

Which Attributes Are Most and Least Important to Patients When Considering Gout Flare Burden Over Time? A Best-worst Scaling Choice Study

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ABSTRACT. *Objective.* Several factors contribute to the patient experience of gout flares, including pain intensity, duration, frequency, and disability. It is unknown which of these factors are most important to patients when considering flare burden over time, including those related to the cumulative experience of all flares, or the experience of a single worst flare. This study aimed to determine which flare attributes are the most and least important to the patient experience of flare burden over time.

Methods. Participants with gout completed an anonymous online survey. Questions were aimed at identifying which attributes of gout flares, representing both individual and cumulative flare burden, were the most and least important over a hypothetical 6-month period. A best-worst scaling method was used to determine the importance hierarchy of the included attributes.

Results. Fifty participants were included. Difficulty doing usual activities during the worst flare and pain of the worst flare were ranked as the most important, whereas average pain of all flares was considered the least important. Overall, attributes related to the single worst gout flare were considered more important than attributes related to the cumulative impact of all flares.

Conclusion. When thinking about the burden of gout flares over time, patients rank activity limitation and pain experienced during their worst gout flare as the most important contributing factors, whereas factors related to the cumulative impact of all flares over time are relatively less important.

Key Indexing Terms: activities of daily living, gout, outcome assessment, pain

Gout flares are experienced as self-limiting attacks of severe joint pain, swelling, redness, and heat.^{1,2,3,4} Although successful long-term urate-lowering therapy can mitigate the symptoms and burden of gout flares,⁵ many patients experience frequent and painful flares that affect many aspects of their lives, including physical function, social and family life, and physiological well-being.^{6,7} Gout flares are sporadic and unpredictable, with most patients experiencing recurrent flares with pain-free inter-critical periods.

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Key to the long-term management of gout is a focus on reducing flare severity and flare frequency.⁵ Gout flare measurement is therefore an important treatment response criterion. The Outcome Measures in Rheumatology (OMERACT) group considers gout flares as a core outcome domain for long-term studies of gout,⁸ yet how gout flares should be measured in these studies is yet to be determined.⁹

The primary factor contributing to the lack of a standardized method for assessing flare burden over time is the wide variation in the pattern of gout flares. Although a typical gout flare has been classified as reaching maximal pain in 1 day, with resolution of symptoms within 14 days,¹⁰ there is considerable heterogeneity in the pattern of gout flares over time in relation to pain intensity, duration, and frequency.¹¹ Consequently, there is inconsistency in the methods used to measure and report flares in long-term studies of gout.^{6,12,13} The most common method used in clinical trials to capture flares over time is to report the proportion of patients experiencing at least 1 flare during the follow-up period without any further information about flare severity.¹² A very small number of studies also captures patient-reported attributes related to pain severity, such as the average peak pain of individual flares on a 0- to 10-point numerical rating scale, or the total number of days over the follow-up period with a pain score > 5.¹² The variation in methods used to measure and report gout flares over time also makes it difficult to compare therapies across

studies, and demonstrates the need for a consistent measurement tool.

Additionally, it is not known which aspects of the flare experienced over time are of greatest importance to patients, and specifically, whether the cumulative experience of all flares over a follow-up period is more important than the experience of a single flare (e.g., the worst flare). Qualitative research has shown that the patient experience of a gout flare is multidimensional,⁷ and pain, duration, and impact on function all contribute to the overall severity of an individual flare.⁶ Despite the important contribution of activity limitation to the severity of an individual flare,^{6,7} the impact on function due to gout flares is not routinely captured in long-term gout studies.¹² Capturing the patient perception of flare severity in a way that reflects this multidimensional experience would clearly provide a more meaningful representation of the cumulative burden of gout flares over time in long-term studies.

An important step in developing tools to measure flare burden is to understand what patients view as being most important to the burden of gout flares over time. This study aimed to determine which attributes of flares are experienced by patients to be most and least important to the burden of flares over time.

METHODS

Design. This cross-sectional study involved an anonymous online survey using a best-worst scaling (BWS) methodology¹⁴ to identify which attributes of gout flares are the most and least important to patients when considering the burden of flares over time.

