National Institute for Health and Care Excellence

Guideline version (Final)

Gout: diagnosis and management

[L] Evidence review for optimum frequency of monitoring

NICE guideline NG219

Evidence reviews underpinning recommendation 1.5.15 and research recommendations in the NICE guideline

June 2022

Final

National Institute for Health and Care Excellence

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ISBN: 978-1-4731-4603-7

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1.1 Review question: What is the optimum frequency of serum urate level monitoring for people continuing on urate-lowering therapies for gout?

1.1.1 Introduction

Urate-lowering therapies for gout are long-term medications, often taken lifelong. With any treatment involving medication there is a need to monitor it to ensure it remains safe and effective at the prescribed dose. In gout monitoring is via measuring serum urate level to ensure it is within the targeted range. This is important because unless the serum urate is within the targeted range the urate lowering therapy will not be effective. For people who have reached therapeutic range good practice is to continue monitoring to check adherence and avoiding potential adverse effects for long-term treatment. However current practice is highly variable with many people only receiving serum urate monitoring *ad hoc* after a gout flare.

This aim of this review is to evaluate the optimum frequency of monitoring people on urate lowering therapy who have achieved serum urate level target.

1.1.2 Summary of the protocol

For full details see the review protocol in Appendix A.

Table 1: PICO characteristics of review question

Population	Inclusion: Adults (18 years and older) with gout who are having their serum urate level monitored. These patients have already reached target serum urate level and are continuing treatment. Strata: • People with CKD (stage 3) • People with CKD (stages 4-5) • People without CKD or people with CKD stages 1-2 • Mixed population (people with CKD and people without CKD) Exclusion: People with calcium pyrophosphate crystal deposition, including pseudogout
Interventions	Different monitoring frequencies, examples: • Every six months • Every year • Every two years
Comparisons	• Compared to each other • Control (no monitoring)

Outcomes	All outcomes are considered equally important for decision making and therefore have all been rated as critical: • health-related quality of life (e.g. as described by SF-36, Gout Assessment Questionnaire (GAQ) and the Gout Impact Scale (GIS) or other validated gout-specific HRQoL measures • patient global assessment of treatment success (response to treatment) (e.g. Likert scales, visual analogue scales (VAS), numerical ratings scales (NRS)) • pain (measured on a visual analogue scale (VAS) or numerical rating scale such as the five-point Likert scale, or reported as pain relief of 50% or greater) • joint swelling/joint inflammation • joint tenderness • serum urate level • frequency of flares • tophi • admissions (hospital and A&E/urgent care) • GP visits Timepoints: Short-term 6 months, medium 6-12 months, long-term 12+ months
Study design	RCT Systematic reviews of RCTs If insufficient RCT evidence is available (no or little evidence for interventions/comparisons), search for non-randomised studies (prospective and retrospective cohort studies will be considered if they adjust for key confounders: • Age • Gender Published NMAs will be considered for inclusion.

1.1.3 Methods and process

This evidence review was developed using the methods and process described in Developing NICE guidelines: the manual. Methods specific to this review question are described in the review protocol in Appendix A and the methods document.

Declarations of interest were recorded according to NICE's conflicts of interest policy.

1.1.4 Effectiveness evidence

1.1.4.1 Included studies

No relevant clinical studies comparing different monitoring strategies were identified.

See also the study selection flow chart in Appendix C.

1.1.4.2 Excluded studies

See the excluded studies list in Appendix J.

1.1.5 Summary of studies included in the effectiveness evidence

No evidence was identified for this review.

1.1.6 Summary of the effectiveness evidence

No evidence was identified for this review.

1.1.7 Economic evidence

1.1.7.1 Included studies

No health economic studies were included.

1.1.7.2 Excluded studies

Two economic studies relating to this review question were identified but were excluded due to a combination of limited applicability and methodological limitations [8, 14]. These are listed in Appendix J, with reasons for exclusion given.

1.1.8 Economic model

This topic was identified as medium – high modelling priority area but no clinical or economic evidence was identified for this review question. Subsequently, a costing analysis was undertaken to determine the number of flares which need to be avoided (per person per year) for the cost of annual monitoring to break even.

