Exploration of Musculoskeletal Diseases

Open Exploration

Open Access Commentary

# Should all people starting urate-lowering therapy for gout receive anti-inflammatory prophylaxis?

Edward Roddy[1,2]*, James A. Prior[1,2], Christian D. Mallen[1,2]

[1]School of Medicine, Keele University, ST5 5BG Keele, UK

[2]Haywood Academic Rheumatology Centre, Midlands Partnership University NHS Foundation Trust, ST6 7AG Staffordshire, UK

***Correspondence:** Edward Roddy, School of Medicine, Keele University, ST5 5BG Keele, UK. e.roddy@keele.ac.uk

**Academic Editor:** Cesar Diaz-Torne, Autonomous University of Barcelona, Spain

**Received:** September 17, 2024 **Accepted:** October 29, 2024 **Published:** November 15, 2024

**Cite this article:** Roddy E, Prior JA, Mallen CD. Should all people starting urate-lowering therapy for gout receive anti-inflammatory prophylaxis? Explor Musculoskeletal Dis. 2024;2:521–8. https://doi.org/10.37349/emd.2024.00076

## Abstract

Co-prescription of anti-inflammatory prophylaxis with colchicine, non-steroidal anti-inflammatory drugs (NSAIDs), or corticosteroids when initiating urate-lowering therapy (ULT) for gout is recommended in clinical guidelines to prevent ULT-induced flares and optimise adherence to ULT. Colchicine prophylaxis is highly clinically and cost-effective and there has been great interest recently in its cardioprotective effects. However, one in four people initiating ULT without prophylaxis in randomised trials do not have a gout flare within six months of initiation, raising the question of whether all people initiating ULT for gout should receive prophylaxis. Uptake of prophylaxis varies and appears to be common in secondary care settings but less commonly used in primary care, where most people with gout are managed and gout may be less severe. Recent clinical guidelines have highlighted that the patient's perspective is important and that the pros and cons of prophylaxis should be discussed with people with gout initiating ULT. Uptake of prophylaxis seems likely to be influenced by perception of an individual's risk of ULT-induced flares, as well as concerns about adverse events, polypharmacy, drug interactions, and cost. We advocate a personalised approach between people with gout and clinicians to reach shared treatment decisions when considering co-prescription of prophylaxis when initiating ULT, empowering people with gout to make decisions about their care.

## Keywords

Gout, urate-lowering therapy, colchicine

Long-term treatment of gout involves taking urate-lowering therapy (ULT), most commonly with allopurinol or febuxostat. National and international guidelines recommend starting ULT at low dose and increasing gradually over a number of months to lower the serum urate below a therapeutic biochemical target level (treat-to-target) [1–4]. New crystal formation is therefore prevented and existing crystals dissolve gradually so that flares cease, tophi reduce in size, and long-term joint damage is prevented, effectively 'curing' gout [5]. One barrier to successful ULT is the tendency for flares to increase in frequency

after initiation of ULT or dose increases. As well as causing significant pain and disability, such ULT-initiated flares may be perceived by people with gout and practitioners as exacerbating the severity of gout, leading to ULT being stopped [6]. Clinical guidelines therefore recommend that colchicine, non-steroidal anti-inflammatory drugs (NSAIDs), or corticosteroids can be co-prescribed when initiating ULT in order to prevent ULT-induced flares [1–4].

