

# Treat to target in gout

<b>Submission date</b> 17/04/2019	<b>Recruitment status</b> No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
<b>Registration date</b> 12/06/2019	<b>Overall study status</b> Ongoing	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
<b>Last Edited</b> 08/04/2025	<b>Condition category</b> Musculoskeletal Diseases	<input type="checkbox"/> Individual participant data <input checked="" type="checkbox"/> Record updated in last year

## Plain English summary of protocol

### Background and study aims

Gout is a common arthritis that affects one in forty people in the UK. It results from a high level of uric acid in the body which forms urate crystals inside the joints. From time to time, these crystals shake loose from their deposit and cause severe joint pain and swelling. These flares usually last for one to two weeks. Flares are treated with anti-inflammatory tablets such as ibuprofen. However, anti-inflammatory tablets do not dissolve the urate crystals. Other tablets such as allopurinol can lower the uric acid level to below a target level, and slowly dissolve the crystals. These are safe treatments that have been used for many years. However, whether their use reduces the number of gout flares is unknown. The aims of this study are to find out if long-term use of tablets such as allopurinol reduces the number of gout flares and improves well-being and to also find out if this treatment is cost-effective for the NHS.

### Who can participate?

Patients aged 18 years and over with gout who have had a flare of gout in the previous 12 months

### What does the study involve?

Participants are randomly allocated to receive one of the following two treatments: allopurinol with the dose gradually increased aimed at reducing blood uric acid to below target level, or usual gout care from their GP including the option to start allopurinol depending on symptoms. People in the first group need treatment visits with a practice nurse in order to adjust the dose of allopurinol to reduce uric acid level sufficiently to allow the urate crystals to dissolve. In addition to the visits to increase the dose of allopurinol, there are three other visits for people taking part in the study. These visits occur at study start, and yearly for 2 years. Information on health, wellbeing and medication use are collected, and blood pressure, height, weight, kidney function and uric acid level are measured at the visits. People taking part in the study are asked to record details of each gout flare they experience while in the study. The main outcome of the study is the number and severity of gout flares. This and the other information collected are compared between the groups. The cost of treatment and overall wellbeing are used to find out if this treatment is cost-effective for the NHS. After the 2-year study ends, participants are asked to continue to provide information about gout flares for a further 2 years. Information about other illnesses, hospital admissions and medications prescribed are collected from their GP. The information collected is compared between the groups.

What are the possible benefits and risks of participating?

Any medications that will be advised to be used for gout in this study will be currently available treatments that will be prescribed in line with guidelines. As with any medication, the treatments for gout can sometimes cause side effects but it is rare to suffer any serious upset. The researchers currently do not know the benefit to patients taking part in the study. However, this study will help them to learn more about how gout should be treated and improve the care of patients with gout in the future.

Where is the study run from?

The study is being run from the University of Nottingham and the Keele Clinical Trials Unit is managing the study. The study is recruiting patients in East Midlands, West Midlands and Wessex (UK)

When is the study starting and how long is it expected to run for?

The study plans to start recruitment in summer 2019 and patients will be in the study for 2 years with an additional 2-year long-term follow-up.

Who is funding the study?

National Institute of Health Research (NIHR) Health Technology Assessment (HTA) programme (UK)

Who is the main contact?

Steff Garvin  
s.garvin@keele.ac.uk

### **Study website**

<https://www.keele.ac.uk/t2t>

## **Contact information**

### **Type(s)**

Scientific

### **Contact name**

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Public

### **Contact name**

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## Additional identifiers

### EudraCT/CTIS number

Nil known

### IRAS number

263669

### ClinicalTrials.gov number

Nil known

### Secondary identifying numbers

19023; HTA 17/82/02, IRAS 263669

## Study information

### Scientific Title

What is the clinical and cost effectiveness of using a goal-directed allopurinol-based treat-to-target protocol in people with recurrent gout flares?

### Acronym

T2T

### Study objectives

To evaluate the effectiveness of allopurinol-based treat-to-target ULT versus usual general practitioner (GP) care on number of gout flares over 2 years.

