Analysis of gout remission definitions in a randomised controlled trial of colchicine prophylaxis for people with gout initiating allopurinol

Adwoa Dansoa Tabi-Amponsah[1], Lisa K Stamp[2], Anne Horne[1], Jill Drake[3], Sarah Stewart[1,4], Greg Gamble[1], Keith J Petrie[5], Nicola Dalbeth[1]

Key Indexing Terms: Gout, Remission, Colchicine

ADT-A is supported by a University of Auckland Health Research Doctoral Scholarship.

1. A.D. Tabi-Amponsah, BBiomedSc(Hons). A. Horne, MBChB. S. Stewart, PhD. G. Gamble, MSc. N. Dalbeth, MD, FRACP. Department of Medicine, The Faculty of Medical and Health Sciences, University of Auckland, Auckland, New Zealand
2. L. K. Stamp, PhD, FRACP. Department of Medicine, University of Otago, Christchurch, Christchurch, New Zealand
3. J. Drake, RN. Department of Rheumatology, Immunology and Allergy, Te Whatu Ora Health New Zealand Waitaha Canterbury, Christchurch, New Zealand
4. S. Stewart, PhD. School of Clinical Sciences, Faculty of Health and Environmental Sciences, Auckland University of Technology, Auckland, New Zealand.
5. K.J. Petrie, PhD. Department of Psychological Medicine, Faculty of Medical and Health Sciences, University of Auckland

Conflict of interest: Nicola Dalbeth has received consulting or speaker fees from AstraZeneca, Dyve Biosciences, Horizon, Selecta, Arthrosi, JW Pharmaceutical Corporation, PK Med, LG Chem, JPI, PTC Therapeutics, Protalix, outside the submitted work. Lisa Stamp

has received royalties from Up-to-Date and consulting fees from Pharmac NZ. The other authors have no conflicting interests to report.

Corresponding author: Professor Nicola Dalbeth, Department of Medicine, Faculty of Medical and Health Sciences, University of Auckland, 22-30 Park Ave, Grafton, Auckland, New Zealand. Email: n.dalbeth@auckland.ac.nz.

Ethical approval was obtained from the Health and Disability Ethics Committee, New Zealand (18/STH/156), and all participants provided written informed consent.

Abstract

Objective: To investigate the effect of colchicine prophylaxis on gout remission when commencing urate lowering therapy (ULT), and illness perceptions of people in remission, using two definitions of gout remission.

Methods: Data from a 12-month double-blind placebo-controlled trial of 200 people with gout commencing allopurinol were analyzed. Participants were randomly assigned to prophylaxis with 0.5mg daily colchicine or placebo for six months, followed by six months of additional follow-up. Gout remission was assessed using the 2016 preliminary definition or simplified definition without patient reported outcomes. Illness perceptions were assessed using a gout-specific brief illness perception questionnaire (BIPQ).

Results: In the first six months, few participants were in remission according to either the 2016 preliminary definition (3% for colchicine and 4% for placebo) or the simplified definition (7% for colchicine and 12% for placebo). In the second six months, after study drug (colchicine or placebo) discontinuation, fewer participants in the colchicine group than in the placebo group were in remission according to the 2016 preliminary definition (4% vs. 14%, p=0.03), and the simplified definition (14% vs 28%, p=0.02). Participants fulfilling remission using either definition had more favorable perceptions about their gout symptoms and illness concerns, as well as consequences, when using the simplified definition.

Conclusion: Using either definition, six months of colchicine prophylaxis when initiating ULT does not provide an advantage in the fulfilment of gout remission. People fulfilling either definition report fewer symptoms, lower concern about their gout, and when using the simplified definition, are less affected by gout.

Significance and Innovation

- Colchicine prophylaxis is recommended by major rheumatology guidelines when commencing ULT.
- This is the first study to investigate the role of anti-inflammatory prophylaxis for the fulfilment of gout remission.
- Six months of colchicine prophylaxis when initiating ULT did not provide an advantage in the fulfilment of gout remission, and lower odds of gout remission were observed in the six months after stopping colchicine prophylaxis.
- Both the 2016 preliminary definition and simplified definition demonstrate high construct validity with positive illness perceptions about gout.

