

What Represents Treatment Efficacy in Long-term Studies of Gout Flare Prevention? An Interview Study of People With Gout

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ABSTRACT. *Objective.* The patient experience of gout flares is multidimensional, with several contributing factors including pain intensity, duration, and frequency. There is currently no consistent method for reporting gout flare burden in long-term studies. This study aimed to determine which factors contribute to patient perceptions of treatment efficacy in long-term studies of gout flare prevention.

Methods. This study involved face-to-face interviews with people with gout using visual representations of gout flare patterns. Participants were shown different flare scenarios over a hypothetical 6-month treatment period that portrayed varying flare frequency, pain intensity, and flare duration. The participants were asked to indicate and discuss which scenario they believed was most indicative of successful treatment over time. Quantitative data relating to the proportion of participants selecting each scenario were reported using descriptive statistics. A qualitative descriptive approach was used to code and categorize the data from the interview transcripts.

Results. Twenty-two people with gout participated in the semistructured interviews. All 3 factors of pain intensity, flare duration, and flare frequency influenced participants' perception of treatment efficacy. However, a shorter flare duration was the most common indicator of successful treatment, with half of participants (n = 11, 50%) selecting the scenario with a shorter flare duration over those with less painful flares.

Conclusion. Flare duration, flare frequency, and pain severity are all taken into account by patients with gout when considering treatment efficacy over time. Long-term studies of gout should ideally capture all these factors to better represent patients' experience of treatment success.

Key Indexing Terms: flare, gout, treatment efficacy

Gout is a common inflammatory arthritis caused by monosodium urate crystal deposition in tissues¹ and is characterized by episodes of painful joint inflammation known as *gout flares*. Gout flares are sporadic and unpredictable, with patients typically experiencing recurrent flares interspersed with pain-free intercritical periods. The patient experience of gout flares is multidimensional, causing major disability and affecting many

aspects of the patients' lives, including physical function, social and family life, physiological well-being, and self-care.^{2,3}

Measurement of gout flares is recognized by the Outcome Measures in Rheumatology (OMERACT) group as a core outcome domain for clinical research investigating the long-term treatment of gout.⁴ However, there is no standardized method for measuring flare burden over time in clinical trials, and there is inconsistency in the methods used to measure and report flares in long-term studies of gout flare prevention.⁵

Measurement of gout flares is made particularly challenging by the wide variation in flare patterns over time, which differ in frequency, pain intensity, and flare duration.⁶ 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.⁷ The multidimensional patient experience of gout flares clearly goes far beyond what is routinely measured in research or clinical settings.^{7,8} There is also discordance evident between physicians and patients on the presence of a gout flare, where patient-reported flares associated with less pain, swelling, and warmth are not regarded as flares by physicians.⁹

There is a need to establish a standardized method for measuring gout flares that can be used in clinical research

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investigating the efficacy of treatments targeting flare prevention. An important step is to gain an understanding of which aspects of gout flares are most important to patients when considering treatment efficacy. This knowledge would allow research, management, and treatment of patients with gout to more accurately address and target areas of most concern to patients experiencing flares. This study aimed to determine which factors contribute to patient perceptions of treatment efficacy in long-term studies of gout flare prevention.

METHODS

Design. This study involved semistructured face-to-face interviews with people with gout using visual representations of gout flare patterns. A critical realism epistemological position was used to analyze the data to understand which factors of gout flares are considered to be indicative of treatment efficacy over time.

Participants. Ethical approval for the study was obtained from the University of Auckland Human Participants Ethics Committee (UAHPEC 023965). Participants in this study were recruited for a qualitative interview study, which has been reported previously.² The sample size in the study was determined by a purposive sampling framework to ensure a broad and diverse representation of demographic variables (age, ethnicity, sex) and gout disease characteristics (disease duration, tophaceous gout, flare frequency). Recruitment occurred concurrently with analysis and continued until theoretical saturation was reached. In brief, patients with gout according to the American College of Rheumatology/European League Against Rheumatism 2015 Gout Classification Criteria¹⁰ were recruited from existing databases of patients with gout who have participated in research at the Clinical Research Centre, University of Auckland, and had consented to be contacted for future studies. The inclusion criteria were age over 18 years and English speaking. Participants were excluded if they had a cognitive impairment or had other forms of autoimmune inflammatory arthritis. The sampling framework ensured that participants represented demographic diversity (age, sex, ethnicity) and gout disease characteristics (disease duration, flare frequency).