### Ethics approval required

Ethics approval required

### Ethics approval(s)

Approved 10/06/2019, North West - Liverpool East Research Ethics Committee (Barlow House, 3rd Floor, 4 Minshull Street, Manchester, M1 3DZ, United Kingdom; +44 (0)207 104 8345, +44 (0) 207 104 8019; nrescommittee.northwest-liverpooleast@nhs.net), ref: 19/NW/0310

### Study design

Parallel-arm multicentre randomized controlled trial with 1-year internal pilot and 2-year long-term extension phase

### Primary study design

Interventional

### Secondary study design

Randomised controlled trial

**Study setting(s)**

GP practice

**Study type(s)**

Treatment

**Participant information sheet**

Not available in web format, please use contact details to request a participant information sheet

**Health condition(s) or problem(s) studied**

Gout

**Interventions**

Participants will be randomised to one of two interventions. Randomisation: 1:1 individual randomisation stratified by region and prior intolerance to Colchicine.

Intervention arm 1: Allopurinol-based treat-to-target Urate Lowering Treatment (ULT) (delivered by practice nurses in primary care). Patients will have commence on a dose of 100 mg of allopurinol or have this increased by 100 mg if already on treatment. Treatment will follow 'a treatment-to-target' approach, i.e. patients will be prescribed low-dose ULT initially, and the dose increased monthly, guided by blood-test results, until the urate level is sufficiently below the saturation point (i.e. less than 360  $\mu\text{mol/L}$ ). Other ULTs will be prescribed if allopurinol is not tolerated.

Intervention arm 2: Usual GP care: Patients will be advised to consult their GP as usual and receive treatment for gout flares and urate lowering treatment according to GP's usual practice.

Each participant in the study for 4 years, 2 years each in the RCT and long-term extension respectively.

**Intervention Type**

Drug

**Phase**

Not Applicable

**Drug/device/biological/vaccine name(s)**

Allopurinol

**Primary outcome measure**

Number of gout flares in the first 2 years measured by patient initiated SMS service or acute gout flare diary

**Secondary outcome measures**

1. Number of gout flares in months 1-12, measured by self-report using SMS or gout flare diary
2. Number of gout flares in months 13-24, measured by self-report using SMS or gout flare diary
3. Tophus count, measured by visual inspection at baseline, year 1 and year 2
4. Size of largest tophus, measured using vernier calipers at baseline, year 1 and year 2

5. Daily pain score measured by self-report using SMS or gout flare diary during gout flare
6. Quality of life measured by EQ-5D-5L during gout flares
7. GIS after flare resolution, measured by completing a questionnaire at baseline, year 1 and year 2 and during gout flares
8. Serum urate: proportion hitting the target serum urate level ( $<360\text{ }\mu\text{mol/L}$ ) and continuous variable at year 1 and 2, measured from a blood sample taken at baseline and year 1 and year 2 post randomisation research visits
9. Quality of life measured by EQ-5D-5L between gout flares at baseline, year 1 and year 2
10. ULT (name and dose) measured by self-report during treatment visits and at year 1 and year 2
11. Treatment satisfaction measured by TSQM-II at year 1 and year 2 post randomisation
12. Returned pill count documented on a CRF at research year 1 and year 2 post randomisation visits
13. Compliance with ULT measured by MMAS-8 scale at year 1 and year 2
14. Serum creatinine and estimated GFR measured from a blood test at screening, year 1 and year 2 and during treatment visits in the intervention arm
15. Urine albumin-creatinine ratio measured from a urine sample at baseline, year 1 and year 2
16. Primary-care consultations for gout, measured by self-report and general practice record search at year 4
17. Hospitalizations due to gout, measured by self-report and general practice record search at year 4
18. Other prescriptions for treating flares of gout, measured by general practice record search at year 4
19. Investigations for gout, measured by general practice record search at year 4
20. Incident cardiovascular diseases, hypertension, diabetes, measured by general practice record search at year 4
21. Incidence or progression of CKD, measured by: general practice record search at year 4
22. Death, measured by general practice record search at year 4
23. Adverse events (AE), measured by self-report at 2 years
24. Cost-effectiveness, measured by health economic analysis of all data at 2 years