The costing analysis estimated the total cost of annual monitoring for people who have achieved target serum urate levels and the total cost of a gout flare. The total cost of monitoring was divided by the total cost of a gout flare to obtain a value for the number of flares avoided for annual monitoring to break even.

The cost of annual monitoring

The cost of annual monitoring was estimated for two patient populations:

1. People with gout with comorbidities
2. People with gout without comorbidities

Monitoring for people with gout once they have achieved target serum urate levels is relatively simple whereby a blood test is taken to measure serum urate levels. If serum urate levels are above target, ULT will be adjusted until people reobtain target levels. ULT treatment for people with gout with a number of comorbidities is the same for people without comorbidities, with the exception of people with CKD where lower doses of allopurinol are prescribed. The committee noted it is very common for people with CKD to have gout, so

clinicians are well informed on how people with gout and CKD should be managed. In addition, people with more severe CKD are likely to be treated in secondary care and monitoring of serum urate levels can be conducted in an appointment visiting a rheumatologist.

The committee concluded the cost of monitoring for people without comorbidities would be more expensive as an additional appointment would be required for these group of people. Whereas monitoring for gout for people with comorbidities could be conducted alongside additional appointments people receive for other comorbidities.

The costs of monitoring for people with gout with comorbidities are presented in Table 2.

Table 2: Cost of monitoring for people with comorbidities

Resource	Cost per hour	Cost per min	Time (mins)	Total cost
Nurse (Band 5)[a]	£42	£0.70	9.25[b]	£6.48
GP[a]	£238	£3.96	5[b]	£19.82
Blood test[c]				£3.10
Total cost				**£29.40**

Sources:(a) PSSRU 2020[3], including qualification costs (excluding individual and productivity costs)
(b) Based on committee opinion
(c) NHS reference costs 2019/20[11]

The costs of monitoring for people with gout without comorbidities are presented in Table 3.

Table 3: Cost of monitoring for people without comorbidities

Resource	Cost per hour	Cost per min	Time (mins)	Total cost
Nurse (Band 5)[a]	£42	£0.70	18.5[b]	£12.95
GP[a]	£238	£3.96	12.5[b]	£49.55
Blood test[d]				£3.10
Total cost				**£65.61**

Sources:(a) PSSRU 2020[3], including qualification costs (excluding individual and productivity costs)
(b) Based on committee opinion
(c) NHS reference costs 2019/20[11]

These costs were multiplied by the proportion of people with gout with and without comorbidities provided by Guthrie et al.[6]. The proportion of people with gout with comorbidities was 86.90% and the proportion of people without comorbidities was 13.10%. This resulted in a total cost for annual monitoring of £34.14.

The cost of a gout flare

The cost of a gout flare was estimated for a total of eight different scenarios and presented in Table 4. The methodology for obtaining the cost of a gout flare can be found in Evidence review G.

Table 4: Cost of a gout flare

Scenario	Hospital	GP visit	Repeat prescription	Self-managed	Total cost of a gout flare
Scenario 1	1%	25%	54%	20%	£30.52
Scenario 2	5%	25%	50%	20%	£55.64
Scenario 3	1%	25%	44%	30%	£28.49
Scenario 4	5%	25%	40%	30%	£53.61

Scenario	Hospital	GP visit	Repeat prescription	Self-managed	Total cost of a gout flare
Scenario 5	1%	15%	64%	20%	£29.61
Scenario 6	5%	15%	60%	20%	£54.59
Scenario 7	1%	15%	54%	30%	£27.22
Scenario 8	5%	15%	50%	30%	£52.20

Results

The number of gout flares required for annual monitoring to break even was estimated by dividing the cost of a gout flare by the cost of annual monitoring. The results of the costing analysis are presented in Table 5.

Table 5: Results for the number of gout flares required to be avoided per person for the cost of monitoring to break even

Scenario	Number of gout flares avoided per person for the cost of monitoring to break even
Scenario 1	1.12
Scenario 2	0.61
Scenario 3	1.20
Scenario 4	0.64
Scenario 5	1.15
Scenario 6	0.63
Scenario 7	1.26
Scenario 8	0.65

Based on the results of the eight scenarios the average number of flares which need to be avoided per person, per year, for annual monitoring to break even ranges from 0.61 – 1.26.

