Evaluation of an Instrument Assessing Influence of Gout on Health-Related Quality of Life

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ABSTRACT. ***Objective.*** To evaluate the reliability and validity of an instrument assessing the influence of gout (acute and chronic) on health-related quality of life (HRQOL).

Methods. Focus groups were used to examine the content of an existing Gout Assessment Questionnaire ($GAQ_{1.0}$). $GAQ_{2.0}$ was developed, consisting of a section describing the impact of gout on HRQOL [Gout Impact (GI)] and 4 sections describing subjects' gout overall and demographic data. The $GAQ_{2.0}$ and the Medical Outcomes Study Short Form-36 Version 2 (SF-36v2) were completed by gout patients in 3 US cities. GI scales were examined using clinical judgment, review of item statistics, Rasch analysis, and confirmatory factor analysis.

Results. Subjects (n = 308) were predominantly male (90.2%), Caucasian (75.9%), with a mean age 62.2 ± 11.8 years. Half the subjects (49.7%) reported ≥ 3 attacks in the past year. Two-week test-retest reliability for each scale was good (0.77 to 0.89) for all 5 GI scales. All scales achieved high sufficient (0.86 to 0.89) or excellent (0.93 to 0.97) ratings based on 10-item adjusted alpha coefficients. Correlations and tests among known groups indicated subjects with more severe gout had higher GI scores (i.e., greater gout impact). GI scores correlated more highly with patient-reported measures of gout severity than the SF-36v2 and several traditional measures of gout severity.

Conclusion. The $GAQ_{2.0}$ is an instrument for measuring the impact of gout on HRQOL. The GI section exhibited acceptable reliability and validity characteristics. Future studies should assess GI responsiveness, minimally important differences, and psychometric properties in other patient populations. (First Release Oct 15 2008; J Rheumatol 2008;35:2406–14; doi:10.3899/jrheum.080506)

Key Indexing Terms:
GOUT QUALITY OF LIFE PSYCHOMETRICS SF-36V2
PATIENT-REPORTED OUTCOMES GOUT ASSESSMENT QUESTIONNAIRE

Gout is a debilitating disease estimated to affect about 2% of those ages 45 to 65 years and 3% of those over 65[1]. Its prevalence appears to be increasing worldwide due to a variety of possible factors (e.g., environment, racial, hereditary)[2]. Although the debilitating physical influence of an acute attack is intuitive, the overall impact of gout on patients' health-related quality of life (HRQOL) has not been well studied. It is estimated that gout resulted in 37 million days of restricted activities during a 3-year period (1979–1981) in the United States[3]. Roughly half of patients participating in a recent gout clinical trial reported, at baseline, that gout interfered with movement, work, recreational activities, and enjoyment of life during an acute attack[4]. A large proportion (43%) of these patients also reported experiencing gout-related pain between acute attacks. Patients with tophaceous gout have reported greater physical functioning disability than those without tophi[5-7]. Two recent studies indicated that patients with chronic stable gout who rated gout as their main health concern also assigned greater disutility to gout and were willing to pay more money each month for a cure than other gout patients[8,9].

A recent review of current measures for assessing gout outcomes acknowledged the importance of assessing patient-reported outcomes (PRO) within gout clinical trials; however, the investigators found only measures for self-reported pain levels and patient global assessment of treatment in the literature[10]. In addition, a study seeking consen-

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sus among rheumatologists included HRQOL in its list of domains to consider as mandatory for studies of chronic gout[11]. Common PRO instruments used in rheumatology such as the Health Assessment Questionnaire (HAQ) and the shorter HAQ Disability Index (HAQ-DI) are able to identify physical disability associated with gout[12]. However, the HAQ-DI assesses only the patient's usual functioning ability over the past week and does not assess the effects of disease on the broader emotional and psychological components of HRQOL. A recently developed PRO, the Gout Assessment Questionnaire ($GAQ_{1.0}$), measures the impact of gout both during and between acute attacks[13]. However, the $GAQ_{1.0}$ has not met the OMERACT (Outcomes Measures in Rheumatology Clinical Trials) filter criteria for robust measurement tools (truth, discrimination, and feasibility) nor the standards for PRO proposed by the US Food and Drug Administration[14,15]. The content of the $GAQ_{1.0}$ was based on a literature review as well as limited clinician and patient interviews. Psychometric testing was conducted using data from 126 subjects enrolled in two Phase 2 trials for an investigational anti-gout agent. Seven domains (scales) of the instrument were identified — gout concern, well-being, gout pain and severity between attacks, productivity, treatment convenience, treatment satisfaction, and treatment bother). Initial testing supported the instrument's reliability, validity, and responsiveness in the clinical trial population studied[13]. Although this was encouraging, several limitations of the initial $GAQ_{1.0}$ remained to be addressed to satisfy the OMERACT filters and to expand its use outside the clinical trial context. Content was based on limited patient input; several of the scales were specific to the clinical trial treatment, and clinical and background data needed for interpretation outside of a clinical trial were not included in the $GAQ_{1.0}$. The objectives of our study were to examine and broaden the content of the $GAQ_{1.0}$ to enhance its use in clinical practice, and to evaluate the psychometric properties of the new $GAQ_{2.0}$ in a large community-based population.

MATERIALS AND METHODS

Generally accepted steps of instrument development and testing were considered for this study[16]. The measurement goal was to assess the impact of gout [chronic and acute (i.e., during attack)] on HRQOL in adult patients. HRQOL domains of physical, emotional, social function, and occupation or work activities were considered, along with clinical symptoms of gout. These domains reflect broad components of HRQOL: physical functioning, social and role functioning, and mental health[17].

