

Diagnosis and Management of Gout. Systematic Literature Reviews of the 3e Initiative 2011-2012

The 3e (Evidence, Expertise, and Exchange) Initiative in Rheumatology is a multinational collaborative task force aiming at developing recommendations for rheumatologists' daily clinical practice. This program addresses practical questions that rheumatologists face every day, by combining both systematic literature reviews (SLR) and opinions from international experts.

Since 2006, the 3e Initiative has successively taken interest in the management of ankylosing spondylitis¹, the use of methotrexate in rheumatoid arthritis², the management of patients with undifferentiated peripheral inflammatory arthritis³, and the management of pain by pharmacotherapy in inflammatory arthritis⁴.

For its fifth project, the 3e Initiative investigated the diagnosis and management of an old, but apparently increasingly prevalent disease, namely gout. Today, it is the most common form of inflammatory arthritis in industrialized countries, affecting 1% to 2% of men in Western countries⁵. Although progress has been made in understanding its pathogenesis, treatment, and several questions remain concerning how to implement best practice in clinical settings.

Participants in the 3e Initiative on Diagnosis and Management of Gout project included 474 clinical experts in rheumatology from 14 countries. Using a Delphi process, a panel of experts drawn from among participants selected 10 questions relevant for daily practice:

1. Under which circumstances can a diagnosis of gout be made on clinical grounds, with or without laboratory tests or imaging; and when is identification of crystals necessary?⁶
2. Should patients with hyperuricemia and/or the diagnosis of gout be screened routinely for comorbidities and cardiovascular risk factors?⁷
3. What is the role of glucocorticoids, colchicine, nonsteroidal antiinflammatory drugs, anti-interleukin 1, and paracetamol in the management of acute gout?⁸
4. Which lifestyle changes (such as diet, alcohol intake, weight loss, smoking and/or exercise) are efficacious in the treatment/prevention of gout?⁹
5. What is the efficacy, cost-efficacy, and safety of urate-lowering therapy (allopurinol, as well as febuxostat, peg-uricase, benzbromarone, and probenecid) in the treatment of gout? Which sequence of urate-lowering therapy or combinations of therapies should be recommended?¹⁰
6. When introducing urate-lowering therapy, what is the

best treatment to prevent an acute attack and for how long should it be continued? What is the optimum time to start urate-lowering therapy after an acute attack of gout?¹¹

7. How do common comorbidities (such as metabolic syndrome, and cardiovascular, gastrointestinal, and renal disease) influence the choice of gout-specific drugs (such as colchicine, allopurinol, and other urate-lowering therapy) in acute gout flare, chronic gout, and as prophylaxis for acute flare?¹²

8. What should the treatment target be and how should patients with gout be followed (i.e., using which measures; e.g., patient-reported outcomes, clinical and biochemical and/or imaging outcomes)?¹³

9. How should tophi be managed?¹⁴

10. Can we prevent gouty arthritis, renal disease, and cardiovascular events by lowering serum uric acid levels in patients with asymptomatic hyperuricemia? If yes, what should the target levels be?¹⁵

The experts then discussed and debated a series of SLR based on the above questions and, via a voting process, came to a set of 10 recommendations on the diagnosis and management of gout¹⁶.

The present supplement gathers the 10 SLR. Each review covers a different aspect of the disease and the series as a whole shows all the supporting evidence for the recommendations. Among the SLR, 4 are copublished with the Cochrane Collaboration^{8,9,10,14}, among which one is based upon 4 Cochrane reviews⁸.

We would like to thank all our expert rheumatologists, the scientific committee members, and the fellows for their collaboration and their impressive work to achieve the high-level scientific content of this fifth 3e Initiative.

DÉSIRÉE van der HEIJDE, MD, PhD,

Rheumatology Department,
Leiden University Medical Center,
Leiden, The Netherlands;

RACHELLE BUCHBINDER, MBBS (Hons), MSc, PhD, FRACP,

Monash Department of Clinical Epidemiology,
Cabrini Hospital,
and Department of Epidemiology and Preventive Medicine,
School of Public Health and Preventive Medicine,
Monash University,
Melbourne, Victoria, Australia

Derived from the 3e Gout program, which was sponsored by AbbVie Inc. Logistical and administrative support for the 3e Gout meetings was provided by Margaux Orange, Paris, France; this work was funded by AbbVie Inc. AbbVie employees were present during the 3e meetings, but

did not influence the scientific discussions. AbbVie did not review the content or have influence on this manuscript. Address correspondence to Dr. van der Heijde; E-mail: mail@dvanderheijde.nl

ACKNOWLEDGMENT

The authors acknowledge the work of all members of the 3e scientific committees and all participants in the national meetings.