Participants. Participants were recruited by email invitation from existing databases of patients with gout (meeting the American College of Rheumatology/European League Against Rheumatism 2015 Gout Classification Criteria¹⁰), who had previously taken part in research at the Clinical Research Centre, University of Auckland, Aotearoa/New Zealand, recruited through public advertising and primary and secondary clinics, and had consented to be contacted for future studies. All invited participants were aged > 18 years and had a good understanding of the English language. Participants were not invited to participate if they had a cognitive impairment or had other forms of autoimmune inflammatory arthritis. Participant information sheets were included in the email invitations and consent to participate was assumed by completion of the survey. Participants represented demographic diversity (age, gender, ethnicity) and gout disease characteristics (disease duration, flare frequency). Ethical approval for the study was obtained from the Auckland Health Research Ethics Committee (AHREC AH3358).

Although sample size calculations are not yet available for BWS methodologies,¹⁵ a minimum of 20 participants has been recommended to estimate reliable models.¹⁶

Selection of gout flare attributes. The selection of gout flare attributes included in the experiment was based on a content analysis of methods used to measure and report gout flare prevention outcomes in long-term clinical trials¹² and from attributes identified as contributing to the burden of individual flares from qualitative interview studies of participants with gout.^{6,7} Four attributes represented the cumulative burden of all flares (average pain of all gout flares, number of gout flares, total number of days of all gout flares, and average difficulty doing usual activities during all gout flares), and 3 attributes represented the burden of individual flares (pain of the worst gout flare, number of days of the longest gout flare, and difficulty doing usual activities during the worst gout flare).

BWS choice experiment. BWS, also known as “object case,” is a conjoint analysis method that provides information on the most preferred but also

least preferred attribute and is used to determine the importance hierarchy of the attributes.¹⁴ BWS has the advantage of including a large number of attributes and is regarded to be less cognitively burdensome than other choice experiment designs.¹⁷

For each choice task, participants were asked to identify the most important and least important attributes that make the overall burden of flares worse for them over a hypothetical 6-month period. An example of a survey question is shown in Figure 1. The experimental design was based on a balanced incomplete block design with 7 items (representing the 7 attributes), and 7 choice tasks with 4 item options in each. Each pair of attributes was compared twice, meaning each attribute appeared in 4 choice tasks in total. The maximum number of times each attribute could have been chosen as most important (or least important), was 200 (50 participants × 4 choice tasks).

The survey was developed through consultation with a patient research partner (PRP) to ensure the wording of the attributes and the survey itself were clear and understandable to patients.

Data collection. All data for the BWS experiment were collected in an online survey using Google Forms (version 0.8). The survey was also used to collect gout history data for all participants including demographic and gout disease characteristics. Prior to the 7 choice tasks, participants were asked to complete some practice questions to familiarize themselves with the attributes of interest. Participants were provided with the following introductory text before beginning the experiment: “We are interested in finding out what is important when deciding how badly gout attacks affect you over time. For this exercise, we would like you to imagine that you have experienced multiple gout attacks over a 6-month period. You will now be shown a total of 7 questions. For each question you will be shown a list of FOUR things. We would like you to select ONE thing that is the most important when deciding how badly gout attacks affect you over the 6-month period. AND we would like you to select ONE thing that is the least important when deciding how badly gout attacks affect you over the 6-month period. You will notice there is some repetition across the questions. Please read each question carefully and answer all the questions. There is no right or wrong answer.”

Data analysis. The BWS analysis was undertaken in RStudio (version 1.3.959; RStudio Team) using the support.BWS package.^{18,19}

This analysis calculated the best (B) and worst (W) scores for each attribute representing the number of times that attribute was chosen as most and least important, respectively. The best-minus-worst (BW) score was also calculated to rank the attributes from most to least important. In addition, mean BW scores were calculated for each attribute, with positive values indicating the attribute being chosen more often as most important, and negative values indicating the attribute being chosen more often as least important. To standardize the score, the BW score was divided by the total number of occurrences of that attribute and adjusted for the sample size,²⁰ resulting in a value ranging from -1 to 1. Finally, the standardized BW ratio score was calculated as the square root of the total best score divided by the total worst score, resulting in a coefficient indicating the choice probability relative to the most important attribute, which was given a coefficient of 1.00.^{17,21,22}

Finally, a conditional logit model was fitted to the data to explore all pairwise comparisons between the variables. Estimated coefficients (β) and their standard errors were reported alongside the asymptotic *t* value and *P* value (under the null hypothesis, in which the coefficient is zero) to demonstrate which items were significantly more important for each comparison.

RESULTS

Participant characteristics. A total of 147 patients were invited by email to participate in the online survey, and of these, 57 (39%) responded to the online survey. Data from 7 participants were excluded due to incomplete responses, leaving a total of 50 participants included in the analysis. Demographic and gout

Which ONE is the most important when deciding how badly gout attacks affect you over a 6-month period? And which ONE is the least important when deciding how badly gout attacks affect you over a 6-month period?