1.1.9 Unit costs

Relevant unit costs are provided below to aid consideration of cost effectiveness.

Table 6: Unit costs

Resource	Unit costs
Primary care Practice Nurse (Band 5), cost per hour[(a)]	£42
General Practitioner, cost per consultation (9.22 mins)[(a)]	£37
Cost of blood test (excluding time to take blood)[(b)]	£3-£4

1. *Source: PSSRU 2020[3], including qualification costs (excluding individual and productivity costs)*
2. *Source: NHS reference costs 2019/2020[11]: directly accessed pathology services, haematology and phlebotomy respectively.*

1.1.10 Evidence statements

Economic

- No relevant economic evaluations were identified.

1.1.11 The committee's discussion and interpretation of the evidence

1.1.11.1. The outcomes that matter most

The committee considered the following outcomes as important for decision making health-related quality of life, patient global assessment of treatment success, pain, joint swelling/joint inflammation, joint tenderness, serum urate level, frequency of flares, tophi, admission (hospital and A&E/urgent care) and GP visits.

Studies that reported serum urate level outcomes would be of particular interest because changes to levels after the target had been reached would require the prescriber to intervene to bring the serum urate level back within the target range. Studies that reported changes at different timepoints would guide the committee in their recommendation on what the frequency of monitoring serum urate should be.

The committee decided to combine joint swelling and joint inflammation as they agreed that these outcomes are synonymous for people with gout. To help guide recommendations the committee were interested in the different frequencies of monitoring reported and decided to categorise time points reported in the included studies by short-term (up to 6 months), medium-term (6 to 12 months) and long-term (more than 12 months).

1.1.11.2 The quality of the evidence

No evidence was identified. The committee decided to make a consensus recommendation based on their clinical experience.

The committee noted the recommendation made for a treat-to-target ULT strategy which would indicate a requirement to monitor a person's serum urate levels. As no evidence was found and annual monitoring would have a resource impact because it would be a change in practice the committee decided to make a research recommendation on the optimum frequency of serum urate level monitoring in people who have achieved target serum urate level.

1.1.11.3 Benefits and harms

The committee agreed that one of the reasons for continuing to monitor a person's serum urate level when they have achieved the target serum urate level is to detect any subsequent rises in the level, which can occur with age, new medications (e.g. diuretics), decline in renal function, or as a result of changes in lifestyle. Rises in the serum urate level above target would necessitate more intensive ULT to lower the level again. The committee noted that changes in serum urate level occurs quickly usually within months, therefore regular monitoring would identify changes early and facilitate early intervention. Adherence to ULT was discussed, and the committee noted that people tend to stop treatment if they feel better, however continuing ULT as prescribed is important as serum urate levels rise quickly after a person stops taking ULT, leading to a recurrence of symptomatic gout.

The committee discussed that in current practice the frequency and delivery of serum urate level monitoring is highly variable, and decisions are usually based on individual factors after discussion with the patient. More often, visits by patients to clinical practice are triggered by gout flares and only then would a health professional measure a person's serum urate level. However, the committee were in agreement that this was not sufficient as the goal of monitoring is to maintain the person at the target level and prevent future gout flares rather than flare management. The committee agreed based on their experience that annual monitoring of serum urate levels would be an appropriate frequency as this would provide enough time to see the result of prescribing urate lowering therapy on serum urate levels and then to adjust treatment as required. The committee acknowledged this would also reflect the British Society of Rheumatology's guidance to carry out annual serum urate level checks. The committee agreed that monitoring is also an opportunity to review treatment, adherence and address any concerns the person may have. NICE guidelines on medicine adherence (CG76) recommend regular review of medicines and at least annual review is accepted as good practice. The data available from the multimorbidity and clinical guidelines research project[6] on the prevalence of comorbidities in people with gout indicated that the large majority (83%) of people with gout have comorbidities. They would require monitoring for these other conditions and any medications required to treat them, therefore, the committee concluded monitoring of ULT could be done as part of another appointment and not involve extra appointments. NICE guidelines on CKD recommend review (including blood tests) annually or more often. The monitoring of urate level annually and the management of ULT is therefore likely to be included among review of other medicines and treatments.

