**Title:** The Role of diet in serum urate concentration

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Hyperuricaemia is a well-established risk factor for the development of gout[1] and the role of sustained hyperuricaemia in the pathogenesis of monosodium urate crystal formation and gout is well understood.[2] Dietary factors have been thought to predispose to hyperuricaemia and gout for centuries, and recent epidemiological studies have suggested a role for excessive consumption of meat, seafood, sugar-sweetened soft drinks, fructose and alcoholic drinks, particularly beer and spirits, whereas coffee, low-fat dairy products and vitamin C may have a protective effect.[3]

In a linked article, Major and colleagues undertook a meta-analysis of cross-sectional food frequency questionnaire data from five US cohort studies to test individual foods for associations with serum urate and to compare the variance in serum urate levels explained by dietary and heritable factors. Their findings replicate the results of previous epidemiological studies, identifying seven foods associated with raised serum urate (beer, spirits, wine, potatoes, poultry, soft drinks, meat) and eight foods associated with reduced serum urate (eggs, peanuts, cold cereal, skimmed milk, cheese, brown bread, margarine, non-citrus fruit). Associations between serum urate levels and potatoes, peanuts and margarine are novel and require corroboration in other cohorts. However, their key new finding is that dietary scores explained a much smaller proportion of the variation in serum urate levels (<0.3%) than common genome-wide single nucleotide variants (23.9%).

The authors advise against generalising their findings to people with gout, because people with gout were excluded from the analysed cohorts, or those of non-European ancestry. People with kidney disease or using diuretics were also excluded so that the relationships between dietary and genetic factors and primary hyperuricaemia could be examined. Future studies should examine the variance in serum urate associated with secondary causes such as kidney disease and diuretics, which are likely to have significant influence in clinical populations, so as to understand the relative contributions of dietary, genetic and comorbid influences. The data presented relate to variation in serum urate attributable to dietary factors and do not constitute evidence of lack of effectiveness of dietary interventions to lower serum urate levels in people with established hyperuricaemia or gout. Furthermore, dietary factors have been implicated in the pathogenesis of gout in two ways; first, as a risk factor for hyperuricaemia as investigated in this study, and second, as a trigger for flares of acute gout.[4,5] Whether and which dietary factors trigger acute flares is not the subject of this study but is often of considerable interest to people with gout.[6]

Despite the authors’ caution against extrapolating their findings, it is unlikely that the aetiology of hyperuricaemia in the studied populations is drastically different to those with clinically-evident gout and it is this latter group to which the results are of most clinical relevance. Whilst the study does not provide evidence to change or ignore the recommendations of clinical guidelines that patients with gout should be advised to modify the content of their diet where consumption of certain high-risk foods is excessive,[7,8] it does have wider implications for people with gout and those who care for them. Gout is frequently poorly managed with only a third of patients prescribed definitive urate-lowering therapy[9] and only a minority of those on such treatment having it escalated to achieve the target serum urate level required to rid the body of causative crystals, prevent flares and shrink tophi.[10] Reasons underlying suboptimal management are not fully understood but patients’ and practitioners’ poor understanding of gout, its causes and treatment are thought to be important factors.[11,12]

People with gout often experience stigma arising from the societal misconception that gout is a humorous self-inflicted condition caused by dietary habits and an unhealthy lifestyle,[6,13] a view which is also pervasive amongst healthcare professionals and in portrayals of gout in lay media.[13,14] As a result, patients are often reluctant to seek help or consult for fear that they will not be taken seriously or will be blamed for their lifestyle habits,[13,15] meaning that practitioners are often unaware that patients have troublesome symptoms. When patients do present, they are frequently given inaccurate or conflicting information which trivialises gout and misrepresents its causes and treatment.[11,13] Hence, valuable opportunities to initiate treatment may be missed. The study by Major et al provides important evidence that much of patients’ preponderance to hyperuricaemia and gout is non-modifiable, countering these harmful but well-established views and practices and providing an opportunity to address these significant barriers to reducing the burden of this easily treatable condition.