	Most important	Least important
Pain of your 'worst' gout attack over the 6 months	<input type="radio"/>	<input type="radio"/>
Average pain of all your gout attacks over the 6 months	<input type="radio"/>	<input type="radio"/>
Difficulty doing your usual activities during your 'worst' gout attack over the last 6 months	<input type="radio"/>	<input type="radio"/>
Number of days of your longest gout attack over the last 6 months	<input type="radio"/>	<input type="radio"/>

Figure 1. Example of a survey question for best-worst scaling analysis.

disease characteristics of the included participants are shown in Table 1. The majority of participants were New Zealand European middle-aged males and 90% had experienced at least 1 gout flare in the previous 12 months, with 58% experiencing 1–4 gout flares in the previous 6 months.

Attributes of gout flares most important to the burden of flares. BWS count statistics for each attribute are shown in Table 2. Difficulty doing usual activities during the worst gout flare was ranked as the most important attribute contributing to the burden of flares over the hypothetical 6-month period, evident by the highest mean BW score of 1.46. The second most important attribute was pain of the worst gout flare (mean BW score = 1.20). The least important attribute was the average pain of all gout flares, with the lowest mean BW score of –1.90, followed by the number of gout flares (mean BW score = –0.48) and the total number of days of all gout flares (mean BW score = –0.38). The number of days of the longest gout flare and the average difficulty doing usual activity during all gout flares were attributes of neither high nor low importance, with mean BW scores close to zero (0.06 and 0.04, respectively). Supplementary Figure 1 (available with the online version of this article) illustrates the consistency and level of agreement among all the participants in selecting the most and least important attributes. Average pain of all flares was most consistently ranked by all participants, whereas the greatest variation in importance ranking was observed for the total number of days of all flares.

Figure 2 shows the mean BW scores for each attribute. Attributes representing individual flares were more important to participants when considering the burden of flares over time compared to attributes representing cumulative flares.

Results from the conditional logit model are shown in Table 3. There was no significant difference in ranking between the 2 highest ranked attributes (difficulty doing usual activity during the worst gout flare, and pain of the worst gout flare; $P = 0.36$).

However, both these attributes were ranked significantly higher than the remaining attributes (all $P < 0.001$). The lowest-ranked attribute (average pain of all gout flares) was ranked significantly lower than all other attributes (all $P < 0.001$). There was no significant difference in ranking between number of days of the longest flare, average difficulty of doing usual activity during all gout flares, and number of gout flares (all $P > 0.07$).

DISCUSSION

This study investigated gout flare attributes that were most and least important to patients when considering the burden of flares over a hypothetical 6-month period. Patients ranked the activity limitation and pain experienced during their worst gout flare as the most important factor in considering flare burden over time, whereas attributes related to the cumulative impact of all flares over time were ranked as least important.

The results from this study suggest that when thinking about gout flares experienced during a previous time period, patients focus on the experience of the worst gout flare. Qualitative research has shown that the severity of gout flares can vary considerably from flare to flare.⁶ Severe flares are associated with excruciating pain, resulting in extreme difficulty walking and carrying out activities of daily living, whereas symptoms of more mild flares are described as uncomfortable, with patients still able to perform most daily tasks.⁶ Therefore, it seems plausible that factors associated with a patient's worst gout flare are more influential to overall flare burden compared to the average impact of multiple flares, which may include flares of more mild severity.

In the current study, participants ranked the activity limitation and pain experienced during their worst gout flare as the most important factors contributing to the burden of flares over time. This aligns with previous qualitative research that has highlighted the effect of activity limitation on the patient's day-to-day

Table 1. Participant characteristics (n = 50).

	Median (range) or n (%)
Sex	
Male	46 (92)
Female	4 (8)
Age, yrs	60 (38–83)
Ethnicity	
Asian	4 (8)
Māori	4 (8)
NZ European	33 (66)
Pacific peoples	3 (6)
Other	6 (12)
Disease duration, yrs	10 (1–54)
No. of gout flares in the preceding 6 months	
0	11 (22)
1–4	29 (58)
5–9	5 (10)
≥ 10	5 (10)
Tophaceous gout	17 (34)
Time since last gout flare, months	
< 1	3 (6)
1–4	28 (56)
5–8	11 (22)
9–12	3 (6)
> 12	5 (10)
Currently experiencing a gout flare	
Yes	5 (10)
No	44 (88)
Not sure	1 (2)
Gout medication ^a	
Allopurinol	45 (90)
Probenecid	1 (2)
Colchicine	13 (26)
Prednisone	4 (8)
Pain medication	4 (8)
None of the above	2 (4)
I don't know what medications I am taking	5 (10)

^a 19 participants were on > 1 medication. NZ: New Zealand.