Introduction

Gout is a common inflammatory arthritis resulting from deposition of monosodium urate crystals in the joints and periarticular tissue [1]. Long term management of gout with ULT, treating to a serum urate target <0.36mmol/l, prevents recurrent gout flares and progressive disease [2].

In 2016, a preliminary definition for gout remission was described. This was as follows: absence of gout flares, serum urate <0.36mmol/l, absence of tophi, pain due to gout <2 and patient global assessment of gout disease activity <2 [3]. In a subsequent qualitative study examining patient perspectives of gout remission, patients indicated that the pain domain and patient global assessment domain may be unnecessary when defining gout remission [4]. Based on this, a simplified gout remission definition that utilizes the same domains as the 2016 preliminary gout remission definition but does not include the patient reported outcomes, has been assessed [5]. In a two year trial of intensive urate-lowering therapy for erosive gout, more people fulfilled the simplified definition, and fulfilment of either definition was associated with lower baseline monosodium urate volume measured by dual energy CT [5].

Gout flares are common during initiation of ULT [6-8]. For this reason, major rheumatology guidelines recommend anti-inflammatory prophylaxis for three to six months when commencing ULT to reduce the frequency of gout flares [9-11]. We have recently reported a 12-month double-blind, placebo-controlled, randomized, non-inferiority trial of people with gout commencing allopurinol with a 'start-low go-slow' allopurinol dose escalation approach [12]. This study demonstrated that placebo was not non-inferior to colchicine in prevention of gout flares in the first six months of the trial [12]. In the second six months of the trial (after stopping study drug), gout flares rose in the colchicine group, but not the placebo group. Similar serum urate, tophus, and patient reported outcomes were observed between the two groups. Herein, we report an analysis of this trial, which aimed to investigate the effect of colchicine

prophylaxis on gout remission when commencing urate lowering therapy (ULT), and illness perceptions of people in remission, using the two definitions of gout remission.

Patients and methods

This paper reports an analysis of a 12-month double-blind, placebo-controlled, randomized non-inferiority trial of people with gout recruited from primary and secondary care clinics in Christchurch and Auckland, New Zealand. The full methods and results of the trial have been reported in full [12]. In brief, participants were included if they had gout according to the 2015 American College of Rheumatology (ACR)/European Alliance of Associations for Rheumatology (EULAR) criteria [13], were ≥18 years old, had at least one self-reported gout flare in the preceding six months, met the ACR guidelines recommendation for initiating ULT [10], and a serum urate concentration of ≥0.36mmol/l at screening. Ethical approval was obtained from the Health and Disability Ethics Committee, New Zealand (18/STH/156), and all participants provided written informed consent.

Participants were randomly assigned to colchicine 0.5mg daily or placebo for six months, followed by a further six months of follow-up after study drug discontinuation. All participants commenced allopurinol with 50mg daily (eGFR<60mls/min/1.73m^2) or 100mg daily (eGFR ≥ 60mls/min/1.73m^2), and doses were increased monthly by 50mg or 100mg daily until a serum urate concentration of <0.36mmol/l, or <0.30 mmol/l for those with tophi, was maintained for three consecutive months. Allopurinol was continued indefinitely unless participants experienced an adverse event requiring discontinuation [12].

Outcomes

After the baseline visit, participants attended three-monthly follow-up visits with telephone assessments undertaken in the intervening months. Gout flares, defined as self-reported gout

flares requiring treatment, were recorded at monthly intervals. Serum urate, subcutaneous tophus count, patient global assessment, and pain were recorded at three-monthly intervals. These outcomes reported at the follow-up visits were used to measure gout remission.