1.1.11.4 Cost effectiveness and resource use

No published health economic evidence was identified for this review. However, a costing analysis was conducted to determine the number of flares needed to be avoided per person over a period of one year for annual monitoring to break even to aid consideration of cost-effectiveness.

The costing analysis indicated the average number of flares which need to be avoided per person for annual monitoring to break even ranged from 0.61 – 1.26 dependent on the cost of a gout flare which was used in the analysis. The results of the analysis were sensitive to the proportion of people receiving hospital treatment for their gout flare. When 1% of people were treated in hospital the average number of flares needed to be avoided per person for annual monitoring to break even ranged from 1.12 – 1.26. However, when 5% of people received treatment in hospital for their gout flare the average number of flares needed to be avoided per person for annual monitoring to break even ranged from 0.61 – 0.65.

The committee acknowledged a number of assumptions were required as part of the costing analysis. For the cost of monitoring, health care professional time was based on committee opinion for the cost of a gout flare, the proportion of people being treated in each health care setting, the proportion of people incurring costs associated with hospital treatment for a gout flare, and health care professional time was also based on committee opinion. The

uncertainty surrounding the proportion of people being treated in each health care setting was partly overcome by the eight scenarios analyses run where the proportion of people treated in each health care setting was varied. The committee accepted uncertainty could not be reduced further due to lack evidence and acknowledged this was a limitation of the analysis.

In general, the committee noted there is no specific data available on the number flares prevented as a result of monitoring. In addition, once people have achieved target serum urate levels monitoring is very rarely conducted in clinical practice. Therefore, the committee acknowledged it was challenging to estimate how many flares would be avoided as a result of annual monitoring.

The committee did however note the well-established link between target serum urate levels above 360µmol/L and increased number of gout flares (compared to people with a serum urate level of <360µmol/L) and acknowledged that people who receive monitoring are more likely to remain at target serum urate levels. This is because having serum urate levels measured more frequently than currently observed in clinical practice allows for ULT to be adjusted accordingly if required. Currently people may not realise their serum urate levels have deviated from target until they experience a gout flare. If, as a result of annual monitoring, a change in serum urate level is detected before a gout flare occurs this may mean serum urate levels have not deviated significantly above target levels, which may make it cheaper and less resource intensive to reobtain target serum urate levels. For example, someone may require a higher dose of allopurinol to reobtain target serum urate levels.

The committee also noted people who receive monitoring may be more likely to adhere to their ULT. Due to a lack of understanding that ULTs are a lifelong medication, adherence can be a problem whereby once people are symptom free via treatment, they may believe they no longer to need to take their ULT. In addition, adherence to allopurinol can be worse compared to febuxostat. The committee acknowledged there are number of reasons this may be the case, for example, as result of a potential higher pill burden associated with allopurinol. But also noted this may be because allopurinol is prescribed a first-line treatment option. If people are switched to febuxostat as their second-line treatment option adherence may be better due to a lack of additional treatment options. Overall, employing monitoring for people with gout may help people understand the importance of taking their ULT. The committee also discussed that the lack of monitoring currently provided in clinical practice can diminish people's perceptions of the severity of gout, whereby people with gout may believe their condition is not serious because monitoring is not provided.

The committee recalled the proportion of people experiencing gout flares in the Doherty treat-to-target trial[4] to make inferences about how many flares may be avoided as a result of annual monitoring. In Doherty, both the nurse-led and usual care arms experienced similar levels of flares at baseline: 79.92% and 79.77% respectively experienced two or more flares and 38.04% and 35.11% respectively experienced four or more flares. At 2 years 8.00% and 24.29% of people in the nurse-led and usual care arms respectively experienced two or more flares. Furthermore, 1.15% and 12.39% of people in the nurse-led and usual care arms respectively experienced four or more flares. Of note at 2 years, 94.88% and 88.05% of people in the nurse-led arm achieved a target serum urate level of $<360\mu$mol/and $<300\mu$mol/L respectively. Conversely in the usual care arm, 29.71% and 17.46% of people achieved a target serum urate level of $<360\mu$mol/L and $<300\mu$mol/L respectively. The committee discussed that although this trial did not provide data on the effects of monitoring, it does illustrate the relationship between target serum urate levels and the number of flares, whereby people not achieving target serum urate levels experience a greater number of flares.