Data collection. In-depth, semistructured face-to-face interviews were conducted by a rheumatologist who was not involved in the medical care of the participants (AGG). The interviews took place in a private room at the Clinical Research Centre, University of Auckland, and lasted between 20 and 45 minutes.² The portion of the interviews analyzed in the current study were aimed at understanding how the following 3 factors of gout flares over time are considered by patients to be indicative of successful treatment: pain severity, flare duration, and flare frequency. These factors were chosen based on the current reporting of flare prevention outcomes in gout studies.⁷

The participants were asked to imagine they were taking part in a study testing a new treatment, which aimed to reduce gout flares over a 6-month period. Each participant was presented with 3 different scenarios representing 3 flare patterns over the treatment period: "A single gout flare, which reaches a maximum pain of 10 and lasts 1 week long" (Scenario 1); "A single gout flare, which reaches a maximum pain of 5 and lasts 2 weeks long" (Scenario 2); and "Two gout flares, with each reaching a maximum pain of 5 and lasting 1 week long" (Scenario 3). Participants were also shown each of the 3 scenarios in the form of graphs with time on the X-axis and pain on the Y-axis, providing a visual representation of the scenarios (Figure 1). The 3 flare scenarios were developed by 2 rheumatologists with expertise in gout research (WJT, ND). The scenarios were designed based on data collected through daily flare diaries during a 6-month gout trial and reflect the variable patterns of gout flares over time.⁶ For each visual representation, the area under the pain-time curve was the same. The participants were asked to indicate the scenario that they believed indicated the treatment was working the best and the reason why. An interview schedule containing key focused, open-ended questions and probes was used to encourage conversation.

Each interview was audio-recorded, transcribed ad verbatim, and anonymized to ensure confidentiality. Participants had the opportunity to review the transcripts to check for completeness and representativeness. Demographic and clinical data were also obtained during the participants' study visit, including age at gout onset, ethnicity, gout flares, and treatment history.

Data analysis. Quantitative data relating to the proportion of participants selecting each scenario were reported using descriptive statistics. A qualitative descriptive approach guided study design. Thematic analysis was used to code and categorize the data from the interview transcripts under 3 predetermined themes (pain severity, flare frequency, flare duration). This approach reflects the flexibility of thematic analysis, which allows coding of data to fit within a predetermined framework driven by the researcher's analytic interest in the area.¹¹ The themes were chosen based on the current reporting of flare prevention outcomes in gout studies⁷ and reflect the intentional differences between the 3 flare scenarios used in the interviews. Transcripts were initially coded by a single researcher (JH) using Nvivo software (QSR International Property Ltd., Version 12). Initial coding was reviewed by 2 researchers (SS, ND), and final coding was agreed upon by all authors. Illustrative quotes from transcripts were selected to provide evidence for each theme.

RESULTS

Participant characteristics. A total of 25 eligible patients with gout were invited to participate, of whom 3 declined; 22 participated in the interviews. Demographic and gout disease characteristics are shown in Table 1. The majority of participants were New Zealand European middle-aged males. All participants had experienced at least 1 gout flare in the previous 12 months.

Attributes of gout flares indicative of treatment success. Scenario 1 (a single gout flare that reaches a maximum pain of 10 and lasts 1 week long) was perceived by half of participants (n = 11, 50%) as being indicative of the most successful treatment, followed by Scenario 3 (2 gout flares, each reaching a maximum pain of 5 and each lasting 1 week long) by 8 (36%) participants, and Scenario 2 (a gout flare which reaches a maximum pain of 5 and lasts 2 weeks long) by 3 (14%) participants. Participants commented on flare duration, pain severity, and flare frequency when considering which gout flare scenario was most indicative of successful treatment. Illustrative quotes are shown in Table 2.

Duration. The duration of the flare was the most commonly mentioned attribute considered by patients who perceived Scenario 1 as being most indicative of successful treatment, despite having a maximum pain severity score of 10: "Although the pain is more severe, it only lasts 1 week, rather than having a mild [one that] lasts longer. ... It's probably better having a gout flare for a short amount of time rather than ongoing." (Patient 19, M, 30 yrs). The idea of a gout flare being ongoing and lingering was a key concern for patients, who preferred to get it "over and done with," even if it meant they would get another flare later on (Scenario 3). A shorter flare duration was also considered important to treatment success, because flares of longer duration meant some participants had to take more time off work.

