Diagnosis and Management of Gout: Current State of the Evidence

Focus of This Summary

This is a summary of two systematic reviews. One review evaluated the evidence regarding the accuracy and safety of tests used to initially diagnose gout in the primary care, urgent care, or emergency care setting. The other review examined the evidence base for treating patients with acute gout attacks in the primary care setting. The former systematic review included 27 articles published through February 29, 2016, and is available at *www.effectivehealthcare.ahrq.gov/gout-diagnosis*. The latter systematic review included 154 articles published through March 1, 2016, and is available at *www.effectivehealthcare.ahrq.gov/gout-management.* This summary is provided to assist in informed clinical decisionmaking. However, reviews of evidence should not be construed to represent clinical recommendations or guidelines.

Background

Gout is a form of inflammatory arthritis that presents as joint swelling and pain, referred to as a gout flare or a gout attack. Upon resolution of a gout attack, patients enter a symptom-free period. However, gout attacks recur in many patients. Patients with gout may develop gouty arthritis or tophaceous gout (solid deposits of monosodium urate [MSU] crystals in skin, soft tissue, and joints) in the long term.

Most patients with gout are diagnosed and managed in the primary care, urgent care, or emergency care setting. It is critical to exclude septic arthritis and other causes of inflammatory arthritis in the acute care setting.

Recent guidelines use assessment of MSU crystals in joints and synovial fluid as the gold standard for gout diagnosis along with history and a physical exam. However, joint aspiration for synovial fluid can be challenging to perform in small joints (such as in toes) and to interpret. The role of clinical algorithms (which often draw upon clinical signs, symptoms, and laboratory tests) in the diagnosis of gout is being investigated in clinical studies. Imaging methods (such as dual-energy computed tomography [DECT] and ultrasound) are mainly used in the diagnosis of complex cases of gout.

Treatments for gout attacks include nonsteroidal anti-inflammatory drugs (NSAIDs), colchicine, and corticosteroids to control pain and inflammation.

Nonpharmacological methods advocated for managing hyperuricemia in patients with gout include weight loss, exercise, alcohol restriction, sufficient hydration, and dietary changes. Urate-lowering medications are the primary pharmacological intervention for managing hyperuricemia.

The two systematic reviews summarized here assessed the accuracy of tests to diagnose gout and also examined the evidence regarding the treatment of gout in the primary care setting.

Conclusions

Diagnosis of Gout:

- Two recently developed clinical algorithms to diagnose gout—the Diagnostic Rule and the Clinical Gout Diagnosis—demonstrated sensitivities of 88 percent and 97 percent, respectively, and specificities of 75 percent and 96 percent, respectively, when compared with MSU crystal analysis (*see Table 1*).
  - The strength of evidence (SOE) supporting the use of these clinical algorithms was moderate; these algorithms have not yet been validated in primary care, emergency care, and urgent care settings.
- The strength of evidence regarding the use of DECT (sensitivity: 85–100%; specificity: 83–92%) or of ultrasound (sensitivity: 74%; specificity: 88%) to diagnose gout was low.

Management of Gout:

- Effective treatments for gout attacks include NSAIDs, colchicine, and corticosteroids (high SOE; *see Table 2*).
- Urate-lowering therapy (ULT), including allopurinol and febuxostat, reduced serum urate levels (high SOE; *see Table 3*).
  - ULT did not reduce the frequency of gout attacks during the initial 6 months of therapy (high SOE), likely because of increased risk of gout attacks with initiation of ULT.
  - The increased risk of gout attacks with initiation of ULT was ameliorated with the concomitant use of prophylactic agents (such as colchicine or NSAIDs) against gout attack (high SOE).
  - After 12 months of ULT, the frequency of gout attacks was reduced (moderate SOE).
- The evidence was too limited to determine if dietary and lifestyle changes are effective in managing gout. This does not mean that dietary and lifestyle changes do not work. Clinicians may wish to consult clinical guidelines (*www.guideline.gov*) regarding the role of diet and lifestyle changes in the management of gout.

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Overview of Clinical Research Evidence

- Two clinical algorithms, the Diagnostic Rule and Clinical Gout Diagnosis, were evaluated as tools for diagnosing gout. Both of these algorithms were developed and validated with patients first identified in primary care and whose diagnosis did not include an MSU assessment.
  - **The Diagnostic Rule:** The diagnostic components of this algorithm include clinical characteristics (>1 attack of acute arthritis, maximum inflammation developed within 1 day, redness observed over joints, painful or swollen first metatarsophalangeal joint) and risk factors (hyperuricemia, male sex, hypertension, or >1 cardiovascular disease event). Additional information is available in the article by Janssens and colleagues (Arch Intern Med. 2010 Jul;170[13]:1120-6. PMID: 20625017).
  - **Clinical Gout Diagnosis:** The diagnostic components of this algorithm include clinical characteristics (>1 attack of acute arthritis, maximum inflammation developed within 1 day, monoarthritis/oligoarthritis attack, redness observed over joints, painful or swollen first metatarsophalangeal joint, unilateral tarsal joint attack, tophi) and risk factors (hyperuricemia). Additional information is available in the article by Vazquez-Mellado and colleagues (Clin Rheumatol. 2012 Mar;31[3]:429-34. PMID: 21979446).
- Diagnostic imaging studies that were evaluated in this review included DECT and ultrasound.

