

# Gout Leaders

Best Practice Forum

**Meeting Highlights**

Milan, Italy 2018



# Graphic summary

## The impact of poorly-managed gout



**Gout affects 1-2% of the adult population**



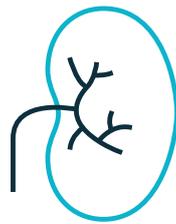
**Left untreated, over 20 years:**

- 70% develop tophaceous gout
- 70% develop irreversible structural joint damage

Associated with comorbidities:



**Cardiovascular**



**Renal**



**Rheumatological**

Untreated gout is linked to a 20-year reduction in quality of life:

— Age/Years

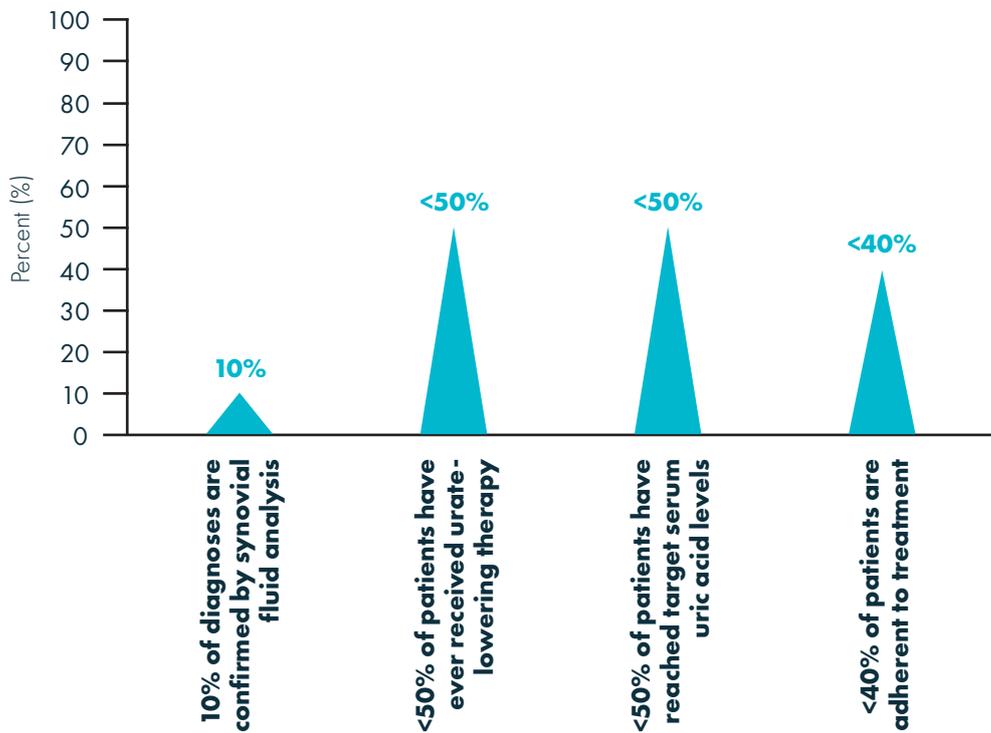


Patients aged 50 years  
with untreated gout...

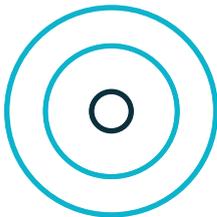


...had the same quality of life as  
healthy people aged 70 years

## Current status of gout management

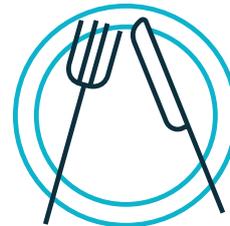


## What does best practice look like?



### Individualised serum uric acid targets:

- <6 mg/dL (most patients; maintenance)
- <5 mg/dL (severe gout; tophi dissolution)



### Diet and lifestyle are not enough in most cases

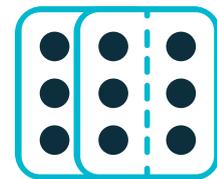
Pharmacotherapy: monitor regularly, and adapt as needed to reach serum uric acid target:



**Increase dose**



**Change medication**



**Combine medications**

# Introduction

Gout is potentially the most curable joint disease, yet the one least often cured. This painful rheumatological condition is among the most frequent causes of inflammatory arthritis. Affecting around 1–2% of adults, it is more prevalent than rheumatoid arthritis (RA), and associated with significant mortality and disability. Fortunately, its pathophysiology is relatively well understood. Of all forms of chronic arthropathy, gout is the one we understand the best.

Why then is management of chronic gout so often inadequate? One answer seems to be that the disease is simply not considered a priority by patients, physicians or the public. Stigma and misconceptions can cause gout to not be treated as the serious chronic disease it really is. Gout is given little emphasis during medical training, and there are few medical educational activities on the subject.