Patient interviews. Two focus groups were conducted to examine the full range of the impact of gout (chronic and acute) on patients' daily lives. The objectives were (1) to generate items regarding the effect of gout on patient's daily life; (2) to determine if the questions and domains of the $GAQ_{1.0}$ were relevant, important, and sufficient; and (3) if the format of the $GAQ_{1.0}$ was easy to read, understand, and complete. Patients with acute or chronic gout of varying severity were recruited from investigators' clinics to participate in one of two 90-minute sessions. General working definitions (although not exhaustive) of severity groupings, based on consensus of experienced rheumatologists, were as follows for mild, moderate, and severe gout: Mild = no visible tophi, no chronic gout medications, and fewer than 3 attacks per year; Moderate = no visible tophi, but chronic use of gout medications, or 3 or more attacks per year; Severe = visible tophi, or chronic use of gout medications, and 3 or more attacks per year.

Subjects completed a questionnaire comprising 14 items from the $GAQ_{1.0}$ assessing gout impact on HRQOL (trial-specific questions were deleted) and 18 items related to clinical descriptors, treatment, gout history, and demographic data. An interview guide was used to elicit ways subjects believed gout affected their daily life overall and then in terms of physical function, social interactions, occupational function, and psychological state. Results were recorded (written, audio, video) and reviewed by the authors to identify possible new items and confirm current items of the $GAQ_{1.0}$ to retain. The revised draft $GAQ_{2.0}$ was reviewed by a panel of researchers with expertise in creating and evaluating PRO instruments and 5 rheumatologists. This revised $GAQ_{2.0}$ was pretested with 6 subjects. The final $GAQ_{2.0}$ consisted of a gout impact (GI) section (primarily original $GAQ_{1.0}$ content) and 4 additional sections to collect clinical, background, and economic data to aid interpretation. The GI section of the $GAQ_{2.0}$ assesses the impact of gout on HRQOL domains and was the subject of psychometric testing in this study.

Community validation study. The $GAQ_{2.0}$ was tested in a large, community-based survey of gout patients in 3 US cities, San Diego, Cincinnati, and Minneapolis. The objectives were to (1) confirm the factor structure of the GI section of the $GAQ_{2.0}$ and (2) test the reliability (test-retest and internal consistency) and validity (content and construct) of the GI section for measuring the impact of gout on HRQOL domains in a community-based population.

The sample was recruited from gout patients attending a variety of clinics (e.g., family practice, internal medicine, rheumatology), using physician in-office recruitment, patient response to clinic posters, and local newspaper advertisements. Patients across a broad range of gout severity were sought. Inclusion criteria were age between 18 and 85 years, history or presence of gout as determined by a physician (per American College of Rheumatology preliminary criteria[18]), ability to read and/or understand informed consent and independently complete questionnaires in English, and provision of contact information for the physician currently treating gout.

Patients were enrolled and completed study questionnaires either in-office or by telephone and mail. Subjects completing the questionnaires received a $25 gift card. Twenty percent of subjects were randomly selected to complete a second questionnaire 2 weeks after receipt of their first completed questionnaires and received an additional $15 gift card.

Subjects completed the $GAQ_{2.0}$ and the standard Medical Outcomes Study Short Form 36 Version 2 (SF-36v2). The $GAQ_{2.0}$ consisted of 55 questions divided into 5 sections: impact of gout on HRQOL (GI section: 27 items), descriptors of subject's gout overall (6 items), recent gout attacks (6 items), treatment of gout (4 items), and gout history and demographics (12 items). The GI section responses were Likert-type scales (e.g., strongly agree to strongly disagree; all of the time to none of the time). Questions in other sections were answered via multiple choice, visual analog scale, or write-in responses.

The SF-36v2 is a generic health status measure containing 36 items assessing 8 domains[19]. It consists of 4 physical health scales [physical functioning (10 items), bodily pain (2 items), role limitations due to physical health perceptions (4 items), and general health perceptions (5 items)]; 4 mental health scales [mental health (5 items), role limitations due to emotional problems (3 items), vitality (4 items), and social functioning (2 items)]; and a health transition scale (1 item). The 8 SF-36v2 scales can be summarized into Physical Component Summary (PCS) and Mental Component Summary (MCS) scores[20].

Subjects provided permission to contact their physicians, who were sent a fax to collect data for gout diagnosis and date, diagnosis confirmation method, presence of tophi, study subject's highest and most recent serum urate levels, and physician's subjective rating of gout severity.

Sample size and data analyses. The sample-size target considered the general requirement for confirmatory factor analysis (i.e., 5 to 20 times the number of subjects as instrument items) and indicated a sample of between 135 and 540 would be adequate[21].

Descriptive statistics were calculated for all $GAQ_{2.0}$ variables. Frequency distributions were used to describe the responses to categorical variables. For continuous variables and scales, descriptive statistics included means, standard deviations, and ranges. Scales for the GI section of the $GAQ_{2.0}$ were examined using clinical judgment, review of item statistics (including Rasch analysis), and confirmatory factor analysis. Based on qualitative data from the patient interviews and quantitative data from the earlier study of the $GAQ_{1.0}$ we hypothesized 5 domains: 3 related to gout overall — gout concern overall, medication side effects, and unmet gout treatment need — and 2 related to experiences during an attack — gout concern during attacks and well-being during attacks. Item statistics (item-total scale correlations and alpha coefficient) were first reviewed to determine items that may need to be removed from a scale. Item statistics and Rasch analysis (rating-scale model) were used to test final items of the scales. Values between 1.3 and 0.7 for the mean-square item fit statistics (infit and outfit) were used to identify items to retain in a scale[22]. Infit assesses unexpected responses to items with an item severity near the respondent's disease severity level, while outfit assesses unexpected responses to items with an item severity different from the respondent's disease severity level. Structural equation modeling was used to perform a structural confirmatory factor analysis of the latent structure of the scales of the $GAQ_{2.0}$. The model was constructed so that each of the scales influenced only the items that were associated with it. No other relationships between items or residuals were included in the model. Goodness of fit was assessed by root mean-square measurement error. Scales were scored from 0 to 100, higher scores on each scale indicating "worse condition" or "greater gout impact." Scales were scored if responses were available for at least half of the scale items.