Table 1: Accuracy of Diagnostic Methods for Gout With MSU Analysis as the Reference Standard: Key Findings

Diagnostic Method	N Studies	N Subjects	Finding	SOE
Clinical algorithm: The Diagnostic Rule	3	1383	**Sensitivity:** 88% **Specificity:** 75%	●●○
Clinical algorithm: Clinical Gout Diagnosis	3	1383	**Sensitivity:** 97% **Specificity:** 96%	●●○
Dual-energy computed tomography	4	235	**Sensitivity:** 85% to 100% **Specificity:** 83% to 92%	●○○
Ultrasound	8	633	**Sensitivity:** 74% **Specificity:** 88%	●○○

MSU = monosodium urate; N = number; SOE = strength of evidence

Table 2: Effectiveness of Treatments for Acute Gout Attack: Key Findings

Strategy	N Studies	N Subjects	Finding	SOE
Colchicine	2 RCTs	229	Reduces pain when compared with placebo	●●●
	1 RCT	184	A lower dose of colchicine is as effective as a higher dose but with fewer side effects	●●○
NSAIDs[†]	1 RCT and observational data	30 (in RCT)	Reduce pain	●●●
	16 RCTs	1280	No differences among NSAIDs in effectiveness	●●○
Corticosteroids	4 RCTs	297	Reduce pain as much as NSAIDs	●●●
Animal-derived ACTH (not commonly used in clinical practice)	2 RCTs	107	Reduces pain as much as NSAIDs	●●○

ACTH = adrenocorticotropic hormone; N = number; NSAIDs = nonsteroidal anti-inflammatory drugs; RCT = randomized controlled trial; SOE = strength of evidence

[†] The known anti-inflammatory action of these agents was considered when assessing SOE.

Strength of Evidence Scale[††]

- High: ●●● High confidence that the evidence reflects the true effect. Further research is very unlikely to change our confidence in the estimate of effect.
- Moderate: ●●○ Moderate confidence that the evidence reflects the true effect. Further research may change our confidence in the estimate of effect and may change the estimate.
- Low: ●○○ Low confidence that the evidence reflects the true effect. Further research is likely to change our confidence in the estimate of effect and is likely to change the estimate.
- Insufficient: ○○○ Evidence either is unavailable or does not permit a conclusion.

[††] The overall evidence grade was assessed based on the ratings for the following domains: study limitations, directness, consistency, precision, and reporting bias. Other domains that were considered, as appropriate, included dose-response association, plausible confounding, and strength of association (i.e., magnitude of effect). For additional details on the methodology used to assess strength of evidence, please refer to: Owens DK, Lohr KN, Atkins D, et al. AHRQ series paper 5: grading the strength of a body of evidence when comparing medical interventions—Agency for Healthcare Research and Quality and the Effective Health-Care Program. J Clin Epidemiol. 2010 May;63(5):513-23. PMID: 19595577.

Table 3: Effectiveness of Strategies for Managing Hyperuricemia in Patients With Gout: Key Findings

Strategy	N Studies	N Subjects	Finding	SOE
Management of hyperuricemia				
ULT vs. placebo	4 RCTs	1378	Reduces serum urate	●●●
	2 RCTs	1129	Does not decrease the risk of acute gout attacks within the first 6 months	●●●
	1 open-label extension study	NR	Reduces the risk of acute gout attacks after 1 year	●●○
Febuxostat vs. allopurinol	1 RCT	2269	No difference in serum urate-lowering effect	●●●
	1 systematic review	NR	No statistically significant differences in overall adverse events	●●●
	Subgroup of 1 RCT	2269	Age and race do not affect the efficacy of either drug	●○○
Prophylactic therapy with colchicine or NSAIDs	3 RCTs	4103	Reduces the risk of acute gout attacks when initiating ULT	●●●
	1 RCT	190	Longer durations of prophylaxis (>8 weeks) are more effective than a shorter duration when initiating ULT	●●○
	3 RCTs	4103		
Monitoring treatment				
Treating to a specific target serum urate level	1 systematic review and 8 studies	NR	Reduces the risk of gout attacks	●○○

N = number; NR = not reported; NSAIDs = nonsteroidal anti-inflammatory drugs; RCT = randomized controlled trial; SOE = strength of evidence; ULT = urate-lowering therapy

Table 4: Adverse Effects Associated With Pharmacological Agents Used To Manage Gout

