

## Medical News &amp; Perspectives

# Chronic Disease Approaches Needed to Curb Gout's Growing Burden

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**G**out's bad rap as disease of dietary excess has sometimes obscured the complex, chronic nature of the disease and led to ineffective care for many patients.

But mounting evidence that gout is a chronic metabolic disease caused by a mix of genetic, environmental, and lifestyle factors is beginning to change that. Experts hope the growing pipeline of drugs targeting the genetics of both the acute and chronic stages of the disease will bring more patients relief. These new tools, along with existing tried-and-true drugs, evidence-based comprehensive care models, and lifestyle advice borrowed from other chronic diseases may help patients and clinicians address gout's many facets more effectively.

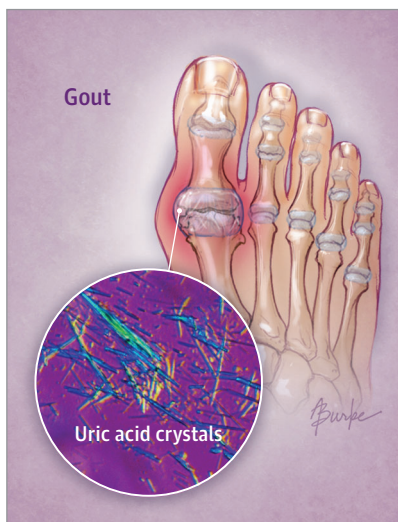
Gout is common in the United States, affecting about 4% of adults. It develops when high levels of uric acid form crystals in patients' joints, causing inflammation and severe pain. Recent research warns that prevalence may be increasing fueled by rising rates of gout risk factors like obesity, hypertension, kidney disease, and hyperlipidemia. Growing use of diuretics or other medications that increase uric acid levels may also be contributing. This has led to more hospitalizations for gout, higher health care costs, and a substantial public health challenge. The growing population of older adults, who are disproportionately affected by the disease, is expected to increase the need for gout care. Despite all this, patients often go untreated or undertreated, which can damage joints or worsen comorbid conditions.

## Diet Misconceptions

As the so-called disease of kings, gout's stigma of gluttony lingers among patients and physicians and may stand in the way of better care.

"The only thing [patients] know is that gout's associated with obesity and from stories it's related to overindulgence of food or alcoholic beverages, so they're

ashamed to even admit to their own family members that they're suffering from gout," said N. Lawrence Edwards, MD, a rheumatologist and chair of the Gout & Uric Acid Education Society (GUES).



"Most patients with gout don't even know that it's a form of arthritis," Edwards added. A 2016 online survey of a nationally representative sample of 1000 US adults, including 103 people with a gout diagnosis, found 71% didn't know gout was a form of arthritis and 55% of the patients with gout weren't aware either. About half who had gout said they were embarrassed by their condition and that they believe it's their fault.

Indeed, diet has been the subject of much finger-pointing when it comes to gout. Red meat, alcohol, sugar-sweetened soft drinks, and seafood have all been implicated. In its 2012 guideline, the American College of Rheumatology (ACR) advised people with gout to avoid purine-rich organ meats such as liver and to limit shellfish and sardines. But the guideline indicates that such dietary changes are likely to yield only a 10% to 18% decrease in uric acid levels—not enough to dissolve uric acid crystals.

Rheumatologist Nicola Dalbeth, MD, a gout expert at the University of Auckland

in New Zealand who helped draft the 2012 recommendations, doesn't advocate a low purine diet for more practical reasons. "It's just unpalatable and not sustainable for most people," she said.

Following a low purine diet can also have unintended consequences, explained Hyon Choi, MD, a rheumatologist and director of clinical epidemiology at Massachusetts General Hospital. Patients on a low purine diet may compensate for the low protein with more carbohydrates or fats, contributing to weight gain and metabolic syndrome that could exacerbate their condition.

In some cases, physicians may inadvertently reinforce gout stigma by overemphasizing dietary interventions that rarely control uric acid sufficiently without medication, Dalbeth said. In fact, a Cochrane Library review found little high-quality evidence to support or refute the use of lifestyle modifications in gout.

Patients may also be reticent to take medications if they believe diet alone can help.

"The patients believe, 'If I was just more astute about watching what I eat, then I wouldn't have the gout, so I'm not going to take the medicines,'" Edwards said. Studies have linked genetic variations in uric acid transporters in the kidneys and gut to both excess uric acid levels and to gout, suggesting that excess production or poor clearance of uric acid contribute. Only about 10% of patients with excess uric acid levels develop gout and environmental factors likely contribute, according to a study of twins. Hypertension, kidney disease, high cholesterol, obesity, being male, and early menopause also increase the risk of developing gout. Newer treatment strategies emphasize these multiple contributors.

"[Patients] don't appreciate that this is really a metabolic disease that's genetically determined and needs to be treated seriously, just like blood pressure and heart disease and kidney disease," he added.