Gout remission using the 2016 preliminary definition (absence of gout flares, absence of tophus, serum urate <0.36mmol/l, pain <20mm, patient global assessment <20mm on 0-100mm scale [3]) and simplified definition (same domains without the patient reported outcomes [4]) were assessed over three-month and six-month timeframes. Supplementary Table 1 outlines the individual remission domains analysed for fulfilment of the preliminary definition and simplified definition over these time periods. Neither the pain questionnaire nor the patient global assessment questionnaires used in the study were specific to gout.

Illness perceptions about gout were assessed using a gout-specific brief illness perception questionnaire (BIPQ) which measured participant concerns, understanding, and emotional responses about gout. The BIPQ is a reliable and valid tool for assessing patients' beliefs and views about their illness [14], and the gout-specific BIPQ has been used in prior gout research [15-19]. The specific questions were consequences (how much gout affects the patient's life), timeline (how long the patient thinks gout will continue), personal control (how much control the patient has over their gout), treatment control (how much the patient's medication can control gout), identity (severity of gout symptoms), concern (how concerned the patient is about their gout), understanding (how well the patient feels they understand their gout), and emotional response (how much gout affects the patient emotionally). Each question was rated by patients on a 0-10 Likert scale, with higher scores indicating stronger endorsement of the question.

Statistical analysis

Demographics and clinical features were summarised using standard descriptive statistics including mean, standard deviation (SD), median, interquartile range (IQR), count, and

percent as appropriate. Comparison of proportions between those fulfilling and not fulfilling the 2016 preliminary definition, simplified definition and individual remission domains were analysed using Pearson's Chi-square test for independent groups and McNemar's test for paired data. Binary logistic regression was used to measure the association between these remission definitions and the colchicine and placebo group.

Cohen's kappa coefficient was used to assess the agreement between the 2016 preliminary definition and simplified definition in measuring gout remission. Kappa <0 was considered 'no agreement,' 0 to 0.20 'slight agreement,' 0.21 to 0.40 'fair agreement,' 0.41 to 0.60 'moderate agreement,' 0.61 to 0.80 'substantial agreement' and 0.81 to 1.0 'perfect agreement' [20]. The percentage agreement described the observed proportion of all observations in agreement.

Using the general linear model algorithm in SPSS, the BIPQ scores at month 12 were used to compare illness perception between those fulfilling and not fulfilling the 2016 preliminary definition and simplified definition during months 7-12, controlling for baseline BIPQ scores and treatment groups.

In the main trial, there were 24 participants who were lost to follow-up (13 in the colchicine group and 11 in the placebo group) and two participants died (both in the colchicine group) during the study. In the remission analysis, missing data were addressed through multiple imputation using the 'Fully Conditional Specification' (FCS) algorithm with predictive mean matching (PMM) in SPSS. Statistical analysis was performed using SPSS software version 28 and GraphPad Prism software version 9.3.1. $p<0.05$ was used to denote statistical significance.

Results

Clinical features

Clinical features of the study participants are shown in Supplementary Table 2. Most participants were male, with a mean age of 56 years and a mean disease duration of 11 years. At baseline, the median number of gout flares in the preceding six months was two, the mean serum urate concentration was 0.50mmol/l, and a quarter of participants had subcutaneous tophi. The mean pain score was 13 mm, and the mean patient global assessment was 24 mm.

Effect of colchicine prophylaxis on gout remission throughout the study

In the first six months of the trial, 3% of participants in the colchicine group and 4% in the placebo group were in remission according to the 2016 preliminary definition, OR 0.62 [95% CI 0.12 to 3.18)], p=0.57. Similarly, during this time period, 7% of participants in the colchicine group and 12% in the placebo group were in remission according to the simplified definition, OR 0.61 [95% CI 0.22 to 1.68], p=0.34 (Table 1).

In the second six months of the trial, after study drug discontinuation, fewer participants in the colchicine group (4%) were in remission according to the 2016 preliminary definition compared to those in the placebo group (14%), OR 0.29 [95% CI 0.09 to 0.90], p=0.03 (Table 1). Similarly, fewer participants in the colchicine group (14%) were in remission according to the simplified definition during this time period compared to those in the placebo group (28%), OR 0.41 [0.20 to 0.85], p=0.02 (Table 1).