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**References**

1. Dalbeth N, Phipps-Green A, Frampton C, Neogi T, taylor WJ, Merriman TR. Relationship between serum urate concentration and clinically evident incident gout: an individual participant data analysis. *Ann Rheumatic Dis* 2018;77:1048-1052. doi: 10.1136/annrheumdis-2017-212288
2. Choi HK, Mount DB, Reginato AM. Pathogenesis of gout. *Ann Intern Med* 2005;143:499–516. doi: 10.7326/0003-4819-143-7-200510040-00009
3. Roddy E, Choi H. Epidemiology of Gout. *Rheum Dis Clin North Am* 2014; 40: 155–175. doi:10.1016/j.rdc.2014.01.001.
4. Zhang Y, Woods R, Chaisson CE, Neogi T, Niu J, McAlindon TE, et al. Alcohol Consumption as a Trigger of Recurrent Gout Attacks. *Am J Med* 2006;119:13–8. doi:10.1016/j.amjmed.2006.01.020
5. Zhang Y, Chen C, Choi H, Chaisson C, Hunter D, Niu J, et al. Purine-rich foods intake and recurrent gout attacks. *Ann Rheum Dis* 2012;71:1448–53. doi:10.1136/annrheumdis-2011-201215
6. Chandratre P, Mallen CD, Roddy E, Liddle J, Richardson J. “You want to get on with the rest of your life”: a qualitative study of health-related quality of life in gout. *Clin Rheumatol* 2016;35:1197–205. doi:10.1007/s10067-015-3039-2
7. Hui M, Carr A, Cameron S, Davenport G, Doherty M, Forrester H, et al. The British Society for Rheumatology Guideline for the Management of Gout. *Rheumatology* 2017;56:e1–20. doi:10.1093/rheumatology/kex156
8. Richette P, Doherty M, Pascual E, Barskova V, Becce F, Castaneda-Sanabria J et al. Updated EULAR evidence-based recommendations for the management of gout. *Ann Rheum Dis* 2017;76:29-42. doi:10.1136/annrheumdis-2016-209707
9. Kuo C-F, Grainge MJ, Mallen C, Zhang W, Doherty M. Rising burden of gout in the UK but continuing suboptimal management: a nationwide population study. *Ann Rheum Dis* 2015;74:661–7. doi: 10.1136/annrheumdis-2013-204463
10. Cottrell E, Crabtree V, Edwards JJ, Roddy E. (2013). Improvement in the management of gout is vital and overdue: an audit from a UK primary care medical practice. *BMC Family Practice* 2013; 14:170 doi:10.1186/1471-2296-14-170
11. Doherty M, Jansen TL, Nuki G, Pascual E, Perez-Ruiz F, Punzi L, et al. Gout: Why is this curable disease so seldom cured? *Ann Rheum Dis* 2012;71:1765–70. doi: 10.1136/annrheumdis-2012-201687
12. Rai SK, Choi HK, Choi SHJ, Townsend AF, Shojania K, De Vera MA. Key barriers to gout care: a systematic review and thematic synthesis of qualitative studies. *Rheumatology* 2018;57:1282-92 doi:10.1093/rheumatology/kex530
13. Spencer K, Carr A, Doherty M. Patient and provider barriers to effective management of gout in general practice: a qualitative study. *Ann Rheum Dis* 2012; 71:1490-95. doi:10.1136/annrheumdis-2011-200801
14. Duyck SD, Petrie KJ, Dalbeth N. “You Don’t Have to Be a Drinker to Get Gout, But It Helps”: A Content Analysis of the Depiction of Gout in Popular Newspapers. *Arthritis Care Res* 2016; 68:1721-172568 doi:10.1002/acr.22879
15. Lindsay K, Gow P, Vanderpyl J, Logo P, Dalbeth N. The experience and impact of living with gout: a study of men with chronic gout using a qualitative grounded theory approach*. J Clin Rheumatol* 2011;17: 1-6 doi:10.1097/RHU.0b013e318204a8f9