Reliability of the scales was assessed by examining internal consistency (alpha coefficient and Spearman-Brown adjusted alpha to a 10-item scale) and 2-week test-retest intraclass correlation coefficients (ICC) of each scale. Criteria for interpreting alpha coefficients were > 0.90 if excellent and > 0.80 if sufficient[23]. ICC > 0.70 was considered acceptable[24]. Frequency distributions were examined for each question to determine range and normality of response patterns.

Content validity was assessed by patient and rheumatologist reviews of the $GAQ_{2.0}$ during the patient interview phase of the study. Construct validity was evaluated by assessing the degree to which scale scores were associated with measures of gout severity and SF-36v2 scales measuring similar constructs, and by examining differences between known groups of subjects expected to differ based on group membership. Subjects with lower patient-rated or physician-rated severity, attack frequency in past year, and attack pain were hypothesized to have lower (better functioning) GI scale scores. Subjects with lower physical function, role-physical, and bodily pain SF-36v2 scores were expected to have higher (i.e., worse, with greater gout impact) GI scale scores. Subjects with lower role-emotional SF-36v2 scores were expected to have higher (i.e., worse, greater gout impact) GI scale scores. Pearson product-moment correlations < 0.29 were considered to be small, between 0.30 and 0.49 moderate, and > 0.5 large[25]. ANOVA were used to investigate differences on each of the GI scales by serum uric acid (SUA) concentration, occurrence of an attack in past 3 months, and rheumatology versus nonrheumatology physician. *A priori*, subjects with lower SUA concentration, with no attack in the past 3 months, or those being treated by a nonrheumatologist were expected to have lower (i.e., better functioning) GI scale scores.

All study procedures were approved by the University of California, San Diego, San Diego Veterans Administration Medical Center (VAMC), Cincinnati VAMC, University of Cincinnati and Minneapolis VAMC Human Research Protection Programs and met requirements of the US Health Insurance Portability and Accountability Act, and all patients provided informed consent.

Statistical analyses were performed using SPSS version 16.0 (SPSS, Chicago, IL, USA), Win-Steps (MESA Press, Chicago, IL, USA), and AMOS version 16.0 (SPSS) software. Statistical significance was set at $p < 0.05$ for known group comparisons.

RESULTS

Patient interviews. Two focus groups of 10 men with history of established gout of varying severity were conducted in the spring of 2005. Subjects were 52–76 years old, from Asian (4), Caucasian (4), African American (1), and Pacific Island (1) heritage, and were all taking gout medications. Years since gout diagnosis ranged from 1 to 25, and patient-reported gout severity ranged from mild (2) and moderate (5) to severe (3).

Overall, the 14 items assessing gout impact on HRQOL in the focus group questionnaire were deemed important for assessing gout effect on daily life, thus supporting face and content validity. Subjects agreed the questions were easy to understand and complete. However, subjects indicated there were unaddressed areas of gout impact to add. Thus, 6 gout concern items were added to reflect patient experience of additional emotions (anger, depression, happiness), difficulty planning ahead, and feeling of control over their gout. One well-being item was added regarding patients' ability to do what they wanted. Two activity items were added to include social and self-care activities in the productivity concept. Four items were added about medications (positive and negative effects). The resulting 27 items became the GI section of the $GAQ_{2.0}$.

Community validation study. A total of 371 subjects were enrolled in the study assessing the $GAQ_{2.0}$. Of these, 63 (17.0%) did not meet inclusion screening and were dropped or did not return questionnaires, leaving 308 subjects with usable data. A total of 298 (96.8%) subjects completed both $GAQ_{2.0}$ and SF-36v2 and were included in the reliability and validity analyses. Sixty-five (21.8%) of these subjects completed 2-week retest questionnaires ($GAQ_{2.0}$ and SF-36v2).

Physician gout confirmation forms were obtained for 226 subjects (73.4%), with gout diagnosis confirmed for 203 (89.8%; 73% by SUA level and clinical examination, 17% by positive urate-crystal joint aspirate, and 10% by radiographic finding consistent with gout). Of these, 59.1% were treated by a rheumatologist, the mean (SD) most recent SUA level was 7.07 ± 1.90 mg/dl, 26.0% had tophi, and physicians considered gout to be mild, moderate or severe for 56.1%, 31.7% and 12.2% of subjects, respectively. Subjects' demographic and disease characteristics are presented in Table 1.

Scales of the GI. Three items from the "gout concern overall" domain were deleted based on poor item statistics and clinical judgment. Each had poor item to total scale correlations (0.26, –0.51, and –0.08), and the internal consistency of the scale improved with each deletion (Table 2). Confirmatory factor analysis was conducted on the remaining 24 items. Item statistics were acceptable (Table 3). Item-total scale correlations ranged from 0.42 to 0.87, with the "gout medication side effects" and "unmet gout treatment need" scales having lower values, as would be expected

Table 1. Subjects' self-reported characteristics (total study subjects 308).