Pain severity. The lower severity of gout flare pain in Scenarios 2 and 3 was the most important attribute for patients who perceived these scenarios as being most indicative of treatment success over Scenario 1, which had a higher pain severity. A gout flare with less pain severity was considered more manageable

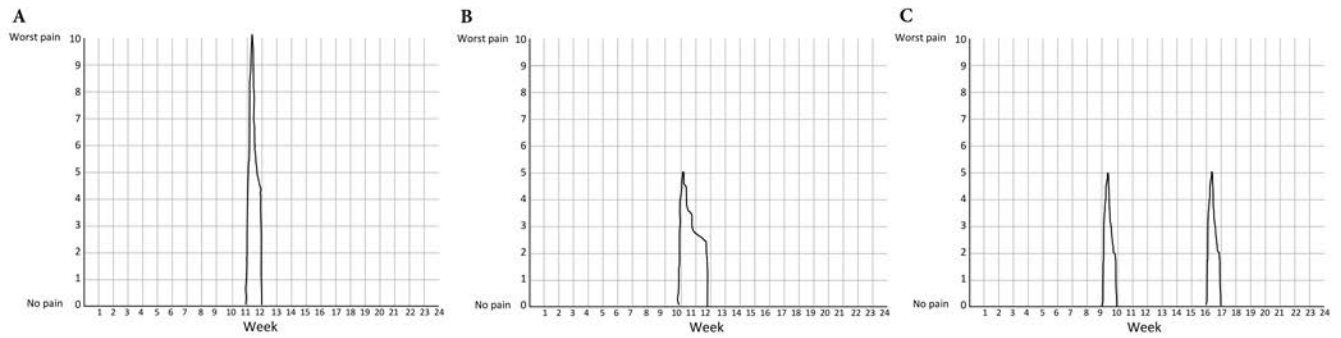


Figure 1. Visual representations of the 3 gout flare scenarios over a hypothetical 6-month period. (A) A single flare with a maximum pain of 10, lasting 1 week. (B) A single flare with a maximum pain of 5, lasting 2 weeks. (C) Two flares with a maximum pain of 5, each lasting 1 week.

Table 1. Participant demographic and clinical characteristics (n = 22).

	Values
Sex, n (%)	
Male	17 (77)
Female	5 (24)
Age, yrs, median (range)	67 (27–84)
Ethnicity, n (%)	
NZ European	12 (55)
Māori	5 (23)
Asian	3 (14)
Pacific Peoples	2 (9)
Disease duration, yrs, mean (range)	11 (0.5–35)
Current urate-lowering therapy, n (%)	20 (91)
Age at onset of gout, yrs, mean (range)	49 (20–81)
No. of flares in the last 6 months, n (%)	
1–4	16 (73)
5–9	2 (9)
≥ 10	4 (18)

by some patients, even if it was for a longer duration: “I would rather have one that’s not so severe, lasting a little bit longer—you know, you can sort of manage it” (Patient 8, M, 44 yrs). Less severe pain allowed participants to engage in a greater level of function and undertake some activities that they would have difficulty with if the pain were more severe. For 1 patient, a flare with severe pain affected his ability to work: “You know, ‘cause working at the prison, I was driving a truck—well, I can’t drive [with a severe flare]” (Patient 8, M, 44 yrs).

Frequency. The single flares in Scenarios 1 and 2 were considered a more successful outcome than multiple flares: “I’d rather deal with it once, you know—yep. I’d rather deal with it once and then be gone with it” (Patient 14, M, 60 yrs). The same patient also commented that if a treatment were successful, “the time between the flare-ups would become longer and longer” (Patient 14, M, 60 yrs). Having a second flare after a period of no flares also made patients frustrated and feel that the treatment was not working.

Table 2. Illustrative quotes of flare attributes considered indicative of treatment success.

Pain severity	<p>“A pain score of 5 is manageable, and for 2 weeks.” [Patient 3, M, 59 yrs]</p> <p>“You’ve got 2 independent flares, each lasting a week and it’s only at 5—well, it’s better than a week of 10, I can assure you.” [Patient 10, M, 73 yrs]</p> <p>“If I compare 5 and 10—a pain of 5 compared to what I reckon was a 10—I could sit around and probably do a lot of things I couldn’t do with [a pain of 10].” [Patient 10, M, 73 yrs]</p> <p>“I would rather have one that’s not so severe, lasting a little bit longer—you know, you can sort of manage it.” [Patient 8, M, 44 yrs]</p>
Flare duration	<p>“You can’t have so much time off work, you know, so I’d rather have [an] intense [flare] lasting a shorter time.” [Patient 8, M, 44 yrs]</p> <p>“Two weeks to recover just sounds horrible...I’d rather have a shorter, sharper pain at the beginning, and then have it go away faster, than have it linger for 2 weeks.” [Patient 12, M, 48 yrs]</p> <p>“I’d prefer to get it over and done within a week, and if it means I’m still going to get another one, I’ll put up with that rather than having it for 2 weeks.” [Patient 1, M, 74 yrs]</p> <p>“A gout flare that lasts for 2 weeks is about...13 days too long.” [Patient 1, M, 74 yrs]</p>
Frequency	<p>“Because it’s just 1 flare-up... I wouldn’t want 2 gout flares.” [Patient 3, M, 59 yrs]</p> <p>“I think I would [have] known the medication is working, if maybe I had a flare of once a week, and then it’s only once a month, and then maybe for 3 months, nothing.” [Patient 4, M, 59 yrs]</p> <p>“Psychologically, you feel like you’ve actually got rid of it, then it comes back again. And so, I think that’s quite frustrating...you feel like you’ve healed yourself and then it comes back again...then you kind of have to go back to the drawing board.” [Patient 11, M, 58 yrs]</p>