Table 2. Summary of best-worst scaling count statistics for each attribute.

	B	W	BW	Rank	Mean BW	Mean Standardized BW	Standardized BW Ratio Score (√BW)
Difficulty doing usual activities during worst gout flare	93	20	73	1	1.46	0.37	1.00
Pain of worst gout flare	80	20	60	2	1.20	0.30	0.93
No. of days of the longest gout flare	41	38	3	3	0.06	0.02	0.48
Average difficulty doing usual activity during all gout flares	50	48	2	4	0.04	0.01	0.47
Total no. of days of all gout flares	40	59	–19	5	–0.38	–0.10	0.38
No. of gout flares	38	62	–24	6	–0.48	–0.12	0.36
Average pain of all gout flares	8	103	–95	7	–1.90	–0.48	0.13

B = best score: number of times each attribute was chosen as most important across all choice tasks it appeared in; W = worst score: number of times that each attribute was chosen as least important across all choice tasks it appeared in; BW = best-minus-worst score (positive values indicate the attribute was chosen more often as most important; negative values indicate the attribute was chosen most often as least important); mean standardized BW = calculated by dividing the BW score by the total number of occurrences of that attribute and adjusted for the sample size, resulting in a value ranging from –1 to 1; standardized BW ratio score = calculated as the square root of the total best score divided by the total worst score, resulting in a coefficient indicating the choice probability relative to the most important attribute, which was given a coefficient of 1.00.

life, including house- and yardwork, family and social activities, and lost work days.^{2,7,23} Despite the importance of this attribute, outcomes related to activity limitation experienced during gout flares are not consistently included in long-term studies of gout flare prevention.^{12,13} The importance of factors related to the worst flare is also consistent with the peak-end theory, in which recalled experiences are dependent on the peak (most intense) point and how the experience ended, rather than the average of the experience or the amount of time one is engaged in that experience.^{24,25} Time to onset of peak pain was not included as an attribute in the current study; however, according to this theory, gout flares that peak in severity early, followed by a gradual resolution phase, may be recalled as less painful than those which peak in severity at the end.^{24,25}

Mean number of gout flares, total number of days in flare, and the mean duration of gout flares, which are common flare prevention outcomes measured and reported in antiinflammatory prophylaxis studies,¹² appear to be less important to patients when considering flare burden over time. This finding supports the variable nature of flare severity and may reflect the finding that a single severe flare is perceived as more important to the overall flare burden than more frequent and lengthy flares of mild severity.

This study has some limitations. First, it should be noted that patients were instructed to imagine a hypothetical scenario when considering the importance of the various flare attributes, and it is possible that patients may have recalled their previous flare experiences during the survey. Considering that patients' remembered experiences may differ from their actual experiences,^{24,25} it should be recognized that undertaking a study of patients experiencing a flare in real time may provide different results. In addition, participants were recruited from a clinical research center in Aotearoa/New Zealand, and only one-third of people invited to participate successfully did so. While efforts were made to avoid selection bias, we cannot be certain that the results are generalizable to all patients with gout. The study population consisted primarily of New Zealand European

