TO THE EDITOR: We read Qaseem and colleagues’ guideline on management of gout (1) with interest. We agree with Neogi and Mikuls’ accompanying editorial recommending that—similar to diabetes mellitus—treatment of gout must not rely solely on symptom relief, because preventing joint destruction and disability is important. However, we are concerned that the guideline takes a step back in the treatment of high serum urate levels, the underlying defect in gout. Qaseem and colleagues cite a lack of knowledge of cost and harms versus benefits of a treat-to-target strategy—one that is widely accepted in clinical practice—and offer an alternate, unproven, new strategy: treat to avoid symptoms.

Qaseem and colleagues do not cite any literature showing more harms with a higher final dose of allopurinol or febuxostat in gout management. Achieving a target serum urate level less than 357 μmol/L (equivalent to <6 mg/dL) is associated with reduction of gout flares, tophi, and costs of medical care. One randomized trial of febuxostat (2) and 2 randomized trials of pegloticase (3) that the Agency for Healthcare Research and Quality evidence report for this guideline regrettably did not include showed that achieving this serum urate target reduced tophi. Tophi are strongly associated with bony erosions and reduced hand function and have a negative physical and psychological effect.

No evidence is provided to support the treat-to-avoid-symptoms strategy proposed. Allopurinol use is actually cost-saving in patients with gout who have 2 or more attacks per year (4), a rare finding in the cost-effectiveness literature related primarily to the low cost of generic allopurinol ($10 for a 90-day supply at discount pharmacies). Measurement of serum urate is similarly inexpensive, costing less than $20. Thus, we believe that the benefit-harms-cost equation based on an evidence-based medicine approach greatly favors a treat-to-target strategy.

A 2004 American College of Physicians guideline addressed the similar dilemma of whether to treat lipid levels to target in patients with diabetes. The authors recommended that the decision be shared between the physician and the patient (5), which would have been the preferred approach for gout as well. Documentation of joint pain, gout flares and their severity, and functional limitations in routine clinical care, which would be necessary in the treat-to-avoid-symptoms strategy proposed, is rare and has low feasibility for widespread implementation. Although we laud the College’s interest in gout management, we believe that this guideline will have adverse public health consequences and move us in the wrong direction at a time when the prevalence of gout is increasing and a more aggressive approach is needed. We suggest that Qaseem and colleagues critically reevaluate these recommendations to avoid doing more harm than good.

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References

IN RESPONSE: Our search identified the randomized controlled trial of pegloticase (1). However, we excluded it because our review focused on the management of gout in primary care and pegloticase was considered to be a drug that primary care physicians do not use. We included Becker and colleagues’ article (2) in both the review (reference 91) and the evidence report (reference 118). In that study, a post hoc analysis revealed the association between serum urate level achieved and reduction in tophi size achieved at week 52; we therefore did not consider it to be hypothesis-testing.

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References
Scientific Misconduct Hurts

TO THE EDITOR: I read Laine’s editorial (1) with interest. I work in the area of diet and risk for chronic diseases and would like to see this paper published. In fact, having read it without knowing that it was retracted, I could not at first understand why. However, its premise reminded me so much of Dansinger and colleagues’ and Gardner and associates’ studies that I easily understood the reason.

I similarly do not understand why Dansinger and colleagues’ manuscript was rejected in the first place. Either Finelli gave it such a bad review that the editors took his word or the reviewers were bamboozled by the currently popular opinion that high-density lipoprotein cholesterol is not an important marker. This is true at present only if designing a drug and, even then, only if the drug is not alcohol.

As for diet and lifestyle interventions, high-density lipoprotein cholesterol (or, better yet, the fasting triglyceride–high-density lipoprotein cholesterol ratio) is the most important marker in a standard lipid test. That genetic influences on high-density lipoprotein cholesterol levels do not affect risk for coronary heart disease merely highlights how important the influences of diet and lifestyle are.

If this manuscript was rejected because it was unfashionable, I expect that fashion to change soon. A proper publication—with changes, of course, if real reviewers deem them necessary—would be the most fitting and just end to this story.

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Reference

IN RESPONSE: Mr. Henderson questions whether Annals did not publish Dansinger and colleagues’ manuscript when we had the opportunity to review it in 2015 because of Finelli’s review, the editors were “bamboozled by the currently popular opinion [about] high-density lipoprotein cholesterol,” or it was “unfashionable.” Many issues factor into Annals’ editorial decision, but those that Mr. Henderson raises did not. The manuscript reported a secondary analysis of a trial that had already been published, and we judged the amount of new information it provided to be limited relative to other papers under consideration. Thus, issues of priority weighed heavily in our decision, because Annals can publish only a small fraction of the many excellent manuscripts that we review.

The actions of the reviewer who stole Dansinger and colleagues’ work were deplorable. We hope that the public disclosure of these actions, retraction of his fraudulent publication, and ensuing effects on his reputation will ensure that “cheaters don’t prosper”—and help to deter other would-be plagiarists. Dansinger’s commendable behavior and essay aimed at preventing such acts (1) are services to the scientific community.

Christine Laine, MD, MPH
Editor in Chief

Disclosures: Disclosures can be viewed at www.acponline.org /authors/icmje/ConflictOfInterestForms.do?msNum=M16-2550.

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Reference

Correction: Update in General Internal Medicine

In a recent Update (1), 2 hazard ratios in a cited article by Lip and colleagues (2) were reported incorrectly. The corrected information is in italics as follows:

Compared with warfarin, a statistically significant lower risk for major bleeding was found with apixaban (HR, 0.53 [CI, 0.39 to 0.71]) and dabigatran (HR, 0.69 [CI, 0.50 to 0.96]), but no difference in risk was found for rivaroxaban (HR, 0.98 [CI, 0.83 to 1.17]). No statistically significant differences were found between dabigatran and apixaban or rivaroxaban. Finally, when apixaban was compared with rivaroxaban, a statistically significant higher risk was found for rivaroxaban (HR, 1.82 [CI, 1.36 to 2.43]).

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References