The Grünenthal Gout Leaders Best Practice Forum set out to help fill this educational gap by providing an opportunity for European rheumatologists to learn, discuss and network with one another. A two-day meeting was held in Milan, Italy on 22 and 23 June 2018,

with 28 rheumatologists from Austria, Italy, Spain and Switzerland. Attendees not only heard presentations given by the internationally renowned faculty, but also actively participated in case study-sharing sessions and a discussion on reaching consensus on best practice.

## Association of gout with rheumatological comorbidities

The Best Practice Forum was opened by Professor Leonardo Punzi, with a presentation on the often-ignored connection between gout and other rheumatological conditions.

The lack of attention paid to rheumatological comorbidities could be due to difficulties in establishing the prevalence of these conditions. However, Professor Punzi believes there is another reason: a widely held misconception that if a joint is affected by a rheumatic disease, it cannot also be affected by a second condition.

He proposed classifying rheumatological comorbidities into three categories, based on the likelihood of their association with gout: probable, possible and controversial or possibly even negatively associated.

The first category incorporates psoriatic arthritis and septic arthritis. Professor Punzi presented data from over 5,000 patients, showing that in patients with an established diagnosis of psoriatic arthritis, 3.3% had serum urate crystals in synovial fluid. This was corroborated by a second study that found the risk of having gout in patients with psoriatic arthritis was nearly six times higher than in patients with no psoriasis. Similarly, European League Against Rheumatism (EULAR) recommendations clearly state that gout and sepsis may coexist and that even during an acute attack of gout, it is prudent to analyse synovial fluid to check for microorganisms causing sepsis. Osteoarthritis falls into the 'possible association' category. Recent evidence has suggested that inflammasome activation in patients with crystal arthropathy may influence the evolution of osteoarthritis.

Finally, RA is an interesting case. Historically, some authors have suggested that RA could protect against gout. However, more recent studies indicate that the prevalence of gout in patients with RA is the same as in the general population.



It is difficult, particularly in polyarticular disease, to always differentiate gout from other arthropathies. The gold standard for diagnosis is to perform synovial fluid analysis and check for urate crystals in every patient. But unfortunately, as Professor Punzi closed his speech by noting, many rheumatologists remain reluctant to perform this test.

### The future of gout

Professor Fernando Pérez-Ruiz focused on three questions in his plenary presentation: what is the current status of gout management, what will the future look like if current practice continues, and how can rheumatologists change the future by altering their practice?

Attendees agreed that current gout management is clearly suboptimal. A recent audit from the United Kingdom showed that only 10% of patients had their diagnosis confirmed by synovial fluid analysis. Fewer than half the patients had also been prescribed urate-lowering therapy (ULT), or had ever reached target serum uric acid (sUA) levels. And it was not only the physicians' actions that were suboptimal, but also the patients': only 30–40% of patients adhered to treatment.

Why does it matter if gout is undertreated? Long-term outcomes seen in patients diagnosed at the end of the last century, when ULT was not yet available, show the stark reality of gout's natural course. As well as experiencing pain and flares, over 70% of the patients developed structural joint damage over 20 years, and this damage is irreversible. All these factors resulted in an incredible 20-year reduction in quality of life.

Professor Pérez-Ruiz painted a bleak picture of the future if this "clinical inertia" continues. The population of gout patients is increasingly getting older, and the proportion with comorbidities is rising. The rate of tophaceous or polyarticular gout is also increasing – but the number of patients receiving ULT therapy is not. The number of hospitalisations for gout, and the associated costs, are now very close to those of RA.

However, he closed on a positive note by showing that it is possible to change. Over the last 10 years in Spain, rates of crystal-confirmed diagnosis, initiation of ULT and achievement of target sUA levels have all increased.

This improvement in disease control has wide-ranging positive effects. For patients, it results in improved mobility, improved ability to perform daily activities, reduced pain and even reduced anxiety or depression. Reduced disability also leads to fewer days of work lost, and therefore good disease control must matter not only to patients and healthcare systems, but to society as a whole.



# Breakout sessions

## — Session 1

### **Gout – more than just flares**

The session led by Dr Tim Jansen examined the chronic pathophysiology of gout. He described the condition as “two diseases for the price of one”: both acute attacks of inflammation due to high inflammasome activity, and crystal depositions due to chronic hyperuricaemia.

Not treating hyperuricaemia can have severe consequences. Left untreated, 70% of patients will have tophaceous gout after 20 years, possibly leading to destruction of bone and cartilage. Tophaceous lesions may occur in the central nervous system, where they can easily be mistaken for malignancy, or even in the kidney or ileum.

sUA levels are also correlated with comorbidities. Untreated gout leads to stiffened vasculature and the risk of cardiovascular complications rises with increased levels of sUA. Kidney function is also negatively associated with uric acid levels.

One interesting question came up on mortality: the dangers of high uric acid are well known, but could a very low sUA level also increase mortality risk? Data from a large study of older people in Taiwan, interestingly, suggests not. Once the study population was corrected for malnourishment, the relationship appeared to be J-shaped. There seems to be limited risk, then, with setting even very low target sUA levels.

