from all groups at OMERACT 9. At the General Assembly plenary session each domain proposed as essential was voted upon. The OMERACT convention had required that 70% of participants vote in favor of a particular domain for it to be retained.

Results. Seventy-seven attendees voted on the proposed

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domains. The breakouts had discussed and proposed some revision to the domains. Five domains were voted as essential for acute gout and 7 for chronic gout (Table 1). Based on consensus from discussions in the breakouts and in the assembled workshop minor clarifications were suggested. The term "activities limitation" was preferred over "functional disability"[9]. For chronic gout, serum uric acid was noted as an essential but surrogate domain that has yet to be proven to coincide with outcomes of concern to patients. The term "acute gout attacks" was preferred over "flares," since translation of "flare" into some non-English languages was thought to be problematic. Figures 1 and 2 illustrate the results of voting to identify essential domains in the inner circle, or ovals, with these minor revisions. Outer ovals include those domains receiving < 70% of votes as well as domains from the previous Delphi exercise, which had not received consideration as essential in the voting. These outer domains were felt to merit consideration for inclusion in selected clinical trials.

Discussion. A multistage process with gout experts and OMERACT 9 participants has been included in the discussion at a special interest group, a formal Delphi process between OMERACT meetings, and a small group/plenary discussion that concluded with plenary voting at OMERACT 9. This led to identification of the listed core domains for outcome measurement in clinical studies of acute and chronic gout.

Information concerning patients' perspective on what is important to them was not presented in plenary sessions at OMERACT because of timetable restrictions, but this was discussed at a meeting of the gout group, which was also attended by 3 patient partners with gout. Data from semi-structured interviews with gout patients in Barcelona, Spain (n = 31) (Diaz-Torne, personal communication); and Gainesville, FL (n = 30) and Cincinnati, OH (n = 49) (Edwards, McTigue, Khanna, Ginsberg, personal communication) showed that the principal concerns of patients with gout were loss of mobility, pain, emotional stress, sleep interference, fear of medication side effects, work and social limitations, joint swelling and deformities, dietary restrictions, and dependency upon others. The most frequently prioritized concerns were pain and mobility problems. These concerns were mostly represented in the proposed core outcome domains and were strongly endorsed by the patient partners present during the group discussion.

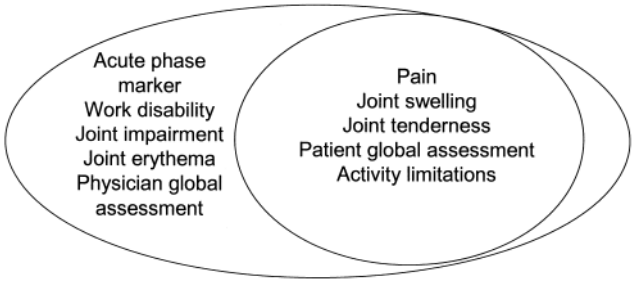

Figure 1. Acute gout studies. Proposed outcome domains in studies of acute gout (domains in the inner oval are mandatory, in the outer oval, discretionary).

An additional means of obtaining the perspective of patients was represented by the International Classification of Functioning, Disability and Health (ICF) core-sets approach, in which categories of the impact of disease were selected for special relevance to a particular disease. The process by which core sets were developed includes patients' perspectives gathered by a standardized quantitative and qualitative methodology[10]. This work has not been accomplished for gout specifically, but an ICF core-set was developed for acute inflammatory arthritis, which explicitly included crystal-associated disease[11]. The ICF Brief Core Set for Body Functions, Body Structures, Activities, Participation and Environmental Factors included 40 ICF categories listed in Table 2. Many of these categories may not be relevant to acute gout, and others do not clearly fall within the domains selected by the OMERACT process. Further work is required to resolve any important omissions from the OMERACT domains highlighted by the ICF Brief Core Set.

The possible importance of developing a responder index or indices was introduced and will be one area for further investigation. For acute gout, pain was identified as the most important domain and it would thus need to carry increased

Table 1. Plenary voting (n = 77) for proposed core (inner circle) domains for gout.