Colchicine prophylaxis is undoubtedly effective. Randomised trials demonstrate that co-prescribing colchicine prophylaxis when initiating ULT reduces the incidence of ULT-induced flares [7]. One small randomised trial (43 participants) undertaken in people initiating allopurinol found that 33% of those randomised to colchicine 0.5 mg twice daily had a flare within the 6-month follow-up period compared with 77% of those receiving placebo [8]. In a more recent larger randomised trial (200 participants), placebo was not non-inferior to colchicine 0.5 mg daily for mean number of flares per month (0.61 vs. 0.35) when initiating 'start low, go slow' treat-to-target allopurinol [9]. The Febuxostat Outcome Research Towards Urate Lowering in the Next Decade-1 (FORTUNE-1) trial randomised 241 adults with gout to febuxostat step-wise dose increase from 10 mg to 40 mg daily only, febuxostat fixed dose 40 mg daily plus colchicine prophylaxis, and febuxostat fixed dose 40 mg daily only, finding that fewer people experienced flares over 12 weeks with febuxostat fixed dose plus colchicine 0.5 mg daily (19%) than with febuxostat fixed dose alone (36%) [10]. There is limited evidence of the effectiveness of prophylactic NSAIDs or glucocorticoids for flare prophylaxis, other than for azapropazone, an NSAID no longer widely used in clinical practice [11].

Colchicine is inexpensive in many countries including the UK and Australia, however, a recent increase in the cost of colchicine in the USA led to a reduction in colchicine initiations and an increase in costs to people with gout [12]. A subsequent 2-arm decision tree cost-effectiveness analysis modelled from both US and Australian inputs found that colchicine was very cost-effective in preventing gout flares when initiating allopurinol compared with placebo, particularly in an Australian setting where colchicine was considerably cheaper [13]. Twice daily colchicine prophylaxis resulted in a cost of $1,276 and 0.49 quality-adjusted life-years (QALYs) compared with $516 and QALY 0.47 for placebo, equating to an incremental cost-effectiveness ratio of $34,004 per QALY gained.

Cardiovascular disease is prevalent in people with gout. In one primary care-based cross-sectional study of 1,079 people with gout, the prevalences of obesity, hypertension, hyperlipidaemia, diabetes mellitus, and chronic kidney disease (CKD) were 35%, 40%, 10%, 16%, and 25% respectively, with 15% of participants having coronary heart disease [14]. There has therefore been great interest recently in the possible cardiovascular benefits of colchicine prophylaxis [15], following large randomised trials that have shown cardioprotective effects of colchicine in people with chronic coronary heart disease or a recent myocardial infarction (MI) [16, 17]. However, to date, there has not been a randomised trial of cardioprotective effects of colchicine in people with gout. A systematic review and meta-analysis of four observational studies including 10,026 participants with gout found that colchicine was associated with a 29% lower risk of MI, although this was not statistically significant (risk ratio 0.71, 95% confidence interval 0.36–1.39), highlighting the need for further robust evidence [18]. The duration of colchicine treatment in the cardiovascular disease trials was often longer than is used for gout flare prophylaxis in clinical practice and since the participants had a history of chronic coronary heart disease or a recent MI, they are likely to have been at higher risk of cardiovascular events than people with gout, many of whom have cardiovascular risk factors but not necessarily established cardiovascular disease. It is therefore unclear whether the potential cardiovascular benefits of colchicine apply to the way it is currently used for gout flare prophylaxis in practice.

Given the clear evidence of effectiveness of colchicine prophylaxis, should all people with gout initiating ULT receive anti-inflammatory prophylaxis? Uptake of prophylaxis appears to be variable and dependent on the clinical setting. Prophylaxis is commonly co-prescribed when ULT is initiated by rheumatologists in the UK (94% of initiations), France (72%), Greece (41%), and by physicians in the USA (90%) [19–21], in contrast to only 25% and 7% of primary care initiations in the UK and Australia respectively [22, 23]. Furthermore, in a large UK primary care-based randomised trial which compared nurse-led treat-to-target ULT with usual primary care for gout, only 1% of participants in the intervention

arm opted for prophylaxis after being offered it when initiating ULT [5]. Although the proportion of participants having a flare during the first year of follow-up was greater in the intervention arm (54.0% vs. 39.8%), this did not prevent excellent adherence to ULT, the vast majority of participants achieving target serum urate levels, or significant clinical improvements in flare rates, tophi, and quality of life at 2 years. The clinical severity of gout and risk of ULT-induced flares are likely to be lower in primary care populations, potentially explaining discrepancies between primary and secondary care prescribing and suggesting that good outcomes can be achieved from ULT without prophylaxis in certain patients. There have been few studies comparing the characteristics of people who receive prophylaxis with those who do not. In a cross-sectional analysis from the secondary care-based Consortium of Rheumatology Researchers of North America (CORRONA) gout registry, people taking prophylaxis had shorter gout duration, more flares, greater healthcare use in the preceding year, greater disease activity and pain, and were more likely to have tophi than those not receiving prophylaxis [24].