**Overall study start date**

01/01/2019

**Completion date**

31/08/2028

## Eligibility

**Key inclusion criteria**

1. Age  $\geq 18$  years
2. Ability to give informed consent
3. Meets the clinical American College of Rheumatology (ACR)/European League Against Rheumatism (EULAR) classification criteria for gout
4.  $\geq 1$  flare of gout in the previous 12 months
5. Serum urate  $\geq 360\text{ }\mu\text{mol/L}$  regardless of current ULT

**Participant type(s)**

Patient

**Age group**

Adult

**Lower age limit**

18 Years

**Sex**

Both

**Target number of participants**

466

**Total final enrolment**

468

**Key exclusion criteria**

1. Previous allopurinol side-effects that contraindicate its prescription
2. Dementia, severe enduring mental illness i.e. mental health illness that makes receiving the study information and initial screening questionnaire from GP a stressful experience
3. Unable to comply with study procedures
4. Life expectancy less than 12 months
5. Cancer treatment, i.e. surgery, radiotherapy, or chemotherapy in the previous 12 months
6. Solid organ transplant
7. Cirrhosis
8. Autoimmune rheumatic disease i.e. rheumatoid arthritis, psoriatic arthritis, systemic lupus erythematosus, connective tissue diseases, vasculitis, giant cell arteritis, polymyalgia rheumatica, inflammatory arthritis associated with inflammatory bowel disease, reactive arthritis, ankylosing spondylitis
9. Inflammatory bowel disease
10. Current long-term daily oral corticosteroid treatment defined as continuous use for  $\geq 30$  days or current immunosuppressive treatments
11. Stage 4/5 CKD i.e.  $\text{eGFR} < 30 \text{ ml/min}$
12. Pregnant, breastfeeding or planning to become pregnant in the next 4 years

**Date of first enrolment**

30/06/2019

**Date of final enrolment**

02/05/2024

**Locations****Countries of recruitment**

England

United Kingdom

**Study participating centre**

**East Midland Clinical Research Network**

Level 1 Knighton Street Outpatients

Leicester Royal Infirmary

Leicester  
United Kingdom  
LE1 5WW

**Study participating centre**  
**West Midland Clinical Research Network**  
Unit 9 Greyfriars Business Park  
Greyfriars Road  
Frank Foley Way  
Stafford,  
United Kingdom  
ST16 2ST

**Study participating centre**  
**Wessex Clinical Research Network**  
Unit 7, Berrywood Business Village  
Tollbar Way  
Hedge End  
Southampton  
United Kingdom  
SO30 2UN

**Study participating centre**  
**London CRNs (Noclar, North London, South London, and Luton Essex and Herts)**  
1st Floor, Bloomsbury Building  
St Pancras Hospital  
4 St Pancras Way  
London  
United Kingdom  
NW1 0PE

**Study participating centre**  
**Yorkshire and Humber CRN**  
Oak House  
Moorhead Way  
Bramley  
Rotherham  
United Kingdom  
S66 1YY

**Study participating centre**

**Thames Valley and South Midlands CRN**

Unipart House

NIHR CRN: Thames Valley And South Midlands Offices Level 2 West

Garsington Rd

Cowley

Oxford

United Kingdom

OX4 2PG

## Sponsor information

**Organisation**

University of Nottingham

**Sponsor details**

East Atrium Jubilee Conference Centre

Jubilee Campus

Nottingham

England

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**Sponsor type**

University/education

**ROR**

<https://ror.org/01ee9ar58>

## Funder(s)

**Funder type**

Government

**Funder Name**

National Institute for Health Research

**Alternative Name(s)**

National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

**Funding Body Type**

Government organisation



**Funding Body Subtype**

National government

**Location**

United Kingdom

## Results and Publications

**Publication and dissemination plan**

The protocol will be available on the NIHR HTA journals library but has yet to be published. The results of this study will be shared at medical conferences and through publication in academic journals.

**Intention to publish date**

31/08/2028

**Individual participant data (IPD) sharing plan**

The datasets generated and analysed during the current study will be available upon request from the Chief Investigator. Requests should be emailed to the sponsor using the sponsor contact details, in which an external data request process will be initiated and considered. Consent from participants will be obtained for use of anonymous data in future research and will be available for 7 years after the study has ended.

**IPD sharing plan summary**

Available on request

**Study outputs**

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">HRA research summary</a>			28/06/2023	No	No