Effect of colchicine prophylaxis on individual remission domains throughout the study

Individual remission domains were examined to understand the reasons for differences in fulfilment of the remission definitions between the two groups. There were no differences in

the serum urate, tophus, and pain domains between the colchicine and placebo groups (Figure 1 and Supplementary Figure 1).

In the first six months of the trial, there were no differences between the colchicine group and placebo group in fulfilment of the gout flares domains, but in the second six months of the trial, after study drug discontinuation, fewer participants in the colchicine group (23%) fulfilled the gout flares domain compared to those in the placebo group (41%), p=0.01 (Figure 1).

In the first six months of the trial, fewer participants in the colchicine group (35%) fulfilled the patient global assessment domain compared to those in the placebo group (49%), p=0.04. Similarly, in the second six months of the trial, fewer participants in the colchicine group (35%) fulfilled the patient global assessment domain compared to the placebo group (51%), p=0.02 (Figure 1).

Agreement between the 2016 preliminary definition and simplified definition

There were significantly more people in remission at either time point according to the simplified definition, p<0.001 (Figure 2). Cohen's kappa analysis showed moderate agreement between the two definitions in the first six months of the trial: κ=0.51 (0.28 to 0.75), p<0.001, with percentage agreement of 94% [95% CI 90% to 97%]. During the second six months of the trial, there was also moderate agreement between the definitions; κ=0.54 (0.40 to 0.70), p<0.001, percentage agreement 88% [95% CI 83% to 92%].

Illness perceptions of people in gout remission

Compared to participants who were not in gout remission according to the 2016 preliminary definition, those in remission reported fewer gout symptoms (lower identity belief scores), p=0.04, and were less concerned about gout (lower concern belief scores) p=0.01 at the month 12 visit (Table 2). There were no significant differences in other BIPQ items.

Similarly, compared to participants who were not in remission according to the simplified definition, those in remission reported fewer symptoms, p=0.002, and were less concerned about gout, p=0.002 at the month 12 visit (Table 3). Additionally, those in remission according to the simplified definition felt their life was less affected by gout (lower consequence belief scores), p=0.002. There were no significant differences in other BIPQ items.

Discussion

For people with gout, an important treatment goal is remission [4]. Absence of gout flares is a key domain contributing to both the 2016 preliminary gout remission definition and the simplified gout remission definition. The use of anti-inflammatory prophylaxis when commencing ULT is recommended to reduce the risk of gout flares. In this study we investigated the effect of colchicine prophylaxis on gout remission when commencing ULT. We found that colchicine prophylaxis for six months when commencing allopurinol does not provide an advantage for reaching gout remission, using either definition, and lower rates of gout remission were observed after stopping colchicine due to higher gout flares. We also investigated illness perceptions of people in remission using either definition. Participants in gout remission had more favorable perceptions of their gout. Specifically, they experienced fewer symptoms of gout, fewer concerns about gout, and, when using the simplified definition, less impact of gout on their lives also.

For both groups, remission was very uncommon in the first six months of starting ULT, and use of colchicine prophylaxis did not lead to more participants in remission using either definition over this time. Participants in this study had a mean disease duration of 11 years, and 25% of participants had tophaceous gout. Prior research has shown that patients with tophi are less likely to achieve remission after starting urate-lowering therapy [21], and it is

possible that remission rates may have been higher in patients with earlier disease duration and less severe disease.

In the last six months of the trial, after discontinuation of study drug, fewer participants in the colchicine group were in remission using either definition compared to those in the placebo group. An increase in gout flares after discontinuing colchicine contributed to the lower rates of remission in the colchicine group. Gout management guidelines recommend the use of anti-inflammatory prophylaxis for three to six months when commencing ULT [10], however it may be that colchicine prophylaxis for longer than six months is needed for the fulfilment of gout remission particularly as it only addresses the gout flares component of gout remission and the other components such tophus reduction can take longer. Other trials have also reported an increase in gout flares after stopping anti-inflammatory prophylaxis when used for shorter periods, which could again influence gout remission when commencing ULT [8,22].