National and international clinical guidelines make varying recommendations regarding how strongly they recommend anti-inflammatory prophylaxis. The 2012 American College of Rheumatology gout guideline and its 2020 update strongly recommended co-prescribing colchicine, NSAID, or prednisolone/prednisone prophylaxis when initiating ULT [1, 25]. Other guideline development groups have made less stringent recommendations concerning prophylaxis in their recent guideline updates than in earlier versions and highlighted that the patient perspective is important and that the pros and cons of prophylaxis should be discussed with people with gout initiating ULT. Whereas the first British Society for Rheumatology gout guideline recommended in 2007 that colchicine (or an NSAID or coxib if colchicine is not tolerated) should be co-prescribed when initiating ULT [26], the 2017 update advocated less strongly that it can be considered [3]. Both the 2016 European Alliance of Associations for Rheumatology (EULAR) and 2022 UK National Institute for Health and Care Excellence (NICE) guidelines recommend discussing prophylaxis with people starting ULT [2, 4]. Whilst recommending colchicine prophylaxis (or NSAID if colchicine is not tolerated) for the first 6 months of ULT, the 2016 EULAR recommendations state that prophylaxis against flares should be fully explained and discussed with the patient [2]. The 2022 NICE guideline advises discussing with the person the benefits and risks of taking medicines (colchicine, NSAID, or low-dose corticosteroid) to prevent gout flares when starting or titrating ULT [4].

There are multiple reasons why people with gout and clinicians may be reluctant to use anti-inflammatory prophylaxis (Table 1). Harm from prophylaxis is likely to be an important consideration. Comorbidities are common in people with gout [14] and the presence of comorbidities, particularly CKD, is a contraindication to NSAIDs and is thought to increase the risk of colchicine toxicity. Gastrointestinal symptoms, particularly diarrhoea, are the most common side-effects of colchicine. In a systematic review of 35 randomised trials of colchicine in the treatment of 18 different conditions, diarrhoea affected 17.9% of participants in the colchicine arms [27]. However, only five trials were undertaken in people with gout, two of which were trials of short courses of colchicine to treat flares rather than longer courses for prophylaxis. In the aforementioned small randomised trial of colchicine prophylaxis by Borstad et al. [8] the incidence of diarrhoea over the 6-month follow-up was 38% in the colchicine arm period compared with 4.5% in the placebo arm. The potential for more serious haematological, neuropathic, or myopathic side-effects, particularly when co-administered with CYP3A4 inhibitors, is a commonly cited concern but the systematic review by Stewart et al. [27] found these to occur infrequently in clinical trials. A more recent large cohort study undertaken in the UK Clinical Practice Research Datalink found that bone marrow suppression, neuropathy, and myalgia occurred more commonly in 13,945 people initiating allopurinol with colchicine than in 13,945 matched individuals initiating without prophylaxis, but absolute incidence rates were uncommon (incidence for each in those receiving colchicine < 120/10,000 person-years) [28]. There were no occurrences of rhabdomyolysis and no consistent associations between adverse events and use of other medications or CKD [29]. In a parallel cohort study, acute kidney injury (incidence 161/10,000 person-years), angina (467/10,000 person-years), MI (157/10,000 person-years), and peptic ulcer disease (82/10,000 person-years) were more common in 25,980 people initiating allopurinol with NSAID prophylaxis than in 25,980 individuals initiating without [28].