Characteristics	n	Question Respondents (%)
Gender	297	
Male		268 (90.2)
Female		29 (9.8)
Race	290	
American Indian		2 (0.7)
Alaska Native		0 (0.0)
Asian		16 (5.5)
Native Hawaiian or other Pacific Islander		5 (1.7)
Black or African American		37 (12.8)
White		220 (75.9)
Other		10 (3.4)
Age, yrs	295	
Mean (± SD)		62.24 (11.75)
Range		28–85
Comorbidities, n (%) Yes		
Hypertension	292	216 (74.0)
Hyperlipidemia	292	172 (58.9)
Kidney problems	278	99 (35.6)
Kidney stones	282	62 (22.0)
Kidney transplant	285	8 (2.8)
Diabetes	287	93 (32.4)
Heart attack or heart failure	286	74 (25.9)
Gout severity, self-reported VAS 0–10	260	
Mean (± SD)		5.42 (3.2)
Range		0.10–10.0
No. of attacks past year, n (%)	296	
Zero		58 (19.6)
1–2		91 (30.7)
3–5		86 (29.1)
6–10		25 (8.4)
> 10		36 (12.2)
Had attack in past 3 months, n (%)	290	
Yes		169 (58.3)
No		121 (41.7)
Gout pain, typical attack (VAS 0–10)	161	
Mean (± SD)		6.72 (2.57)
Range		(0–10)
Type of medication prescribed, n (%)	283	
Medication prescribed (for flares and/or prevention)		262 (92.6)
None prescribed now		21 (7.4)

VAS: visual analog scale.

since these scales had the fewest items. Alpha coefficient if an item was deleted remained stable or decreased, indicating reliability of each scale would not improve if items were deleted. Infit and outfit statistics ranged between 0.74 and 1.32, within the *a priori* specified range, for all but 3 items in the "well-being during attack" scale. These items, which had fit statistics slightly below the *a priori* specified range, were retained because they were deemed to represent concepts important to the patient (e.g., work and recreation). Responses from other patient samples may be used to further investigate and improve these items in the future. The structural confirmatory factor analysis model revealed a root mean-square measurement error of 0.082. Response distributions for each scale were examined for normality, and none deviated significantly, as measured by skewness and kurtosis. The full range of response options was utilized for each GI item, and none of the items appeared to have a floor or ceiling effect. The revised 24-item GI section of the $GAQ_{2.0}$ is presented in the Appendix.

Reliability. Coefficient alpha for the GI scales was sufficient or excellent (0.76 to 0.94) except for "medication side effect" and "unmet gout treatment need" (0.60 and 0.65, respectively; Table 2). All scales achieved a high sufficient (0.86 to 0.89) or excellent (0.93 to 0.97) rating when the 10-item adjusted alpha was considered. Two-week test-retest reliability for each scale was good, ranging from 0.77 to 0.89.

Construct validity. Hypotheses that subjects with lower patient- or physician-rated severity would have lower (better functioning) GI scale scores were generally supported (Table 4). All GI scales were moderately and positively correlated with patient-rated severity (lower gout impact with lower rated gout severity; r = 0.31 to 0.45). Two of the 3 scales related to the overall impact of gout ("gout concern overall," "unmet gout treatment need") were also moderately and positively correlated with physician-rated severity (r = 0.27 and 0.34), while the third ("gout medication side effects") exhibited a small correlation (r = 0.22). Correlation of the 2 "during attack" scales with physician-rated severity was negligible.

Hypotheses that subjects with lower attack frequency and typical attack pain in the last 3 months would report lower (better functioning) GI scores were partially supported (Table 4). Two of the overall impact of gout scales ("gout concern overall" and "unmet gout treatment need") were highly to moderately correlated with attack frequency in the past year (r = 0.51 and 0.43, respectively). The "gout concern overall" scale and one "during attack" scale ("well-being during attack") were moderately correlated with typical attack pain in last 3 months (r = 0.38, and 0.47, respectively).

Hypotheses that subjects with lower physical (physical function, role-physical, bodily pain) and mental (role-emotional) SF-36v2 scores would have higher (i.e., worse, greater gout impact) GI scale scores were only partially supported. When all subjects were considered, small, negative correlations were observed between the 2 "during attack" scales and the physical function and role physical SF-36v2 scales (r = –0.22 to –0.32; Table 5). All GI scales were only weakly correlated with the bodily pain SF-36v2 scale (r = –0.05 to –0.19) and the SF-36v2 PCS (r = –0.10 to –0.20). However, when only subjects who had had an attack in the past 3 months (58.3%, n = 169) were considered, the correlation between the 2 "during attack" GI scales and physical function, role-physical, and bodily pain were higher and reached the moderate range (r = –0.24 to –0.41).

When all subjects were considered, the strongest and most consistent correlation between GI and SF-36v2 scales was observed for the 2 "during attack" scales and the mental SF-36v2 scales, social function, role-emotional, and

Table 2. Internal consistency analysis scale versions.

Scale	No. Items	Items Included or Deleted*	Coefficient alpha	Coefficient alpha – 10**
Overall				
Gout concern overall	7	All items: a-f + m	0.61	0.69
	6	1 a-e + m	0.81	0.87
	5	1 a-e	0.88	0.94
	4	1 a-d	0.93	0.97
Gout medication side effects	2	All items: 1 f and 1 l	0.60	0.88
Unmet gout treatment need	3	All items: 1 j, 1 m, and 1 n	0.65	0.86
During attack				
Well-being during attack	11	All items: 2 a–d, 3 a-g	0.94	0.93
Gout concern during attack	4	All items: 1 g, h, i, k	0.76	0.89

* Item numbers and letters are from GI version used in study and will not match revised version of GI in the Appendix since renumbering occurred when items removed. ** Spearman-Brown adjusted alpha to a 10-item scale.