This study also showed that people in remission according to the 2016 preliminary definition reported fewer gout symptoms and were less concerned about their gout. When remission was defined using either the 2016 preliminary definition or the simplified definition, participants reported fewer gout symptoms, were less concerned about their gout and when using the simplified definition, also felt less affected by gout. This finding illustrates that, in terms of defining gout remission, the simplified definition has high construct validity. The value of patient reported outcomes in defining remission has been greatly debated for other rheumatic diseases [23]. However, our study suggests that a definition without the patient reported outcomes may be more sensitive in identifying people in gout remission. This is an important finding as the simplified definition may be more feasible for use in both clinical practice and research settings. It is also important to note that the simplified remission definition could be overestimating the rates of remission, and that the exclusion of pain and patient global assessment may mean some participants are incorrectly classified as being in

gout remission. Further analysis could aim to evaluate alternative definitions for gout remission including introducing more lenient thresholds for the patient reported outcomes. This approach has been taken with definitions of RA remission recently, with a change of the patient global assessment of disease activity threshold to 2 cm [24].

Strengths of this study include the double-blind, randomized approach, the measurement of OMERACT core outcome domains, and the six-month follow-up after discontinuation of colchicine/placebo interventions. A potential limitation of this study is its 12-month study duration which did not enable the assessment of gout remission over longer follow-up. Another limitation of this study is the absence of gout-specific pain and patient global assessment questionnaires. The patient global assessment domain may have been influenced by more adverse events in the colchicine group [12], resulting in lower proportions of participants in the colchicine group fulfilling the patient global assessment domain compared to those in the placebo group.

In summary, six months of colchicine prophylaxis did not provide an advantage in achieving gout remission when initiating ULT and decreased the odds of gout remission after colchicine discontinuation. People in remission using either definition report fewer symptoms, have a lower concern about their gout, and, when using the simplified definition, are less affected by gout. The simplified definition has high construct validity, feasibility, and sensitivity for identifying people in remission and may be sufficient to define gout remission.

References

1. Dalbeth N, Merriman TR, Stamp LK. Gout. Lancet 2016;388:2039-52.
2. Stamp LK, Frampton C, Morillon MB, et al. Association between serum urate and flares in people with gout and evidence for surrogate status: a secondary analysis of two randomised controlled trials. The Lancet Rheumatology 2022;4:e53-e60.
3. de Lautour H, Taylor WJ, Adebajo A, et al. Development of Preliminary Remission Criteria for Gout Using Delphi and 1000Minds Consensus Exercises. Arthritis Care Res (Hoboken) 2016;68:667-72.
4. Tabi-Amponsah AD, Stewart S, Hosie G, Horne A, Dalbeth N. The Patient Experience of Gout Remission: A Qualitative Study. ACR Open Rheumatol 2023.
5. Tabi-Amponsah AD, Stewart S, Gamble G, et al. Dual Energy Computed Tomography (DECT) Urate Volume Predicts Fulfillment of Gout Remission After Two Years of Intensive Urate Lowering Therapy. ACR Convergence 2023 .San Diego, USA.
6. Becker MA, Schumacher HR, Espinoza LR, et al. The urate-lowering efficacy and safety of febuxostat in the treatment of the hyperuricemia of gout: the CONFIRMS trial. Arthritis Res Ther 2010;12:R63.
7. Efficacy and Tolerability of Pegloticase for the Treatment of Chronic Gout in Patients Refractory to Conventional Treatment. JAMA 2011;306:711.
8. Becker MA, Schumacher HR, Jr., Wortmann RL, et al. Febuxostat compared with allopurinol in patients with hyperuricemia and gout. N Engl J Med 2005;353:2450-61.
9. Richette P, Doherty M, Pascual E, et al. 2016 updated EULAR evidence-based recommendations for the management of gout. Ann Rheum Dis 2017;76:29-42.
10. FitzGerald JD, Dalbeth N, Mikuls T, et al. 2020 American College of Rheumatology Guideline for the Management of Gout. Arthritis Care Res (Hoboken) 2020;72:744-60.
11. Hui M, Carr A, Cameron S, et al. The British Society for Rheumatology Guideline for the Management of Gout. Rheumatology 2017;56:1056-9.