DISCUSSION

This study investigated factors associated with gout flares that are perceived by patients with gout to be the most indicative of successful treatment. Flare duration, flare frequency, and pain severity all influenced how patients perceived treatment success. Although these factors are interrelated, flare duration appeared to be an important factor when patients were considering treatment efficacy.

Some patients were willing to experience more severe pain, such as a pain score of 10 compared to that of 5, if the duration of the flare were shorter. A recurrent idea highlighted among patients in the current study was the notion of not wanting to deal with the flare any longer than they had to. The main reasons behind this were the effect that flare duration had on the individual's ability to work, socialize, and even carry out simple tasks around the home. Flare duration is rarely measured and reported in long-term gout studies,⁷ and reporting methods are inconsistent, with authors reporting either the mean duration of individual flares or the total number of gout flare days over the follow-up period.

In the current study, patients selected scenarios with single flares as indicative of treatment success over those with multiple flares, suggesting that frequency of flares does play a role in whether patients perceive treatment to be working. This finding is consistent with existing qualitative research in which more frequent flares have a greater impact on work life and taking days off work, psychological well-being, and the ability to plan in advance.³ A quantitative survey of 1100 people with gout also reported a reduction in perceived treatment satisfaction as the number of flares increased.¹² However, two-thirds of patients who experienced 5 or more flares in the previous year also reported satisfaction with treatment,¹² highlighting the importance of factors other than flare frequency that may be driving patient-perceived treatment efficacy. Pain severity appeared to be the least influential of the 3 factors perceived as indicative of treatment efficacy. Pain severity is a dominant theme in the overall patient experience of gout^{2,3} and is recommended by OMERACT as a mandatory outcome measure for both acute studies of gout flares and studies investigating the long-term management of gout.⁴ The current findings suggest that a reduction in flare pain severity alone may not be as important to patients with gout when thinking about treatment success; duration and frequency of the flares must also be considered.

This study explored the patient perspective on what factors influence treatment efficacy; however, there are limitations with the study. First, although the 3 flare scenarios were based on data collected from patient flare diaries,⁶ patient research partners were not directly involved in the design of the scenarios. In addition, although the sample size was small with only 22 participants, this was a qualitative study in which recruitment and analysis occurred simultaneously, with qualitative experts stating new information is rarely generated after interviewing 20 participants.¹² The majority of these participants were New Zealand European middle-aged males and despite these findings aligning with the trends in gout prevalence, generalizability of the findings may be reduced for people with gout of non-European

ethnicity. The influence of participant characteristics (including sex) and disease characteristics (including flare history and comorbidities) on patient-perceived treatment efficacy was also not examined as part of this study; it therefore remains unknown whether such factors play a role. Further, all participants in this study were recruited from databases of patients with gout who had participated in previous research, including trials of urate-lowering therapy; this may have influenced their perceptions of the importance of the flare characteristics examined in the current study. Additionally, this study only investigated the influence of pain severity, flare duration, and flare frequency. Other factors not assessed in the current study, including activity limitation, have also been shown to be important to the burden of flares^{2,3} and may have influenced the perception of treatment success. Finally, it remains unclear whether factors related to an individual flare (i.e., the worst flare) or the cumulative effect of flares over time has greater importance to patients when considering treatment efficacy. Further research is required to address these points in order to develop a standardized tool that comprehensively and consistently captures the burden of gout flares over time.

This study provides a number of novel observations. First, we have shown that flare duration is the most important factor when patients are considering treatment efficacy. In addition, pain severity, although important, was the least influential of the 3 factors in patients' perceptions of treatment success. This is a novel finding and suggests that patients prefer to have flares of shorter duration and less frequency, rather than less pain. Considering that flare duration is not routinely measured in long-term studies of gout, these findings have important implications for future research. Further, these insights will be valuable when developing a standardized tool for capturing flare burden over time in long-term studies of flare prevention.

In conclusion, this study highlights the interrelated factors of flare duration, flare frequency, and pain severity, which are all considered by patients when thinking about treatment efficacy over time. Long-term studies of gout should ideally capture all these factors to better represent patients' perceptions of treatment success.

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