**Table 1. Reasons for and against all people with gout receiving anti-inflammatory prophylaxis when initiating ULT**

| For | Against |
|---|---|
| ULT-induced flares are common and often lead ULT to be stopped | 1 in 4 people with gout do not experience ULT-induced flares, even without prophylaxis |
| Prophylaxis reduces the incidence of ULT-induced flares, improving long-term adherence to ULT | 'Start low, go slow' ULT leads to fewer ULT-induced flares than historical fixed dosing |
| Colchicine prophylaxis is cost-effective | Risk of adverse events |
| Potential CV benefits of colchicine | Drug interactions, polypharmacy |
| Difficulty predicting who is most at risk of ULT-induced flares | Difficulty predicting who is most at risk of adverse events |
| - | Financial burden of prescription costs to individuals |
| - | Some people may prefer the 'pill in the pocket' approach to treat flares than regular prophylaxis |

-: no data. CKD: chronic kidney disease; CV: cardiovascular; ULT: urate-lowering therapy

Patient and clinician perceptions of a person's individual risk of ULT-induced flare are also likely to be a key factor determining use of prophylaxis. A large secondary care cohort study of 8,828 people with gout initiating ULT found that 68% had at least one flare within 12 months of initiating ULT [30]. Colchicine, NSAIDs, and corticosteroids were taken by more than 80% of participants at baseline and during the 12-month follow-up period, although the duration of treatment and whether this was to treat a flare or for prophylaxis was not stated. In the placebo arms of two randomised trials of colchicine prophylaxis by Borstad et al. [8] and Stamp et al. [31] 77% and 73% of participants respectively had a flare within six months of initiating allopurinol suggesting that approximately one-quarter of people initiating ULT without prophylaxis in secondary care do not appear to flare in the first six months following ULT initiation and arguably do not require prophylaxis. Furthermore, whereas the risk of ULT-induced flares is high when initiating ULT at historical fixed doses (e.g., allopurinol 300 mg daily), contemporary practice of starting at low dose and increasing the dose gradually leads to fewer flares [7, 10]. There have been few studies of other risk factors for ULT-induced flares. Secondary care-based cohort studies and an analysis nested in the aforementioned non-inferiority trial by Stamp et al. [9] have suggested that older age, having a high serum urate or C-reactive protein level, more comorbidities, having a flare in the month preceding ULT initiation, higher allopurinol starting dose, taking diuretics, and not taking prophylaxis were associated with greater risk of ULT-induced flares, but risk factors investigated did not include the presence of tophi, which might also be expected to influence likelihood of a ULT-induced flare [30–32]. Only one study investigated whether prior flare frequency increased the risk of a ULT-induced flare, finding that people having at least two flares in the 6 months prior to ULT initiation were no more likely to experience a ULT-induced flare than those having only one flare in the prior 6 months [31]. Identifying clinical characteristics that influence an individual's risk of ULT-induced flares may allow use of prophylaxis to be tailored and personalised [7].

Whilst recent guideline recommendations suggest that the perspectives of people with gout about prophylaxis should inform treatment decisions, little is known about what the perspectives of patients and prescribers are and what influences uptake of prophylaxis. Qualitative research studies highlight that people with gout are aware that ULT can precipitate flares and that prophylaxis is available to prevent these [6, 33, 34]. One study from New Zealand of patients' perceptions and experiences of taking colchicine highlighted their concerns about polypharmacy and potential side-effects that can affect adherence [34]. Our clinical experience is that people with gout may be concerned that taking prophylaxis requires them to take additional tablets, which can be compounded by the need for gastroprotection if taking an NSAID or corticosteroids and/or bone protection if taking corticosteroids. Conversely, people with gout may find prophylaxis particularly acceptable if they have had frequent or severe flares or bad experiences of ULT-induced flares previously. However, existing studies have not explored the factors which influence people with gout to opt for prophylaxis, their information needs to support this decision, or their views on the relative merits of prophylaxis versus the 'pill in the pocket' approach, the main alternative to prophylaxis, which involves having medication to treat a flare available to be taken as soon as the flare starts [2]. It seems likely that some people with gout may prefer to manage ULT-induced flares as they arise rather than take regular prophylaxis, depending on their previous experience of flares (frequency, severity, and

duration) and ULT (if taken previously), their perception of their individual flare risk, and their concerns about polypharmacy and adverse events.