Table 3. Item statistics.

Item	Item — Total Scale Correlation	Coefficient alpha If Item Deleted	Infit	Outfit
Gout concern overall				
1.a	0.78	0.92	1.32	1.30
1.b	0.82	0.91	1.02	1.02
1.c	0.87	0.89	0.76	0.74
1.d	0.85	0.89	0.86	0.86
Gout medication side effects				
1.f	0.42	NA	1.01	0.96
1.l	0.43	NA	0.99	0.96
Unmet gout treatment need				
1.j	0.43	0.59	1.07	1.09
1.m	0.51	0.47	0.95	0.91
1.n	0.44	0.58	0.99	0.95
Well-being during attack				
2.a	0.66	0.94	1.65	1.38
2.b	0.74	0.94	1.20	1.14
2.c	0.75	0.94	1.03	0.97
2.d	0.70	0.94	1.38	1.27
3.a	0.60	0.94	1.35	1.60
3.b	0.76	0.94	0.78	0.83
3.c	0.71	0.94	1.11	1.34
3.d	0.86	0.93	0.60	0.61
3.e	0.81	0.93	0.69	0.66
3.f	0.81	0.93	0.73	0.77
3.g	0.85	0.93	0.54	0.52
Gout concern during attack				
1.g	0.54	0.72	1.08	1.06
1.h	0.54	0.72	1.02	1.02
1.i	0.65	0.65	0.81	0.80
1.k	0.51	0.73	1.08	1.09

NA: Not applicable since the scale is a 2-item scale.

mental health (r = –0.34 to –0.43; Table 5). Correlation of the "gout concern overall" scale with these 3 SF-36v2 scales also approached moderate magnitude (r = –0.26 to –0.29). Thus, a moderate, or near, correlation was observed for the SF-36v2 MCS for all GI scales except the 2 treatment-related scales ("gout medication side effects" and "unmet gout treatment need"). As with the physical SF-36v2 scales, the correlation for the 2 "during attack" GI scales and the mental health domains of the SF-36v2 was higher when only subjects who had experienced an attack in the past 3 months were considered (r = –0.43 to –0.55).

The patient's rating of their overall gout severity was more highly correlated with all GI scales (r = 0.31 to 0.45) than any of the SF-36v2 scales (r = –0.17 to –0.25) or other traditional measures of gout severity [i.e., recent SUA concentration, presence of tophi, or number of joints involved

Table 4. Construct validity: Pearson correlations gout impact scales versus clinical characteristics. Correlations are for descriptive purposes and were not analyzed for significance.

	Patient-rated Severity, r (n)	Physician-rated Severity, r (n)	Attack Frequency, Past Year, r (n)	Typical Attack Pain, Past 3 Months r (n)
Overall				
Gout concern overall	0.45 (258)	0.27 (178)	0.51 (293)	0.38 (222)
Gout medication side effects	0.31 (257)	0.22 (178)	0.26 (293)	0.13 (222)
Unmet gout treatment need	0.34 (254)	0.34 (177)	0.43 (289)	0.19 (218)
During attack				
Well-being during attack	0.36 (256)	0.02 (174)	0.06 (289)	0.47 (218)
Gout concern during attack	0.45 (258)	0.17 (178)	0.19 (293)	0.21 (222)

Differences in number of subjects for each correlation due to missing item responses (patient-rated severity and attack frequency past year) and lower number of subjects with physician supplied data (physician-rated severity) or lack of attack occurrence past 3 months (typical attack pain past 3 months).

Table 5. Construct validity: Pearson correlations gout impact (GI) versus SF-36v2. Correlations are for descriptive purposes and were not analyzed for significance.

	Physical Function	Role Physical	Bodily Pain	General Health	Vitality	Social Function	Role Emotional	Mental Health	Physical Summary Score	Mental Summary Score
Overall										
Gout concern overall	–0.20 (294)	–0.19 (292)	–0.19 (292)	–0.23 (294)	–0.21 (293)	–0.28 (294)	–0.26 (291)	–0.29 (293)	–0.16 (288)	–0.28 (288)
Gout medication side effects	–0.14 (294)	–0.12 (292)	–0.05 (292)	–0.13 (294)	–0.11 (293)	–0.20 (294)	–0.12 (291)	–0.18 (293)	–0.10 (288)	–0.17 (288)
Unmet gout treatment need	–0.12 (290)	–0.20 (288)	–0.17 (288)	–0.21 (290)	–0.19 (289)	–0.28 (290)	–0.22 (287)	–0.20 (289)	–0.15 (284)	–0.24 (284)
During attack										
Well-being during attack	–.027 (290)	–0.32 (288)	–0.19 (288)	–0.29 (290)	–0.36 (289)	–0.41 (290)	–0.38 (287)	–0.43 (289)	–0.20 (284)	–0.43 (284)
Gout concern during attack	–0.26 (294)	–0.22 (292)	–0.12 (292)	–0.22 (294)	–0.24 (293)	–0.37 (294)	–0.34 (291)	0.42 (293)	–0.13 (288)	–0.39 (288)

in typical attack (r = 0.06, 0.17, and 0.21, respectively)]. Similarly, attack frequency was more highly correlated with the 3 "overall" GI scales (r = 0.26 to 0.51) than the SF-36v2 scales (r = –0.18 to –0.23), except social function (r = –0.28), recent SUA (r = 0.20), and presence of tophi (r = 0.22). The "gout concern overall" and "well being during attack" GI scales were more highly correlated with typical attack pain in past 3 months (r = 0.38 and r = 0.47) than any of the SF-36v2 scales (r = –0.14 to –0.34) or other traditional measures of gout severity [i.e., recent SUA, presence of tophi, number of joints involved in typical attack (r = 0.16, 0.05, and 0.13, respectively)].