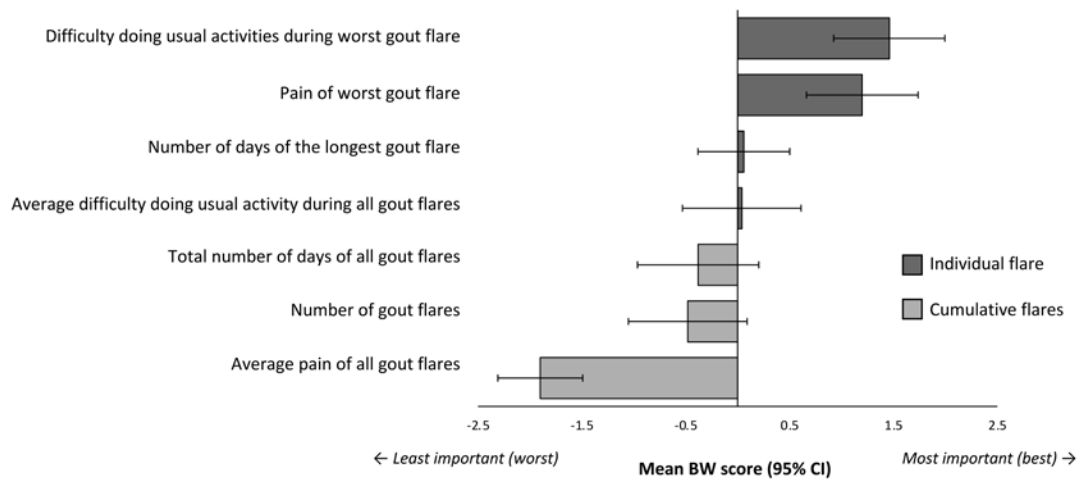


Figure 2. Bar chart showing mean best-worst (BW) scores (95% CI) for each attribute. Positive scores indicate that attribute was chosen more frequently as the most important, while negative scores indicate that attribute was chosen more frequently as the least important.

men, and while this is representative of the largest group of people in Aotearoa/New Zealand with gout, it is possible that the experience of women or other ethnic groups may differ; for example, Maori and Pacific peoples in Aotearoa/New Zealand experience frequent flares and high burden of severe disease.²⁶ Further, only 20% of the participants who completed the survey reported no history of flares in the previous 12 months, and it may be possible that participants with poorly controlled gout were more motivated to participate. It is also possible that flare history, which was recalled retrospectively, may be influenced by recall bias and may not reflect true flare occurrence. In addition,

BWS surveys can be repetitive and cognitively challenging. Data from 7 participants who responded to the online survey were excluded from analysis due to failure to choose both a “best” and “worst” attribute for each choice task, suggesting that some participants may have had difficulty understanding the instructions provided. However, a PRP was involved in the development of the survey to ensure it was clear and understandable to the target population. Further, there are a number of participant-specific factors that may have contributed to the way the various attributes were ranked, which may explain the degree of heterogeneity observed among participants in the importance

Table 3. Best-worst scaling conditional logit regression results showing pairwise comparisons between all attributes.

		Difficulty Doing Usual Activities During worst Gout Flare	Pain of Worst Gout Flare	No. of Days of the Longest Gout Flare	Average Difficulty Doing Usual Activity During All Gout Flares	Total No. of Days of All Gout Flares	No. of Gout Flares
Pain of worst gout flare	β	-0.13	-	-	-	-	-
	SE	0.14					
	<i>P</i>	0.36					
No. of days of the longest gout flare	β	-0.69	-0.56	-	-	-	-
	SE	0.14	0.14				
	<i>P</i>	< 0.001	< 0.001				
Average difficulty doing usual activity during all gout flares	β	-0.69	-0.56	0.00	-	-	-
	SE	0.14	0.14	0.14			
	<i>P</i>	< 0.001	< 0.001	0.99			
Total no. of days of all gout flares	β	-0.88	-0.75	-0.20	-0.20	-	-
	SE	0.14	0.14	0.14	0.14		
	<i>P</i>	< 0.001	< 0.001	0.16	0.16		
No. of gout flares	β	-0.93	-0.80	-0.24	-0.25	-0.05	-
	SE	0.14	0.14	0.14	0.14	0.14	
	<i>P</i>	< 0.001	< 0.001	0.08	0.07	0.70	
Average pain of all gout flares	β	-1.64	-1.51	-0.95	-0.95	-0.75	-0.70
	SE	0.15	0.15	0.15	0.15	0.14	0.14
	<i>P</i>	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001

β = conditional logit regression coefficient. Negative β values indicate attributes in column 1 are less important compared to attributes in row 1. Values in bold are statistically significant. SE: standard error of β .

hierarchy of some of the attributes. Unfortunately, the sample size in the current study was not sufficiently powered to examine this statistically.¹⁶ Future research may therefore explore whether factors such as employment status and demographic or gout disease characteristics, including flare history, influence patient perspectives on gout flare burden. Current flare status has shown to influence patient perceptions of disease activity.²⁷

In conclusion, when thinking about the burden of gout flares over time, patients rank activity limitation and pain experienced during their worst gout flare as the most important contributing factors, whereas factors related to the cumulative impact of all flares over time are relatively less important. Future studies investigating gout flare prevention should consider capturing outcomes related to the worst gout flare experienced during the follow-up period, specifically those related to activity limitation and pain.

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ONLINE SUPPLEMENT

Supplementary material accompanies the online version of this article.

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