In conclusion, ULT-induced flares can be a significant clinical problem, which contributes substantially to suboptimal adherence to ULT and poor outcomes in people with gout. There is robust evidence of the effectiveness and safety of colchicine to prevent flares when initiating ULT but limited evidence for NSAIDs or corticosteroids. However, not all people with gout experience a flare after initiating ULT, even without prophylaxis, and some may not wish to take flare prophylaxis, preferring to manage flares as they arise (Table 1). We advocate a personalised approach between people with gout and clinicians to reach shared treatment decisions when discussing the possibility of co-prescribing prophylaxis, which explores their views about prophylaxis, makes them fully aware of its benefits and risks (including those of different therapeutic options for prophylaxis), the alternatives to it (the 'pill in the pocket' approach), and what they should do in the event of a flare (including not stopping ULT), and provides them with a prescription for flare treatment that they can take as soon as a flare occurs. This approach not only provides a safety net for patients should a flare occur but also empowers them to make decisions about their care.

## Abbreviations

CKD: chronic kidney disease

EULAR: European Alliance of Associations for Rheumatology

MI: myocardial infarction

NICE: National Institute for Health and Care Excellence

NSAIDs: non-steroidal anti-inflammatory drugs

QALYs: quality-adjusted life-years

ULT: urate-lowering therapy

## Declarations

### Author contributions

ER: Conceptualization, Writing—original draft, Writing—review & editing. JAP: Writing—review & editing. CDM: Conceptualization, Writing—review & editing. All authors read and approved the submitted version.

### Conflicts of interest

CDM is director of the National Institute for Health and Care Research (NIHR) School for Primary Care Research. The views expressed are those of the author(s) and not necessarily those of the NIHR or the Department of Health and Social Care.

### Ethical approval

Not applicable.

### Consent to participate

Not applicable.

### Consent to publication

Not applicable.

### Availability of data and materials

Not applicable.

### Funding

Not applicable.