Known-groups validity. Generally, hypotheses that subjects with lower SUA and no attack in the past 3 months would have lower (better functioning) GI scale scores were supported for the 3 "overall impact of gout" scales (Table 6). Mean scores for the "gout concern overall" and "unmet gout treatment need" scales were lower for subjects with lower versus higher SUA levels (p = 0.001 and p = 0.012). Mean scores for all 3 overall impact of gout scales were lower for subjects who had not experienced an attack in the past 3 months versus those who had (ps < 0.001).

The "gout concern during attack" was the only "during attack" GI scale that varied significantly among levels of a known group, with subjects with no attack in the past 3 months scoring lower (lower gout impact) than subjects who had experienced an attack (p = 0.001). The hypothesis that subjects being treated by a nonrheumatologist would have lower (better functioning) GI scale scores was not supported since no significant differences in any GI mean scale scores were detected.

DISCUSSION

The purpose of our study was to create an instrument for assessing gout impact (acute and chronic) on HRQOL in clinical practice. We broadened the content of a previously developed gout assessment questionnaire ($GAQ_{1.0}$) and evaluated the psychometric properties of the gout impact (GI) section of the resulting new $GAQ_{2.0}$.

Results of patient interviews identified areas of gout impact to add to the original $GAQ_{1.0}$. Rheumatologist reviews identified clinical and background data needed for interpretation outside a clinical trial setting. PRO expert reviews enhanced the questionnaire structure, content, and

Table 6. Known-groups validity, gout impact (GI) scales for clinical groups.

	Serum Uric Acid Level, < 6, 6-10, > 10 mg/dl		Attack in Past 3 Months, Yes/No		Treating Physician Specialty, Rheumatologist vs Not Rheumatologist	
	F	p	F	p	F	p
Overall						
Gout concern overall	6.80	0.001	97.30	< 0.001	0.300	0.584
Gout medication side effects	0.49	0.614	14.61	< 0.001	1.37	0.244
Unmet gout treatment need	4.54	0.012	50.47	< 0.001	0.006	0.937
During attack						
Well-being during attack	1.45	0.234	0.001	0.981	0.108	0.742
Gout concern during attack	2.13	0.122	12.70	0.001	0.482	0.488

format. The new $GAQ_{2.0}$ consists of 5 sections. The first section allows subjects to describe the impact of gout on HRQOL (GI section), and the remaining 4 allow subjects to describe their gout overall, recent gout attacks, treatment of gout, and gout history and demographics. The revised 24-item GI section comprises 5 scales representing the impact of gout overall and during an attack.

Field testing the $GAQ_{2.0}$ in a community-based sample of gout patients allowed for a fairly robust test of practical administration issues as well as the psychometric properties of the GI portion of the new instrument. Overall, the $GAQ_{2.0}$ proved to be an acceptable instrument for collecting data from a wide variety of patients that would be relevant to community and clinical trial settings. A high response and completion rate indicated patient acceptance and demonstrated the viability of self-administration via a mail survey and in a clinic setting.

The internal consistency and test-retest reliability of scales in the GI portion of the $GAQ_{2.0}$ were acceptable. The 2 shorter scales, "medication side effects" and "unmet gout treatment need," had internal consistency correlations slightly lower than the prespecified level. However, when an alpha coefficient that adjusted for the number of items in a scale was considered, the internal consistency was in the high-sufficient range for each scale. Both these treatment-related scales represent broad constructs and should not be interpreted as measuring a specific medication or treatment's effectiveness. While the reliability of the GI appears adequate for comparisons between groups of subjects, further testing is needed to allow use for individual patient comparisons.

Validity results were generally positive, with all GI scales moderately correlated with patient rating of gout severity. The 3 overall impact scales were also correlated with physician rating of gout severity, although the magnitude was less, which may be expected for several reasons, one of which would be the variable time since patient-physician contact. The most consistent results were observed for the "gout concern overall" scale, which was moderately correlated with all clinical characteristics and differed between almost all known groups tested. The remaining 2 overall gout impact scales ("gout medication side effects" and "unmet gout treatment need") were most closely correlated with patient report of attack frequency. These 2 scales are treatment-related, the success of which would be related to frequency of attack.

The 2 "during attack" scales were most correlated with attack-related variables (e.g., typical attack pain in last 3 months), and the "gout concern during an attack" scale differed significantly between subjects who had versus those who had not had an attack in the past 3 months. The "during attack" scales would be expected to be most related to the within attack experience as opposed to the more global clinical characteristics (e.g., attack frequency) or non-patient-reported variables (e.g., SUA, physician-rated severity).

With regard to the SF-36v2, the strongest correlations were observed between the 2 "during attack" GI scales and mental SF-36v2 scales. Only weak to small correlations were observed between GI scales and physical SF-36v2 scales when all subjects were considered. However, when only subjects who had had an attack in the past 3 months were considered, correlation of GI and physical and mental SF-36v2 scales increased to levels closer to, yet lower than those observed for the function ability focused HAQ-DI in a more severe gout population[12]. The correlations for subjects with an attack in the past 3 months were also similar to those observed in a recent study including 3 well validated migraine-specific HRQOL instruments[26]. The authors in that study reported correlations between 0.26 and 0.32 for each instrument (all scales) and the SF-36v2 PCS scale. Gout, like migraine, is a chronic condition with episodic flares of pain and related symptoms. Therefore, lower correlation between broad, overall measures of physical health may be expected in groups of subjects with a wide range of time since their last attack.