Intervention	Adverse Effects
Colchicine	■ Gastrointestinal symptoms, fatigue, and headache ■ Rare adverse effects include leukopenia, aplastic anemia, neuromuscular toxicity, and rhabdomyolysis ■ Overdose in adults and children can be fatal
NSAIDs	■ Dyspepsia, abdominal pain, headache, and reduced kidney function ■ Rare adverse effects include bone marrow suppression, aseptic meningitis, and dermatological adverse events ■ Serious adverse effects include gastrointestinal perforations, ulcers, and increased risk of heart attack or stroke that can lead to death
Corticosteroids	■ Dysphoria and mood disorders, elevation in blood glucose, high blood pressure, weight gain, insomnia, and fluid retention may occur with short-term use
Allopurinol	■ Nausea, upset stomach, diarrhea, and elevated liver enzymes ■ Rare but serious adverse effects include toxic epidermal necrolysis (TEN), Stevens-Johnson syndrome (SJS), bone marrow suppression, and drug rash with eosinophilia and systemic symptoms (DRESS) syndrome
Febuxostat	■ Abdominal pain, diarrhea, musculoskeletal pain, liver function abnormalities, nausea, arthralgia, and rash ■ Rare but serious adverse effects include cardiovascular thromboembolic events, hepatic failure, TEN, SJS, and DRESS

NSAIDs = nonsteroidal anti-inflammatory drugs

Gaps in Knowledge

Clinical algorithms for diagnosing gout

- Diagnostic clinical algorithms such as the Diagnostic Rule and Clinical Gout Diagnosis need to be validated more broadly in primary care, emergency care, and urgent care settings.

Diet, lifestyle, and complementary and alternative medicine therapies for managing gout

- There has been limited research regarding how specific dietary changes (reducing intake of dietary purines, red meat, shellfish, sugary drinks, or alcohol; increasing intake of cherries, modified milk products, or supplemental vitamin C) or lifestyle changes (achieving weight loss) affect symptomatic outcomes in patients with gout.
- Evidence is insufficient to determine the effectiveness of traditional Chinese medicine (e.g., acupuncture, herbal mixtures) in improving symptomatic outcomes in patients with gout.

Urate-lowering therapy for managing hyperuricemia in patients with gout

- While lowering serum urate levels should minimize clinical gout sequelae, the exact target level has yet to be formally evaluated in randomized controlled trials, and guidelines vary in the recommended target levels.

Effectiveness of therapy for gout in subpopulations

- The efficacy of pharmacological therapies for gout when stratified by patient demographics, comorbid conditions, disease severity, or clinical presentation remains to be determined.

Additional Issues

- When initiating ULT, comorbidities and the benefits and harms of prophylactic agents should be considered (e.g., possible contraindications of NSAIDs in patients with cardiovascular disease, renal disease, or both).
- The studies assessing treatment interventions for gout did not clearly state if they enrolled patients in the primary care setting. The applicability of the findings of this review to patients with gout in the primary care setting is unclear.

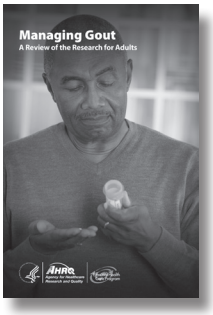
What To Discuss With Your Patients and Their Caregivers

- What a gout attack is and how to prevent the recurrence of gout attacks
- The effectiveness of the various treatment strategies for gout
- The adverse effects associated with the various treatment strategies
- The role of ULT in patients with gout and the potential adverse effects of long-term use

Although further evidence is needed, providers may wish to discuss diet and lifestyle with their patients, as such discussions may offer general health benefits and are commonly supported by guidelines (*www.guideline.gov*).

- It may be prudent to counsel patients on maintaining a healthy diet, losing weight, and exercising to promote general health.
- It may also be prudent to advise patients to limit high-purine foods (especially organ meats), shellfish, sugar-sweetened beverages, and alcohol and to maintain hydration.

Companion Resource for Patients



Managing Gout: A Review of the Research for Adults is a free companion to this clinician research summary. It can help patients and their caregivers talk with their health care professionals about the various options that are available for treating gout.

Ordering Information

For electronic copies of this clinician research summary, the companion patient resource, and both of the full systematic reviews, visit *www.effectivehealthcare.ahrq.gov/gout-clinician*. To order free print copies of the patient resource, call the AHRQ Publications Clearinghouse at 800-358-9295.

Source

The information in this summary is based on *Diagnosis of Gout* (Comparative Effectiveness Review No. 158; February 2016) available at *www.effectivehealthcare.ahrq.gov/gout-diagnosis* and *Management of Gout* (Comparative Effectiveness Review No. 176; March 2016) available at *www.effectivehealthcare.ahrq.gov/gout-management*. Both reviews were prepared by the RAND Southern California Evidence-based Practice Center under Contract No. 290-2012-00006-I for the Agency for Healthcare Research and Quality. Additional information comes from the articles "Diagnosis of Gout: A Systematic Review in Support of an American College of Physicians Clinical Practice Guideline" (Ann Intern Med. 2016 Nov 1. DOI: 10.7326/M16-0462. PMID: 27802505) and "Management of Gout: A Systematic Review in Support of an American College of Physicians Clinical Practice Guideline" (Ann Intern Med. 2016 Nov 1. DOI: 10.7326/M16-0461. PMID: 27802478). This summary was prepared by the John M. Eisenberg Center for Clinical Decisions and Communications Science at Baylor College of Medicine, Houston, TX.

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