Naproxen or low-dose colchicine for gout flares in primary care? Response to: 'Open-label randomised pragmatic trial (CONTACT) comparing naproxen and low-dose colchicine for the treatment of gout flares in primary care' by Parperis *et al*

We concluded that naproxen should be considered as first-line treatment for gout flares in primary care based on there being no difference between naproxen and colchicine in pain intensity (the primary outcome), more analgesic use and self-reported side-effects in the colchicine group, and evidence that naproxen was cost-effective.[1] We note the Bayesian meta-analysis by Bally *et al* in which all non-steroidal anti-inflammatory drugs (NSAIDs), including naproxen, were associated with increased risk of myocardial infarction.[2] However, this review was limited by including only studies undertaken in healthcare databases risking bias due to residual confounding and, as the review's authors acknowledge, measuring drug dispensing or prescribing and not actual drug intake. A meta-analysis of individual patient data from 280 randomised trials of NSAID versus placebo found that naproxen did not significantly increase major vascular events or vascular deaths, in contrast to other NSAIDs.[3]

We acknowledge that the colchicine dose in our pragmatic trial differed from that subsequently recommended in the European League Against Rheumatism (EULAR) recommendations.[4] Pragmatic trials evaluate interventions as prescribed, managed and used in routine clinical practice.[5] We used the UK recommended colchicine dose,[6] consistent with the British Society for Rheumatology gout management guideline.[7] Furthermore, the EULAR recommendations advocate a loading dose of colchicine of 1 mg followed by 0.5 mg 1 hour later in patients presenting within 12 hours of flare onset,[4] as per the Acute Gout Flare Receiving Colchicine Evaluation (AGREE) trial,[8] without making a dose recommendation for patients with longer flare durations. Over two-thirds of our participants initiated medication over 24 hours after flare onset, hence the appropriateness of this dose regimen for our trial population is uncertain.

Our findings support informed decision-making based on an assessment of the balance of benefits and harms. Our conclusion was not that naproxen should be considered as the *only* first treatment option for gout flares, as stated by Parperis,[9] but importantly contained the caveat that naproxen should be considered as first-line treatment in primary care *in the absence of contraindications*. While colchicine would be a reasonable first therapeutic option in patients with cardiovascular risk factors, this is consistent with our conclusion that the choice of treatment should be influenced by the presence or absence of comorbidities.

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REFERENCES

1 Roddy E, Clarkson K, Blagojevic-Bucknall M, *et al*. Open-label randomised pragmatic trial (CONTACT) comparing naproxen and low-dose colchicine for the treatment of gout flares in primary care. *Ann Rheum Dis* 2019:pii: annrheumdis-2019-216154.
2 Bally M, Dendukuri N, Rich B, *et al*. Risk of acute myocardial infarction with NSAIDs in real world use: Bayesian meta-analysis of individual patient data. *BMJ* 2017;357.
3 Bhala N, Emberson J, Merhi A, *et al*. Vascular and upper gastrointestinal effects of non-steroidal anti-inflammatory drugs: meta-analyses of individual participant data from randomised trials. *Lancet* 2013;382:769–79.
4 Richette P, Doherty M, Pascual E, *et al*. Updated EULAR evidence-based recommendations for the management of gout. *Ann Rheum Dis* 2016;2017:29–42.
5 Dal-Ré R, Avendaño-Solà C, Bloechl-Daum B, *et al*. Low risk pragmatic trials do not always require participants' informed consent. *BMJ* 2019;1.
6 Joint Formulary Committee. *British National formulary*. 75th edn. London: BMJ Group and Pharmaceutical Press, 2018.
7 Hui M, Carr A, Cameron S, *et al*. The British Society for rheumatology guideline for the management of gout. *Rheumatology* 2017;56:e1–20.
8 Terkeltaub RA, Furst DE, Bennett K, *et al*. High versus low dosing of oral colchicine for early acute gout flare: twenty-four-hour outcome of the first multicenter, randomized, double-blind, placebo-controlled, parallel-group, dose-comparison colchicine study. *Arthritis Rheum* 2010;62:1060–8.
9 Parperis K. Open-label randomised pragmatic trial (CONTACT) comparing naproxen and low-dose colchicine for the treatment of gout flares in primary care. *Ann Rheum Dis*. In Press