Overall, the stronger correlation of GI scales with patient-reported measures of gout severity than observed for the SF-36v2 scales and other traditional measures of gout severity (i.e., recent SUA level, number of joints involved in typical attack, and presence of tophi) indicate the GI pro-

vides a description of gout impact that more closely reflects the patients' experiences.

Study limitations. Study subjects were from 3 US metropolitan areas, thus study results may not be generalizable to other locations. However, enrolling subjects with rheumatology and nonrheumatology physicians and the high response rate broadens the applicability of results across patients at varying gout severity levels. The study sample size was not overly generous. The items in the $GAQ_{2.0}$ and results of its use may be biased toward Caucasians and male patients, as most patient interviews and field testing were conducted in this group. The cross-sectional design of the study did not allow testing of responsiveness and identification of minimally important differences of the GI section of the $GAQ_{2.0}$. Further, longitudinal testing on a more diverse and larger group of patients is needed.

The $GAQ_{2.0}$ is a PRO instrument for measuring the effects of gout on HRQOL in community-based patient populations. It contains the Gout Impact (GI) section to assess the impact of gout (acute and chronic) on HRQOL as well as sections for collecting clinical and background data. The GI section exhibited acceptable reliability and validity characteristics in a community-based sample of patients. While more developmental and validation work is needed, it is a useful tool that correlates more closely with patient-reported measures of gout severity than the SF-36v2 and several traditional measures of gout severity. A study to further develop and test the GI structure, reliability, and validity in an additional patient population is under way. In addition, the study will evaluate the ability of the GI to detect change in gout severity over time and define its minimally clinical important difference. Future studies should also examine the possibility of a reduced form of the $GAQ_{2.0}$ and its GI section to reduce responder burden.

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REFERENCES

1. Adams PF, Hendershot GE, Marano MA. Current estimates from the National Health Interview Survey, 1996. Washington, DC: National Center for Health Statistics. Vital Health Stat 1999;10:1-212. Available from: http://www.cdc.gov/nchs/data/series/sr_10/sr10_200.pdf.
2. Kim KY, Schumacher HR, Hunsche E, Wertheimer AI, Kong SX. A literature review of the epidemiology and treatment of acute gout. Clin Ther 2003;25:1593-617.
3. Roubenoff R. Gout and hyperuricemia. Rheum Dis Clin North Am 1990;16:539-50.
4. Osterhaus JT, Patel P, Palo W, Bakst A, Joseph-Ridge, N. Patient reported outcomes associated with gout: Baseline results from two clinical trials. American College of Rheumatology Annual Meeting, 2005 San Diego CA.
5. Alvarez-Nemegyei J, Cen-Pisté JC, Medina-Escobedo M, Villanueva-Jorge S. Factors associated with musculoskeletal disability and chronic renal failure in clinically diagnosed primary gout. J Rheumatol 2005;32:1923-7.
6. Vazquez-Mellado J, Cruz J, Guzman S, Casasola-Vargas J, Lino L, Burgos-Vargas R. Severe tophaceous gout. Characterization of low socioeconomic level patients from Mexico. Clin Exp Rheumatol 2006;24:233-8.
7. Geletka RC, Hershfield MS, Scarlett THE, Sundy JS. Severe gout is associated with impaired quality of life and functional status [abstract]. Arthritis Rheum 2004;50 Suppl:S340.
8. Khanna D, Mansoor A, Yontz D, et al. The disutility of chronic gout. Qual Life Res 2008;17:815-22.
9. Khanna D, Mansoor A, Yontz D, Ginsburg SS, Tsevat J. Willingness to pay for a cure in patients with chronic gout. Med Decis Making 2008 Mar 18 [Eub ahead of print].
10. Taylor WJ, Schumacher HR, Singh JA, Grainger R, Dalbeth N. Assessment of outcome in clinical trials of gout — a review of current measures. Rheumatology Oxford 2007;46:1751-6.
11. Taylor WJ, Schumacher HR Jr, Baraf HS, et al. A modified Delphi exercise to determine the extent of consensus with OMERACT outcome domains for studies of acute and chronic Gout. Ann Rheum Dis 2008;67:888-91.
12. Alvarez-Hernandez E, Pelaez-Ballestas I, Vazquez-Mellado J, et al. Validation of the Health Assessment Questionnaire Disability Index in patients with gout. Arthritis Rheum 2008;59:665-9.
13. Colwell HH, Hunt BJ, Pasta D, Palo WA, Mathias SD, Joseph-Ridge N. Gout Assessment Questionnaire: Initial results of reliability, validity and responsiveness. Int J Clin Pract 2006;60:1210-7.
14. Boers M, Brooks P, Strand V, Tugwell P. The OMERACT filter for outcome measures in rheumatology. J Rheumatol 1998;25:198-9.
15. U.S. Department of Health and Human Services. Guidance for industry: Patient-reported outcome measures: use in medical product development to support labeling claims [draft]. Available from: http://www.fda.gov/cder/guidance/5460dft.htm
16. Juniper EF, Guyatt GH, Jaeschke R. How to develop and validate a new health related quality of life instrument. In: Spilker B, editor. Quality of life and pharmacoeconomics in clinical trials. 2nd ed. Philadelphia: Lippincott-Raven Publishers; 1996.
17. Bungay KM, Boyer JG, Ware JE. Health related quality of life: an overview. In: Bootman JL, Townsend R, McGhan WF, editors. Principles of pharmacoeconomics. 3rd ed. Cincinnati: Harvey Whitney Books; 2005.
18. Levin RW, Park J, Ostrov B, et al. Clinical assessment of the 1987 American College of Rheumatology criteria for rheumatoid arthritis. Scand J Rheumatol 1996;25:277-81.
19. Ware JE, Sherbourne CD. The MOS 36-item Short-form Health Survey (SF-36): Conceptual framework and item selection. Med Care 1992;30:473-83.
20. Ware JE, Kosinski M, Dewey JE. How to score version 2 of the SF-36® health survey. Lincoln, RI: Quality Metric Inc.; 2000.
21. Suhr DD. Exploratory or confirmatory factor analysis? Paper 200-31 presented at SUGI 31 Meeting, Statistics and Data Analysis Session, San Francisco, California; 2006 March 26. Internet. Available from: http://www2.sas.com/proceedings/sugi31/200-31.pdf. Accessed Sept 23, 2008.
22. Wright BD, Stone MH. Best test design: Rasch measurement. Chicago: MESA Press; 1979.
23. Nunnally JC, Bernstein IH. Psychometric theory. 3rd ed. New York: McGraw Hill; 1994.
24. Fitzpatrick RD, Buxton MJ, Jones DR. Evaluating patient-based outcome measures for use in clinical trials. Health Technol Assess