Acute gout	In Agreement, %	Chronic gout	In Agreement, %
Pain	96	Serum uric acid	83
Joint swelling	79	Flare of gout	84
Joint tenderness	72	Tophus burden	89
Patient global assessment	83	HRQOL	70
Physician global assessment	62	Pain	84
Functional disability	75	Functional disability	77
		Patient global assessment	79
		Physician global assessment	51
		Work disability	49
		Joint inflammation	61

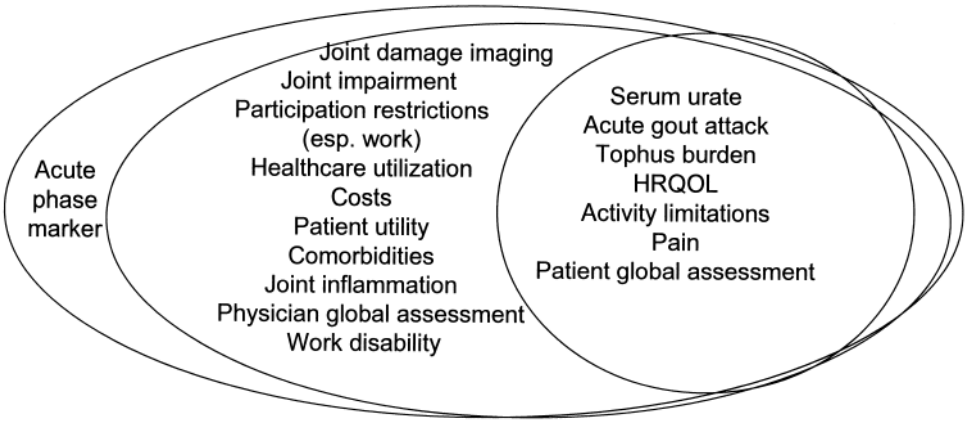

Figure 2. Chronic gout studies. Proposed outcome domains in studies of chronic gout (domains in the inner circle are mandatory; in the next oval, discretionary; and in the outer oval, for research).

Table 2. The International Classification of Functioning, Disability and Health (ICF) brief core set for acute inflammatory arthritis.

ICF code	Category Description	Potentially represented within proposed acute gout domains
b126	Temperament and personality factors	X
b130	Energy and drive functions	X
b134	Sleep functions	X
b152	Emotional functions	X
b280	Sensation of pain	Pain
b415	Blood vessel functions	X
b430	Haematological system functions	X
b435	Immunological system functions	Acute phase marker
b440	Respiration functions	X
b455	Exercise tolerance functions	X
b710	Mobility of joint functions	Joint impairment
b715	Stability of joint functions	Joint impairment
b730	Muscle power functions	X
b780	Sensations related to muscles and movement functions	X
s220	Structure of the eyeball	X
s710	Structure of the head and neck region	X
s720	Structure of the shoulder region	Joint tenderness
s730	Structure of the upper extremity	Joint swelling, tenderness, erythema
s740	Structure of the pelvic region	X
s750	Structure of the lower extremity	Joint swelling, tenderness, erythema
s760	Structure of the trunk	X
s770	Additional musculoskeletal structures relating to movement	X
s810	Structure of areas of skin	X
d230	Carrying out a daily routine	Activity limitations
d410	Changing a basic body position	Activity limitations
d440	Fine hand use (picking up, grasping)	Activity limitations
d445	Hand and arm use	Activity limitations
d450	Walking	Activity limitations
d510	Washing oneself	Activity limitations
d530	Toileting	Activity limitations
d540	Dressing	Activity limitations
d550	Eating	Activity limitations
d845	Acquiring, keeping and terminating a job	Work disability
e110	Products or substances for personal consumption	X
e115	Products and technology for personal use in daily living	X
e120	Products and technology for personal indoor and outdoor mobility	X
e340	Personal care providers and personal assistants	X
e355	Health professionals	X
e410	Individual attitudes of immediate family members	X
e580	Health services, systems and policies	X

weight in any index. A 10-point Likert scale was generally favored for measuring pain, but the adequacy of instruments for measuring in other domains is an area for further development. For various measures at joints, the question whether we should measure a target joint or all joints still needs to be resolved. Progress in validation of measurement instruments is the subject of a companion paper[12].

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