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July 2018 Author Statement Explaining Different Serum Urate Targets in 2012 ACR Gout Guideline and 2018 ACR Electronic Clinical Quality Measures for Gout

The 2012 American College of Rheumatology (ACR) Gout Guidelines[1,2] and the recently published ACR Electronic Clinical Quality Measures (eCQM) for Gout[3] describe different serum urate thresholds, which has created some confusion. We seek to clarify and defend the rationale for different serum urate targets. Firstly, Guidelines and Quality Measures have distinctly different purposes. Secondly, the Guideline recommendation and Quality Measure statement address different populations of gout patients. These differences resulted in the different target levels.

The 2012 ACR Gout Guideline for the management of hyperuricemia[1] states that "serum urate level should be lowered sufficiently to durably improve signs and symptoms of gout, with the target < 6.0 mg/dL at a minimum." (Underlining added for emphasis.) The principal Guideline authors continue to stand by this recommendation that for patients with gout, where hyperuricemia is being actively managed to achieve the goal of clinical remission as noted above, the treat to target strategy ought to have a goal of serum urate < 6.0 mg/dL, at a minimum.

As described in the ACR Electronic Clinical Quality Measures for Gout manuscript, quality measures are meant to be applied to specific populations. For ALL patients on urate lowering therapy regardless of gouty disease activity, the ACR Quality Measure recommends that serum urate should be checked at least once yearly and be < 6.8 mg/dL. This value is the solubility threshold for precipitation of urate under normal physiologic conditions and, as described in the 2012 ACR Gout Guideline, the "foundation [for] an excess body burden of uric acid, manifested in part by hyperuricemia, which is variably defined as a serum urate level greater than either 6.8 or 7.0 mg/dl." This ACR Quality Measure addresses the minimum threshold (for maximum tolerated serum urate) that can be appropriately applied to ALL patients on ULT. For non-palpable, non-tophaceous patients in long-term clinical remission (e.g., no signs or symptoms of gout for years), the clinical description of these patients in remission meets the above management objective (durable improvement/resolution of their gout). For these patients doing well by all clinical metrics (for years), and whose serum urate is less than solubility threshold (6.8 mg/dL), the ACR eCQM voting panel stated and the ACR guideline authors agree that ULT need not be up-titrated simply for the purpose of lowering serum urate < 6.0 mg/dL. Therefore, the minimum level of control for all patients regardless of symptoms should be < 6.8 mg/dL. For all other patients with gout (e.g., any recent symptoms of gout or tophi), the guideline recommendation remains that serum urate should be "< 6 mg/dL at a minimum, and often < 5 mg/dl."

A more detailed discussion explaining the eCQM decision process and supporting data is presented in the eCQM paper, which is excerpted below, for reference.

> *"The conservative sUA target advocated by international organizations is <6 mg/dl, while some situations and guidelines argue for <5 mg/dl [14-16, 18]. eCQMs are meant to define a minimum threshold of care for most patients (with some exceptions), and, therefore, an eCQM threshold (minimum level of quality care) is typically more lenient than clinical guideline statements (optimal level of care). For example, for patients with diabetes mellitus, the NQF measure addressing glycosylated hemoglobin (HbA_{1c}) (NQF-0575) "…looks at the percent of patients whose most recent HbA_{1c} level is less than 8.0%*

during the measurement year" [50]*, recognizing that treatment guidelines may advocate the achievement of even lower HbA_{1c} goals in practice.*

"For patients with continued gout symptoms, it is clear that the treatment target ought to be <6 mg/dl (or lower). For patients in symptomatic remission (but still on ULT), a less stringent criterion could be clinically reasonable. Recent research has begun to question whether ULT can be safely discontinued in some patients whose sUA remains <7 mg/dl (off ULT) [51]*. In this observational cohort, of the 27 patients with sUA remaining <7 mg/dl, no patient was found to have a clinical gout attack during the median 2 years of follow up off ULT. However, frequency of gout attacks rose quickly with higher sUA levels off ULT.*

"The working group ultimately selected the solubility concentration of urate (6.8 mg/dl) [52] *as a physiologically sound but less stringent threshold for quality measurement purposes. The working group reinforced that for patients with symptomatic gout or tophi, sUA <6 mg/dl (or lower) ought to be the goal, but did not want to penalize clinicians whose patients might be in clinical remission with sUAs that might be slightly higher than 6 mg/dl.*

"With a vibrant internal debate about the precise threshold to specify, this eCQM was initially ranked lowest by the TFP (mean rating 6.3), with some members ranking the eCQM very low, voicing concern against promulgating a treatment target >6.0 mg/dl that did not directly align with the ACR gout guideline recommendations. Despite this controversy, the QMS felt that this eCQM was the key component of the overall treat-to-target strategy emphasized in the 2012 ACR gout guidelines, and therefore this eCQM was advanced to testing by the QMS after combining it with M7."

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[1] 2012 American College of Rheumatology guidelines for management of gout. Part 1: systematic nonpharmacologic and pharmacologic therapeutic approaches to hyperuricemia.
Khanna D, Fitzgerald JD, Khanna PP, et. al.
Arthritis Care Res (Hoboken). 2012 Oct;64(10):1431-46.

[2] 2012 American College of Rheumatology guidelines for management of gout. Part 2: therapy and antiinflammatory prophylaxis of acute gouty arthritis.
Khanna D, Khanna PP, Fitzgerald JD, et. al;
Arthritis Care Res (Hoboken). 2012 Oct;64(10):1447-61.

[3] Development of the American College of Rheumatology Electronic Clinical Quality Measures for Gout.
FitzGerald JD, Mikuls TR, Neogi T, Singh JA, Robbins M, Khanna PP, Turner AS, Myslinski R, Suter LG.
Arthritis Care Res (Hoboken). 2018 May;70(5):659-671.