APPENDIX

REVISED GOUT IMPACT (GI) SECTION OF $GAQ_{2.0}$

Please answer every question. Read every question carefully and choose the best answer for you. Questions may be answered by filling in a bubble to indicate your choice.
Some questions in this survey are about your gout overall and some are about only the times you are experiencing pain or swelling of your joints due to your gout. Two important terms are used in this survey:

Gout Attack = time when you are experiencing pain or swelling of your joints because of gout. When a question is about a Gout Attack please only think about what it is like for you when you have joint pain or swelling because of your gout.

Gout Overall = times you have a Gout Attack AND the time Between Attacks when you do not have joint pain or swelling because of gout.

ABOUT HOW GOUT AFFECTS YOUR DAILY LIFE OVERALL

1. Please indicate how much you agree or disagree with each of the statements below. (Mark one answer for each statement.)

	Strongly Agree	*Agree*	*Not Certain*	*Disagree*	*Strongly Disagree*
a. I am worried that I will have a gout attack within the next year.	○	○	○	○	○
b. I am afraid that my gout will get worse over time.	○	○	○	○	○
c. I feel anxious that my gout will interfere with my future activities.	○	○	○	○	○
d. I worry that I will not be able to continue to enjoy my leisure activities as a result of my gout.	○	○	○	○	○
e. I am bothered by side effects from my gout medications.	○	○	○	○	○
f. I am mad or angry when I experience a gout attack.	○	○	○	○	○
g. It is difficult to plan ahead for events or activities because I may have a gout attack.	○	○	○	○	○
h. I feel depressed when I experience a gout attack.	○	○	○	○	○
i. My current medications are effective for treating a gout attack when I have one.	○	○	○	○	○
j. I miss planned or important activities when I have a gout attack.	○	○	○	○	○
k. I worry about long term effects of gout medications.	○	○	○	○	○
l. My current medications do not work well to prevent gout attacks from happening.	○	○	○	○	○
m. I have control over my gout.	○	○	○	○	○

2. During your last gout attack, how much of the time did you experience the following? (Mark one answer for each statement.)

	All of the Time (100%)	*Most of the Time*	*Some of the Time* (about 50%)	*A Little of the Time*	*None of the Time* (0%)
a. Miss work because of your gout symptoms?	○	○	○	○	○
b. Have difficulty working because of your gout symptoms?	○	○	○	○	○
c. Have difficulty with recreational or social activities because of your gout symptoms?	○	○	○	○	○
d. Have difficulty with self care activities such as feeding, bathing, or dressing yourself because of your gout symptoms?	○	○	○	○	○

During your last gout attack, how much did your symptoms interfere with the following things? (Mark one answer for each statement.)

	Not a Bit	*A Little Bit*	*Moderately*	*Quite a Bit*	*Extremely*
a. Your mood?	○	○	○	○	○
b. Your ability to move about?	○	○	○	○	○
c. Your sleep?	○	○	○	○	○
d. Your normal work? (including both work outside the home and housework)	○	○	○	○	○
e. Your recreational activities?	○	○	○	○	○
f. Your enjoyment of life?	○	○	○	○	○
g. Your ability to do what you want to do?	○	○	○	○	○

Scales and items: Gout concern overall (4 items, 1 a-d); Gout medication side effects (2 items, 1 e & k); Unmet gout treatment need (3 items, 1 i,l,m); Well being during attack (11 items, 2 a-d 3 a-g); Gout concern during attack (4 items, 1 f,g,h,j)

1998;2:1-74.
25. Cohen J, Cohen P, West SG, Aiken LS. Applied multiple regression/correlation analysis for the behavioral sciences. 2nd ed. Hillsdale, NJ: Lawrence Erlbaum Associates; 2003.
26. Cole JC, Lin P, Rupnow MFT. Validation of the Migraine-Specific Quality of Life Questionnaire, version 2.1 (MSQ v. 2.1) for patients undergoing prophylactic migraine treatment. Qual Life Res 2007;16:1231-7. Epub 2007 Apr 28.