REFERENCES

1. Sidiropoulos PI, Hatemi G, Song IH, Avouac J, Collantes E, Hamuryudan V, et al. Evidence-based recommendations for the management of ankylosing spondylitis: Systematic literature search of the 3e Initiative in Rheumatology involving a broad panel of experts and practising rheumatologists. *Rheumatology* 2008;47:355-61.
2. Visser K, Katchamart W, Loza E, Martinez-Lopez JA, Salliot C, Trudeau J, et al. Multinational evidence-based recommendations for the use of methotrexate in rheumatic disorders with a focus on rheumatoid arthritis: Integrating systematic literature research and expert opinion of a broad international panel of rheumatologists in the 3e Initiative. *Ann Rheum Dis* 2009;68:1086-93.
3. Machado P, Castrejón I, Katchamart W, Koevoets R, Kuriya B, Schoels M, et al. Multinational evidence-based recommendations on how to investigate and follow-up undifferentiated peripheral inflammatory arthritis: Integrating systematic literature research and expert opinion of a broad international panel of rheumatologists in the 3e Initiative. *Ann Rheum Dis* 2011;70:15-24.
4. Whittle SL, Colebatch AN, Buchbinder R, Edwards CJ, Adams K, Englbrecht M, et al. Multinational evidence-based recommendations for pain management by pharmacotherapy in inflammatory arthritis: Integrating systematic literature research and expert opinion of a broad panel of rheumatologists in the 3e Initiative. *Rheumatology* 2012;51:1416-25.
5. Smith EU, Diaz-Torne C, Perez-Ruiz F, et al. Epidemiology of gout: An update. *Best Pract Res Clin Rheumatol* 2010;24:811-27.
6. Sivera F, Andrés M, Falzon L, van der Heijde DMFM, Carmona L. Diagnostic value of clinical, laboratory and imaging findings in patients with a clinical suspicion of gout: A systematic literature review. *J Rheumatol* 2014;41:3-8.
7. van Durme C, van Ecteld IAAM, Falzon L, Aletaha D, van der Heijde DMFM, Landewé RB. Cardiovascular risk factors and comorbidities in patients with hyperuricemia and/or gout: A systematic review of the literature. *J Rheumatol* 2014;41:9-14.
8. Wechalekar MD, Vinik O, Moi JHY, Sivera F, van Ecteld IAAM, van Durme C, et al. The efficacy and safety of treatments for acute gout: Results from a series of systematic literature reviews including Cochrane reviews on intraarticular glucocorticoids, colchicine, nonsteroidal antiinflammatory drugs and interleukin-1 inhibitors. *J Rheumatol* 2014;41:15-25.
9. Moi JHY, Sriranganathan MK, Falzon L, Edwards CJ, van der Heijde DM, Buchbinder R. Lifestyle interventions for the treatment of gout: A summary of 2 Cochrane systematic reviews. *J Rheumatol* 2014;41:26-32.
10. Kydd AS, Seth R, Buchbinder R, Falzon L, Edwards CJ, van der Heijde DM, et al. Urate-lowering therapy for the management of gout: summary of 2 Cochrane reviews. *J Rheumatol* 2014; 41:33-41.
11. Seth R, Kydd AS, Falzon L, Bombardier C, van der Heijde DM, Edwards CJ. Preventing attacks of acute gout when introducing urate-lowering therapy: A systematic literature review. *J Rheumatol* 2014;41:42-7.
12. van Ecteld IAAM, van Durme C, Falzon L, Landewe RB, van der Heijde DM, Aletaha D. Treatment of gout patients with impairment of renal function: A systematic literature review. *J Rheumatol* 2014;41:48-54.
13. Andrés M, Sivera F, Falzon L, van der Heijde DM, Carmona L. Treatment target and followup measures for patients with gout: A systematic literature review. *J Rheumatol* 2014;41:55-62.
14. Sriranganathan MK, Vinik O, Falzon L, Bombardier C, van der Heijde DM, Edwards CJ. Interventions for tophi in gout: A Cochrane systematic literature review. *J Rheumatol* 2014;41:63-9.
15. Vinik O, Wechalekar MD, Falzon L, Buchbinder R, van der Heijde DM, Bombardier C. Treatment of asymptomatic hyperuricemia for the prevention of gouty arthritis, renal disease, and cardiovascular events: A systematic literature review. *J Rheumatol* 2014;41:70-4.
16. Sivera F, Andrés M, Carmona L, Kydd AS, Moi J, Seth R, et al. Multinational evidence-based recommendations for the diagnosis and management of gout: Integrating systematic literature review and expert opinion of a broad panel of rheumatologists in the 3e initiative. *Ann Rheum Dis* 2014;73:328-35.

J Rheumatol Suppl. 2014 Sept; 92:1–2; doi:10.3899/jrheum.140455