12. Stamp L, Horne A, Mihov B, et al. Is colchicine prophylaxis required with start-low go-slow allopurinol dose escalation in gout? A non-inferiority randomised double-blind placebo-controlled trial. Ann Rheum Dis 2023.

13. Neogi T, Jansen TL, Dalbeth N, et al. 2015 Gout classification criteria: an American College of Rheumatology/European League Against Rheumatism collaborative initiative. Ann Rheum Dis 2015;74:1789-98.

14. Broadbent E, Petrie KJ, Main J, Weinman J. The brief illness perception questionnaire. Journal of psychosomatic research 2006;60:631-7.

15. Dalbeth N, Petrie KJ, House M, et al. Illness perceptions in patients with gout and the relationship with progression of musculoskeletal disability. Arthritis Care & Research 2011;63:1605-12.

16. Serlachius A, Gamble G, House M, et al. Illness Perceptions and Mortality in Patients With Gout: A Prospective Observational Study. Arthritis Care & Research 2017;69:1444-8.

17. Krasnoryadtseva A, Dalbeth N, Petrie K. Does seeing personal medical images change beliefs about illness and treatment in people with gout? A randomised controlled trial. Psychology & Health 2020;35:107-23.

18. Serlachius A, Schache K, Kieser A, Arroll B, Petrie K, Dalbeth N. Association Between User Engagement of a Mobile Health App for Gout and Improvements in Self-Care Behaviors: Randomized Controlled Trial. JMIR mHealth and uHealth 2019;7:e15021.

19. Bergsten U, Dehlin M, Klingberg E, Landgren AJ, Jacobsson LTH. Gender differences in illness perceptions and disease management in patients with gout, results from a questionnaire study in Western Sweden. BMC musculoskeletal disorders 2023;24.

20. Landis JR, Koch GG. The measurement of observer agreement for categorical data. Biometrics 1977;33:159-74.

21. Alvarado-de la Barrera C, López-López CO, Álvarez-Hernández E, et al. Are Target Urate and Remission Possible in Severe Gout? A Five-year Cohort Study. J Rheumatol 2020;47:132-9.

22. Schumacher HR, Jr., Becker MA, Wortmann RL, et al. Effects of febuxostat versus allopurinol and placebo in reducing serum urate in subjects with hyperuricemia and gout: a 28-week, phase III, randomized, double-blind, parallel-group trial. Arthritis Rheum 2008;59:1540-8.

23. van Tuyl LH, Sadlonova M, Davis B, et al. Remission in Rheumatoid Arthritis: Working Toward Incorporation of the Patient Perspective at OMERACT 12. J Rheumatol 2016;43:203-7.

24. Studenic P, Aletaha D, de Wit M, et al. American College of Rheumatology/EULAR remission criteria for rheumatoid arthritis: 2022 revision. Ann Rheum Dis 2023;82:74-80.

Table 1. Six-monthly fulfilment of the 2016 preliminary gout remission definition and the simplified gout remission definition according to randomized group

Six-monthly fulfilment of the 2016 preliminary definition				
	Colchicine N=100	**Placebo N=100**	***OR [95% CI]**	**p-value**
Months 1 to 6	3 (3.0%)	4 (4.0%)	0.62 [0.12 to 3.18]	0.57
Months 7 to 12	4 (4.0%)	14 (14.0%)	0.29 [0.09 to 0.90]	0.03
Six-monthly fulfilment of the simplified definition				
	Colchicine N=100	**Placebo N=100**	***OR [95% CI]**	**p-value**
Months 1 to 6	7 (7.0%)	12 (12.0%)	0.61 [0.22 to 1.68]	0.34
Months 7 to 12	14 (14.0%)	28 (28.0%)	0.41 [0.20 to 0.85]	0.02
*Participants in placebo group were used as the reference				

Table 2. Comparison of month 12 BIPQ scores between those who fulfilled and did not fulfil the 2016 preliminary gout remission definition in the final six months of the trial (months 7-12).