The committee acknowledged estimating the number of flares avoided as a result of annual monitoring was uncertain. The committee discussed the results and noted it was highly likely

annual monitoring would break even or be cost saving when 5% of people with gout receive treatment for a gout flare in hospital (when the average number of flares needed to be avoided per person for annual monitoring to break even ranged from 0.61 – 0.65). The committee concluded it was likely annual monitoring would break even or be cost saving when 1% of people with gout receive treatment for a gout flare in hospital (when the average number of flares needed to be avoided per person for annual monitoring to break even ranged from 1.12 – 1.26). However, they acknowledged there was more uncertainty surrounding this due to a greater of number of flares needed to be avoided for annual monitoring to break even. Due to this uncertainty and the absence of clinical evidence, the committee agreed to make a consider recommendation for annual monitoring to be conducted once people have achieved target serum urate levels.

There is large variation in clinical practice as to how frequently – if at all – monitoring is conducted to measure a person's serum urate level once target serum urate levels have been achieved. In general, the purpose of monitoring is to determine if people are on the correct dose of ULT. Monitoring will involve a clinical professional conducting a blood test to measure a person's serum urate level and ensure serum urate levels are below target. If serum urate levels are above target, the appropriate course of action will be taken (for example, up titration of ULT) by a clinical professional to ensure target levels are subsequently achieved. Because monitoring is rarely conducted in clinical practice this recommendation will likely have an impact on resources as it is a change in practice for a large proportion of the gout population. The impact on resources will be seen in the form of increased staff time and serum urate level testing. As the number of people receiving ULT is expected to increase as a result of the recommendations made in this guideline, this will also increase the number of people being monitored once people achieve target serum urate levels.

1.1.12 Recommendations supported by this evidence review

This evidence review supports recommendations 1.5.15 and the research recommendation on, the optimum frequency of serum urate level monitoring in people with gout when target serum urate level is reached.

1.1.13 References

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Appendices

Appendix A – Review protocols

Review protocol for optimum frequency of serum urate level monitoring for people continuing on urate-lowering therapies for gout

ID	Field	Content
0.	PROSPERO registration number	CRD42021236775
1.	Review title	The optimum frequency of serum urate level monitoring for people continuing on urate-lowering therapies for gout
2.	Review question	What is the optimum frequency of serum urate level monitoring for people continuing on urate-lowering therapies for gout?
3.	Objective	To determine the optimum frequency of serum urate level monitoring for people continuing on urate-lowering therapies in gout
4.	Searches	The following databases (from inception) will be searched: • Cochrane Central Register of Controlled Trials (CENTRAL) • Cochrane Database of Systematic Reviews (CDSR) • Embase • MEDLINE Medline search strategy to be quality assured using the PRESS evidence-based checklist (see methods chapter for full details) Searches will be restricted by: • English language studies • Human studies The searches may be re-run 6 weeks before the final committee meeting and further studies retrieved for inclusion if relevant. The full search strategies will be published in the final review. Medline search strategy to be quality assured using the PRESS evidence-based checklist (see methods chapter for full details).

5.	Condition or domain being studied	Gout (including people with gout and chronic kidney disease)
6.	Population	Inclusion: Adults (18 years and older) with gout who are having their serum urate level monitored. These patients have already reached target serum urate level and are continuing treatment. Strata: • People with CKD (stage 3) • People with CKD (stages 4-5) • People without CKD or people with CKD stages 1-2 • Mixed population (people with CKD and people without CKD) Exclusion: People with calcium pyrophosphate crystal deposition, including pseudogout
7.	Intervention/Exposure/Test	Different monitoring frequencies, examples: • Every six months • Every year • Every two years
8.	Comparator/Reference standard/Confounding factors	• Compared to each other • Control (no monitoring)
9.	Types of study to be included	RCT Systematic reviews of RCTs If insufficient RCT evidence is available (no or little evidence for interventions/comparisons), search for non-randomised studies (prospective and retrospective cohort studies will be considered if they adjust for key confounders: • Age • Gender Published NMAs will be considered for inclusion.
10.	Other exclusion criteria	Non-English language studies. Conference abstracts will be excluded as it is expected there will be sufficient full text published studies available