## — Session 2

### **Treat to target, and monitor regularly**

Professor Pérez-Ruiz began his session by discussing the evidence for a treat-to-target approach. The American College of Physicians stated that there is no evidence for this approach. But if comparisons are made with treat-to-target recommendations for other rheumatological conditions, the evidence for these was also lacking – and the efficacy of the approach has now been shown.

Individualising the target is of the highest importance. For patients with severe gout, a lower target sUA level may be more appropriate than for those with milder gout. Even in initially severe gout, once tophi have been eradicated and crystal deposition dissolved, a higher ‘maintenance’ target may now be appropriate. Target levels for preventing later trouble may be different from the levels needed to treat current problems.

Whatever target is chosen, patients must be monitored to ensure they are on track to reach it. Striking data from Germany showed that fewer than 1% of patients had their sUA tested at least annually. But without monitoring, it is not possible to optimise treatment, ensure safety, support adherence, achieve target sUA levels and eventually improve outcomes.



— Session 3

## Standard care to best practice

Professor Alexander So's session opened with a clinical case. A middle-aged man developed sudden knee pain and swelling. X-rays showed fluid but no other abnormalities. Based on this clinical picture, Prof So asked the audience: how confident are you in diagnosing this patient with gout?

He acknowledged that it may sometimes be necessary to diagnose based on clinical parameters alone, but aspiration remains the gold standard.

Current practice in treatment decisions often does not match best practice. Many patients are only given lifestyle advice, but diet cannot cure gout the way ULT can. Three classes of drugs are available: uricosytics, uricosurics and xanthine oxidase inhibitors (XOIs).

For a disease as common as gout, Prof So expressed his disappointment that there are only two XOIs currently on the market. This lack of treatment choice means many patients are intolerant or unable to reach target sUA on even high doses of these therapies.

However, 90% of patients with hyperuricemia have uric acid underexcretion, rather than overproduction, and therefore uricosurics can be helpful. These drugs can be used on their own but a newly available option is to combine an XOI with a uricosuric, which can lead to better outcomes in reducing flares and tophi and achieving target sUA levels.



# Consensus discussion

The meeting closed with a whole-group discussion on five key topics where international consensus on best practice has not yet been reached.

## How comfortable do you feel with a conservative vs an intensive approach?

More than anything else, treatment approaches must be individualised. Treatment should enable every patient to live without gout flares regardless of their age. Every patient's therapy should aim to help them reach a target sUA level, but exactly what that target level is must be tailored to the individual. 'Conservative' was loosely defined to mean treatment of flares only, whereas 'intensive' treatment included efforts to treat to target. Language is important: 'intensive' is not the same as 'aggressive', and intensive treatment to reach a target sUA level can take place over a prolonged period of time to avoid causing harm.

## Is imaging useful to tailor treatment at any time?

The great majority of attendees currently use imaging (primarily X-ray or ultrasound, although a small number use dual-energy computed tomography (DECT)) to adjust treatment. Tophi seen on imaging leads to intensified treatment, although tapering down of treatment was based on lack of symptoms and not on imaging results. There are also a number of roles for imaging in diagnosis, including identifying an appropriate

joint to puncture. Obtaining imaging results for every patient at diagnosis to determine the extent of their disease was considered a good idea; what is initially considered 'mild' gout may turn out to be tophaceous gout, requiring a far-more-urgent treatment approach. However, more research is needed on the optimum number of joints to screen before any consensus can be reached in that area.

## When diagnosis is confirmed, when do you treat?

There is conflict between the guidelines: EULAR recommends discussing urate-lowering therapy with patients at first diagnosis, while the American College of Rheumatology prefers deferring such treatment until the patient has experienced two flares or develops severe gout. Attendees, on the whole, followed EULAR's approach – but it is important to note that many stated their colleagues do not do the same! This inconsistency in practice even within the same hospital was considered a cause for concern, and there were fears patients could be experiencing a 'lottery' in the standard of care they receive.

## How can we define 'best practice' for gout, and aim for remission for all our patients?

Although attendees generally followed EULAR guidelines for managing gout, they did not follow them stringently for every patient. The reason for this is two-fold: firstly, the guidelines are too long and detailed for regular reading. Secondly, it was considered most important to achieve a target sUA level and to eliminate symptoms. The guideline recommendations for therapy may help to achieve these goals, but they are just that – recommendations, not 'commandments', and clinical judgement and experience is of the utmost importance in deciding when and how to adjust therapy.

## What are the concerns to bear in mind when speaking to patients?

Attendees all agreed that systematic patient education is important and every patient should be informed about the causes of gout, their possible achievable outcomes and the steps that could be taken to reach those outcomes. The patient decides whether or not to take treatment, so they must be convinced of its benefits or else any therapy is doomed to fail. Finally, better education leads to greater empowerment, as patients learn what their test result numbers mean and what they should expect from effective therapy. Empowered patients can compel physicians to provide better care.