	Fulfilled N=18 Mean (95% CI)	Not fulfilled N=182 Mean (95% CI)	Mean difference (95% CI)	p-value
How much does gout affect your life? (Consequences beliefs) 10= severely affects life	0.86 (-0.53 to 2.26)	2.18 (1.75 to 2.63)	1.32 (-0.10 to 2.75)	0.07
How long do you think your gout will continue? (Timeline beliefs) 10= will continue forever	8.78 (6.84 to 10.73)	7.58 (6.99 to 8.16)	-1.20 (-3.22 to 0.80)	0.25
How much control do you feel you have over your gout? (Personal control beliefs) 10= extreme amount	9.02 (7.86 to 10.19)	8.12 (7.70 to 8.54)	-0.90 (-2.12 to 0.32)	0.15
How much do you think your treatment can help your gout? (Treatment control beliefs) 10= extremely helpful	8.96 (7.95 to 9.98)	8.81 (8.42 to 9.21)	-0.15 (-1.21 to 0.91)	0.77
How much do you experience symptoms from your gout? (Identity beliefs) 10=many severe symptoms	0.89 (-0.21 to 2.00)	2.10 (1.72 to 2.50)	1.21 (0.05 to 2.37)	0.04
How concerned are you about your gout? (Concern beliefs) 10= extremely concerned	1.20 (-0.34 to 2.73)	3.40 (2.84 to 3.96)	2.20 (0.63 to 3.77)	0.01
How well do you feel you understand your gout? (Understanding beliefs) 10= very clearly	8.70 (7.71 to 9.69)	8.35 (8.00 to 8.71)	-0.35 (-1.38 to 0.67)	0.48
How does your gout affect you emotionally? (Emotional response beliefs) 10=extremely affected	0.97 (-0.39 to 2.33)	2.10 (1.65 to 2.55)	1.13 (-0.22 to 2.48)	0.08

Table 3. Comparison of month 12 BIPQ scores between those who fulfilled and did not fulfil the simplified gout remission definition in the final six months of the trial (months 7-12).

	Fulfilled N=42 Mean (95% CI)	**Not fulfilled N=158 Mean (95% CI)**	**Mean difference (95% CI)**	**p-value**
How much does gout affect your life? (Consequences beliefs) 10= severely affects life	0.84 (-0.01 to 1.70)	2.39 (1.91 to 2.87)	1.55 (0.61 to 2.48)	0.002
How long do you think your gout will continue? (Timeline beliefs) 10= will continue forever	8.03 (6.94 to 9.14)	7.49 (6.84 to 8.15)	-0.54 (-1.77 to 0.68)	0.39
How much control do you feel you have over your gout? (Personal control beliefs) 10= extreme amount	8.71 (7.94 to 9.48)	8.07 (7.60 to 8.53)	-0.64 (-1.50 to 0.22)	0.15
How much do you think your treatment can help your gout? (Treatment control beliefs) 10= extremely helpful	9.07 (8.38 to 9.75)	8.77 (8.33 to 9.20)	-0.30 (-1.04 to 0.44)	0.44
How much do you experience symptoms from your gout? (Identity beliefs) 10=many severe symptoms	0.80 (-0.01 to 1.62)	2.29 (1.86 to 2.71)	1.49 (0.60 to 2.37)	0.002
How concerned are you about your gout? (Concern beliefs) 10= extremely concerned	1.61 (0.53 to 2.69)	3.59 (2.97 to 4.20)	1.98 (0.83 to 3.12)	0.002
How well do you feel you understand your gout? (Understanding beliefs) 10= very clearly	8.65 (7.97 to 9.33)	8.35 (7.96 to 8.74)	-0.30 (-1.04 to 0.45)	0.43
How does your gout affect you emotionally? (Emotional response beliefs) 10=extremely affected	1.29 (0.42 to 2.16)	2.19 (1.70 to 2.69)	0.90 (-0.06 to 1.86)	0.07