11.	Context	People with gout, on ULT, who have reached the target serum urate level will be continued on ULT in the long-term. They will require monitoring to check for changes in their serum urate level to see if the dosage of ULT requires adjustment. Current practice is variable on how often monitoring is carried out, so this review focuses on how frequent monitoring should be conducted.
12.	Primary outcomes (critical outcomes)	All outcomes are considered equally important for decision making and therefore have all been rated as critical: • health-related quality of life (e.g. as described by SF-36, Gout Assessment Questionnaire (GAQ) and the Gout Impact Scale (GIS) or other validated gout-specific HRQoL measures • patient global assessment of treatment success (response to treatment) (e.g. Likert scales, visual analogue scales (VAS), numerical ratings scales (NRS)) • pain (measured on a visual analogue scale (VAS) or numerical rating scale such as the five-point Likert scale, or reported as pain relief of 50% or greater) • joint swelling/joint inflammation • joint tenderness • serum urate level • frequency of flares • tophi • admissions (hospital and A&E/urgent care) • GP visits Timepoints: Short-term 6 months, medium 6-12 months, long-term 12+ months
13.	Secondary outcomes (important outcomes)	N/A
14.	Data extraction (selection and coding)	EndNote will be used for reference management, sifting, citations and bibliographies. All references identified by the searches and from other sources will be screened for inclusion. 10% of the abstracts will be reviewed by two reviewers, with any disagreements resolved by discussion or, if necessary, a third independent reviewer. The full text of potentially eligible studies will be retrieved and will be assessed in line with the criteria outlined above.

		Evibase will be used for data extraction. 10% of all evidence reviews are quality assured by a senior research fellow. This includes checking: • papers were included /excluded appropriately • a sample of the data extractions • correct methods are used to synthesise data • a sample of the risk of bias assessments Disagreements between the review authors over the risk of bias in particular studies will be resolved by discussion, with involvement of a third review author where necessary. Study investigators may be contacted for missing data where time and resources allow.
15.	Risk of bias (quality) assessment	Risk of bias will be assessed using the appropriate checklist as described in Developing NICE guidelines: the manual For Intervention reviews • Systematic reviews: Risk of Bias in Systematic Reviews (ROBIS) • Randomised Controlled Trial: Cochrane RoB (2.0) • Non randomised study, including cohort studies: Cochrane ROBINS-I
16.	Strategy for data synthesis	• Pairwise meta-analyses will be performed using Cochrane Review Manager (RevMan5). Fixed-effects (Mantel-Haenszel) techniques will be used to calculate risk ratios for the binary outcomes where possible. Continuous outcomes will be analysed using an inverse variance method for pooling weighted mean differences. Heterogeneity between the studies in effect measures will be assessed using the I^2 statistic and visually inspected. An I^2 value greater than 50% will be considered indicative of substantial heterogeneity. Sensitivity analyses will be conducted based on pre-specified subgroups using stratified meta-analysis to explore the heterogeneity in effect estimates. If this does not explain the heterogeneity, the results will be presented pooled using random-effects. If sufficient data is available and it is methodologically appropriate, network meta-analysis (NMA) will conducted.

		• GRADEpro will be used to assess the quality of evidence for each outcome, taking into account individual study quality and the meta-analysis results. The 4 main quality elements (risk of bias, indirectness, inconsistency and imprecision) will be appraised for each outcome. Publication bias is tested for when there are more than 5 studies for an outcome. The risk of bias across all available evidence was evaluated for each outcome using an adaptation of the 'Grading of Recommendations Assessment, Development and Evaluation (GRADE) toolbox' developed by the international GRADE working group http://www.gradeworkinggroup.org/ • Where meta-analysis is not possible, data will be presented and quality assessed individually per outcome. • WinBUGS will be used for network meta-analysis, if possible given the data identified.		
17.	Analysis of sub-groups	Subgroups that will be investigated if heterogeneity is present: None		
18.	Type and method of review	☒	Intervention	
		☐	Diagnostic	
		☐	Prognostic	
		☐	Qualitative	
		☐	Epidemiologic	
		☐	Service Delivery	
		☐	Other (please specify)	
19.	Language	English		
20.	Country	England		
21.	Anticipated or actual start date	4th December 2020		
22.	Anticipated completion date	13th June 2022		
23.	Stage of review at time of this submission	Review stage	Started	Completed
		Preliminary searches	☑	☑
		Piloting of the study selection process	☑	☑