## References

1. FitzGerald JD, Dalbeth N, Mikuls T, Brignardello-Petersen R, Guyatt G, Abeles AM, et al. 2020 American College of Rheumatology Guideline for the Management of Gout. Arthritis Care Res (Hoboken). 2020; 72:744–60. [DOI] [PubMed] [PMC]
2. Richette P, Doherty M, Pascual E, Barskova V, Becce F, Castañeda-Sanabria J, et al. 2016 updated EULAR evidence-based recommendations for the management of gout. Ann Rheum Dis. 2017;76: 29–42. [DOI] [PubMed]
3. Hui M, Carr A, Cameron S, Davenport G, Doherty M, Forrester H, et al. British Society for Rheumatology Standards; Audit and Guidelines Working Group. The British Society for Rheumatology Guideline for the Management of Gout. Rheumatology (Oxford). 2017;56:1056–9. [DOI] [PubMed]
4. Neilson J, Bonnon A, Dickson A, Roddy E; Guideline Committee. Gout: diagnosis and management—summary of NICE guidance. BMJ. 2022;378:o1754. [DOI] [PubMed]
5. Doherty M, Jenkins W, Richardson H, Sarmanova A, Abhishek A, Ashton D, et al. Efficacy and cost-effectiveness of nurse-led care involving education and engagement of patients and a treat-to-target urate-lowering strategy versus usual care for gout: a randomised controlled trial. Lancet. 2018;392: 1403–12. [DOI] [PubMed] [PMC]
6. Harrold LR, Mazor KM, Velten S, Ockene IS, Yood RA. Patients and providers view gout differently: a qualitative study. Chronic Illn. 2010;6:263–71. [DOI] [PubMed] [PMC]
7. Maher D, Reeve E, Hopkins A, Tan JM, Tantiongco M, Ailabouni N, et al. Comparative Risk of Gout Flares When Initiating or Escalating Various Urate-Lowering Therapy: A Systematic Review With Network Meta-Analysis. Arthritis Care Res (Hoboken). 2024;76:871–81. [DOI] [PubMed]
8. Borstad GC, Bryant LR, Abel MP, Scroggie DA, Harris MD, Alloway JA. Colchicine for prophylaxis of acute flares when initiating allopurinol for chronic gouty arthritis. J Rheumatol. 2004;31:2429–32. [PubMed]
9. Stamp L, Horne A, Mihov B, Drake J, Haslett J, Chapman PT, 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;82:1626–34. [DOI] [PubMed]
10. Yamanaka H, Tamaki S, Ide Y, Kim H, Inoue K, Sugimoto M, et al. Stepwise dose increase of febuxostat is comparable with colchicine prophylaxis for the prevention of gout flares during the initial phase of urate-lowering therapy: results from FORTUNE-1, a prospective, multicentre randomised study. Ann Rheum Dis. 2018;77:270–6. [DOI] [PubMed] [PMC]
11. Templeton JS. Azapropazone or allopurinol in the treatment of chronic gout and/or hyperuricaemia. A preliminary report. Br J Clin Pract. 1982;36:353–8. [DOI] [PubMed]
12. Kesselheim AS, Franklin JM, Kim SC, Seeger JD, Solomon DH. Reductions in Use of Colchicine after FDA Enforcement of Market Exclusivity in a Commercially Insured Population. J Gen Intern Med. 2015;30: 1633–8. [DOI] [PubMed] [PMC]
13. Robinson PC, Dalbeth N, Donovan P. Cost-Effectiveness of Colchicine Prophylaxis for Gout Flares When Commencing Allopurinol. Arthritis Care Res (Hoboken). 2021;73:1537–43. [DOI] [PubMed]
14. Bevis M, Blagojevic-Bucknall M, Mallen C, Hider S, Roddy E. Comorbidity clusters in people with gout: an observational cohort study with linked medical record review. Rheumatology (Oxford). 2018;57: 1358–63. [DOI] [PubMed]