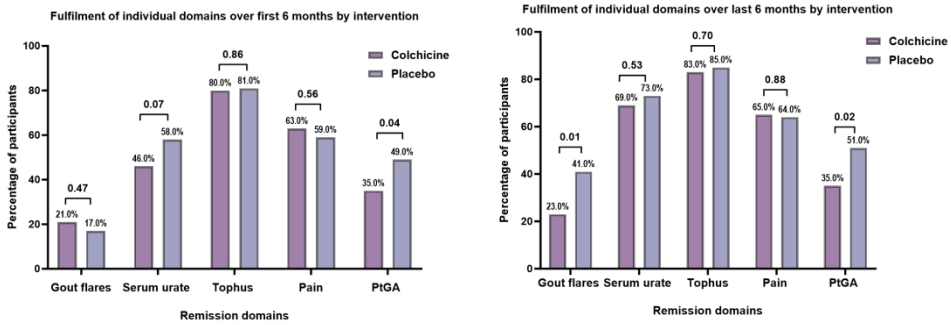

Figure 1. Fulfilment of individual remission domains over six-month periods. Domains were defined as follows: Absence of gout flares over months 1-6 (first six months) and months 7-12 (last six months); Serum urate ≤0.36mmol/l at month 3 and month 6 (first six months) and months 9 and 12 (last six months); Absence of tophus at month 6 (first six months) and absence of tophus at month 12 (last six months); pain <20mm and patient global assessment (PtGA) <20mm at month 3 and month 6 (first six months) month 9 and month 12 (last six months).

190x71mm (300 x 300 DPI)

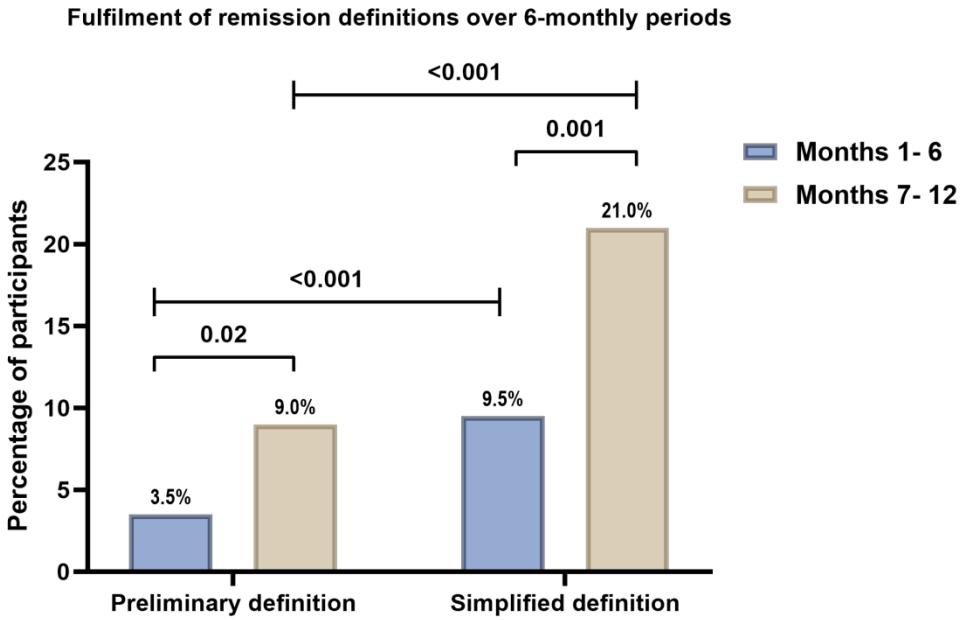

Figure 2. Fulfilment of the 2016 preliminary gout remission definition and simplified gout remission definition over six-month periods for all study participants.

160x105mm (300 x 300 DPI)