## Differing Guidelines

The 2012 guideline was the ACR's first on treating gout. Its treat-to-target approach aims to lower serum uric acid levels below 6 mg/dL in patients with 2 or more flares a year or other indications by using urate-lowering medications long-term with frequent monitoring. But a 2016 [guideline](#) from the American College of Physicians (ACP) suggests a treat-to-symptoms approach emphasizing the use of anti-inflammatory medications to control flares and reserving uric acid-lowering therapy for patients with frequent flares, noting uncertain evidence of the longer-term benefit.

The divergent treatment philosophies likely have to do with both patient preferences and differing physician perspectives. Painful flares demand immediate attention, but in between flares neither patients nor primary care physicians may pay attention to the underlying chronic disease. But rheumatologists frequently encounter patients dealing with the long-term consequences of poorly managed gout, including chronic arthritis, joint damage, and declining kidney function.

"It's like treating 2 different diseases, or trying to explain to patients the 2 different treatment approaches you need to take," explained Leslie Harrold, MD, MPH, associate professor of medicine and orthopedics at the University of Massachusetts Medical School. "One is to affect the acute manifestations, and then the other is to prevent the chronic problems that occur with gout."

When patients and their primary care physicians delay uric acid-lowering treatment until flares become frequent or uric acid crystals collect in soft tissue, the disease is harder to treat and joint damage has already occurred. By then, Edwards noted, "we've missed a window of opportunity."

Discrepancies between the guidelines may be hampering patient care, said Choi, who helped draft the ACR guidelines. In April the ACR and ACP plan to meet to find some common ground. An update to ACR's gout guideline is scheduled for release in 2020. Ultimately, randomized clinical trials comparing the long-term out-

comes of the various approaches may be needed, Choi said.

"Without the strong, clear-cut data, it's difficult to convince each other anything, he said. "At some point, this needs to be resolved with additional data or some sort of consensus and unified guideline."

In the meantime, allopurinol and febuxostat are recommended as first-line uric acid-lowering therapies in both guidelines. Allopurinol can cause allergic reactions in some people, so the ACR recommends a low- and slow-dose escalation.

"Allopurinol is a therapy that's been around for over 50 years," said Dalbeth. "It's a very effective urate-lowering drug."

Unfortunately, many physicians start the medication, but don't monitor uric acid levels or escalate the dose as needed to adequately lower uric acid levels, Edwards noted. A recent [clinical trial](#) by Dalbeth and her colleagues of allopurinol dose escalation shows it is safe and effective.

The US Food and Drug Administration (FDA) recently [alerted](#) clinicians to clinical trial data that showed an elevated risk of heart-related death in patients taking febuxostat compared with allopurinol. The agency continues to evaluate the potential risk. In the meantime, Dalbeth said clinicians may reconsider their options and should discuss the risks and benefits with patients.

"That really does change the calculus somewhat around which therapy we would use as first-line or in those who don't tolerate allopurinol," she said.

The FDA [approved](#) a new uric acid-lowering drug last year for patients who don't reach treatment targets with allopurinol alone. The drug combines allopurinol with lesinurad in the hopes of addressing uric acid overproduction and poor excretion simultaneously. Several other uric acid-lowering drugs that target renal transport proteins implicated in gout by genetic studies are also in the [pipeline](#). They may help patients who don't reach uric acid targets with existing therapies or who can't take existing drugs, according to Harrold.

Drugs that target the inflammatory pathways triggered in gout are also in devel-

opment. Harrold explained that the new anti-inflammatory drugs may be useful to treat the acute phase of the disease, which sets off an inflammatory cascade and causes the release of interleukin 1b.

"Directly inhibiting that mechanism can dramatically decrease the pain associated with gout," Harrold said.

## Chronic Disease Model

Emerging evidence suggests that a chronic disease care model, which simultaneously addresses uric acid levels, lifestyle, and dietary factors, may help better treat patients with gout.

Patient education is a key component of such approaches. For example, starting uric acid-lowering therapy can temporarily trigger flares before the uric acid levels eventually come down, Choi explained. Without education and prophylaxis for these flares, many patients will discontinue the medication, thinking it isn't effective. A [study](#) involving 106 patients with gout who were recruited from primary care clinics in the United Kingdom found that nurse-led education, lifestyle advice, and uric acid-lowering therapy allowed 9 out of 10 patients to meet treatment targets. A similar pharmacist-led intervention was also [found](#) to help US patients reach their targets. Similar models of care that leverage nurses or other clinicians have been successfully used to treat [diabetes](#).

More research is also under way on comprehensive dietary interventions that have proven to be effective in other chronic metabolic diseases like heart disease, hypertension, and diabetes. Studies suggest that the DASH diet, which emphasizes fruits and vegetables, heart-healthy fats, whole grains, and lean meat may [lower uric acid levels](#) and is associated with a [reduced risk](#) of developing gout.

"We need to be looking at the alternative models of care for gout management," Dalbeth said. "[We need to see] gout as a chronic disease and take those chronic care models that are used so often in diabetes, hypertension, anticoagulation and apply them to gout as well." ■

**Note:** Source references are available through embedded hyperlinks in the article text online.