15. Robinson PC, Terkeltaub R, Pillinger MH, Shah B, Karalis V, Karatza E, et al. Consensus Statement Regarding the Efficacy and Safety of Long-Term Low-Dose Colchicine in Gout and Cardiovascular Disease. Am J Med. 2022;135:32–8. [DOI] [PubMed] [PMC]
16. Tardif JC, Kouz S, Waters DD, Bertrand OF, Diaz R, Maggioni AP, et al. Efficacy and Safety of Low-Dose Colchicine after Myocardial Infarction. N Engl J Med. 2019;381:2497–505. [DOI] [PubMed]
17. Nidorf SM, Fiolet ATL, Mosterd A, Eikelboom JW, Schut A, Opstal TSJ, et al.; LoDoCo2 Trial Investigators. Colchicine in Patients with Chronic Coronary Disease. N Engl J Med. 2020;383:1838–47. [DOI] [PubMed]
18. Siddiqui MU, Junarta J, Sathyanarayanan S, Kochar K, Ullah W, Fischman DL. Risk of coronary artery disease in patients with gout on treatment with Colchicine: A systematic review and meta-analysis. Int J Cardiol Heart Vasc. 2023;45:101191. [DOI] [PubMed] [PMC]
19. Roddy E, Packham J, Obrenovic K, Rivett A, Ledingham JM. Management of gout by UK rheumatologists: a British Society for Rheumatology national audit. Rheumatology (Oxford). 2018;57:826–30. [DOI] [PubMed]
20. Oderda GM, Shiozawa A, Walsh M, Hess K, Brixner DI, Feehan M, et al. Physician adherence to ACR gout treatment guidelines: perception versus practice. Postgrad Med. 2014;126:257–67. [DOI] [PubMed]
21. Richette P, Flipo RN, Patrikos DK. Characteristics and management of gout patients in Europe: data from a large cohort of patients. Eur Rev Med Pharmacol Sci. 2015;19:630–9. [PubMed]
22. Cottrell E, Crabtree V, Edwards JJ, Roddy E. Improvement in the management of gout is vital and overdue: an audit from a UK primary care medical practice. BMC Fam Pract. 2013;14:170. [DOI] [PubMed] [PMC]
23. Coleshill MJ, Day RO, Tam K, Kouhkamari M, Caillet V, Aung E, et al. Persistence with urate-lowering therapy in Australia: A longitudinal analysis of allopurinol prescriptions. Br J Clin Pharmacol. 2022;88:4894–901. [DOI] [PubMed] [PMC]
24. Schlesinger N, Etzel CJ, Greenberg J, Kremer J, Harrold LR. Gout Prophylaxis Evaluated According to the 2012 American College of Rheumatology Guidelines: Analysis from the CORRONA Gout Registry. J Rheumatol. 2016;43:924–30. [DOI] [PubMed]
25. Khanna D, Khanna PP, Fitzgerald JD, Singh MK, Bae S, Neogi T, et al. 2012 American College of Rheumatology guidelines for management of gout. Part 2: therapy and antiinflammatory prophylaxis of acute gouty arthritis. Arthritis Care Res (Hoboken). 2012;64:1447–61. [DOI] [PubMed] [PMC]
26. Jordan KM, Cameron JS, Snaith M, Zhang W, Doherty M, Seckl J, et al. British Society for Rheumatology and British Health Professionals in Rheumatology Standards; Guidelines and Audit Working Group (SGAWG). British Society for Rheumatology and British Health Professionals in Rheumatology guideline for the management of gout. Rheumatology (Oxford). 2007;46:1372–4. [DOI] [PubMed]
27. Stewart S, Yang KCK, Atkins K, Dalbeth N, Robinson PC. Adverse events during oral colchicine use: a systematic review and meta-analysis of randomised controlled trials. Arthritis Res Ther. 2020;22:28. [DOI] [PubMed] [PMC]
28. Roddy E, Bajpai R, Forrester H, Partington RJ, Mallen CD, Clarson LE, et al. Safety of colchicine and NSAID prophylaxis when initiating urate-lowering therapy for gout: propensity score-matched cohort studies in the UK Clinical Practice Research Datalink. Ann Rheum Dis. 2023;82:1618–25. [DOI] [PubMed] [PMC]
29. Bajpai R, Partington R, Muller S, Forrester H, Mallen CD, Clarson L, et al. Prognostic factors for colchicine prophylaxis-related adverse events when initiating allopurinol for gout: retrospective cohort study. Rheumatology (Oxford). 2024:keae229. [DOI] [PubMed]
30. Rashid N, Levy GD, Wu YL, Zheng C, Koblick R, Cheetham TC. Patient and clinical characteristics associated with gout flares in an integrated healthcare system. Rheumatol Int. 2015;35:1799–807. [DOI] [PubMed] [PMC]

31. Stamp LK, Horne A, Mihov B, Drake J, Haslett J, Chapman P, et al. Predicting Gout Flares in People Starting Allopurinol Using the Start-Low Go-Slow Dose Escalation Strategy. Arthritis Care Res (Hoboken). 2024;76:1371–8. [DOI] [PubMed]
32. Janssen CA, Oude Voshaar MAH, Ten Klooster PM, Vonkeman HE, van de Laar MAFJ. Prognostic factors associated with early gout flare recurrence in patients initiating urate-lowering therapy during an acute gout flare. Clin Rheumatol. 2019;38:2233–9. [DOI] [PubMed]
33. Richardson JC, Liddle J, Mallen CD, Roddy E, Hider S, Prinjha S, et al. A joint effort over a period of time: factors affecting use of urate-lowering therapy for long-term treatment of gout. BMC Musculoskelet Disord. 2016;17:249. [DOI] [PubMed] [PMC]
34. Rebello C, Thomson M, Bassett-Clarke D, Martini N. Patient awareness, knowledge and use of colchicine: an exploratory qualitative study in the Counties Manukau region, Auckland, New Zealand. J Prim Health Care. 2016;8:140–8. [DOI] [PubMed]