		Formal screening of search results against eligibility criteria	☑	☑
		Data extraction	☐	☐
		Risk of bias (quality) assessment	☐	☐
		Data analysis	☐	☐
24.	Named contact	5a. Named contact National Guideline Centre 5b Named contact e-mail managementofgout@nice.org.uk 5e Organisational affiliation of the review National Institute for Health and Care Excellence (NICE) and National Guideline Alliance / National Guideline Centre / NICE Guideline Updates Team / NICE Public Health Guideline Development Team		
25.	Review team members	From the National Guideline Centre: Gill Ritchie [Guideline lead] Sedina Lewis [Senior systematic reviewer] Audrius Stonkus [Systematic reviewer] Alexandra Bonnon [Health economist] Amber Hernaman [Project manager] Joseph Runicles [Information specialist]		
26.	Funding sources/sponsor	This systematic review is being completed by the National Guideline Centre which receives funding from NICE.		
27.	Conflicts of interest	All guideline committee members and anyone who has direct input into NICE guidelines (including the evidence review team and expert witnesses) must declare any potential conflicts of interest in line with NICE's code of practice for declaring and dealing with conflicts of interest. Any relevant interests, or changes to interests, will also be declared publicly at the start of each guideline committee meeting. Before each meeting, any potential conflicts of interest will be considered by the guideline committee Chair and a senior member of the development team. Any decisions to exclude a person from all or part of a meeting will be documented. Any changes to a member's declaration of interests will be recorded in the minutes of the meeting. Declarations of		

		interests will be published with the final guideline.	
28.	Collaborators	Development of this systematic review will be overseen by an advisory committee who will use the review to inform the development of evidence-based recommendations in line with section 3 of Developing NICE guidelines: the manual. Members of the guideline committee are available on the NICE website: [NICE guideline webpage].	
29.	Other registration details	[Give the name of any organisation where the systematic review title or protocol is registered (such as with The Campbell Collaboration, or The Joanna Briggs Institute) together with any unique identification number assigned. If extracted data will be stored and made available through a repository such as the Systematic Review Data Repository (SRDR), details and a link should be included here. If none, leave blank.]	
30.	Reference/URL for published protocol	[Give the citation and link for the published protocol, if there is one.]	
31.	Dissemination plans	NICE may use a range of different methods to raise awareness of the guideline. These include standard approaches such as: • notifying registered stakeholders of publication • publicising the guideline through NICE's newsletter and alerts • issuing a press release or briefing as appropriate, posting news articles on the NICE website, using social media channels, and publicising the guideline within NICE. [Add in any additional agree dissemination plans.]	
32.	Keywords	[Give words or phrases that best describe the review.]	
33.	Details of existing review of same topic by same authors	[Give details of earlier versions of the systematic review if an update of an existing review is being registered, including full bibliographic reference if possible. NOTE: most NICE reviews will not constitute an update in PROSPERO language. To be an update it needs to be the same review question/search/methodology. If anything has changed it is a new review]	
34.	Current review status	☐	Ongoing
		☐	Completed but not published
		☐	Completed and published
		☐	Completed, published and being updated

		☐	Discontinued
35..	Additional information	[Provide any other information the review team feel is relevant to the registration of the review.]	
36.	Details of final publication	www.nice.org.uk	

Health economic review protocol

Review question	All questions – health economic evidence
Objectives	To identify health economic studies relevant to any of the review questions.
Search criteria	• Populations, interventions and comparators must be as specified in the clinical review protocol above. • Studies must be of a relevant health economic study design (cost–utility analysis, cost-effectiveness analysis, cost–benefit analysis, cost–consequences analysis, comparative cost analysis). • Studies must not be a letter, editorial or commentary, or a review of health economic evaluations. (Recent reviews will be ordered although not reviewed. The bibliographies will be checked for relevant studies, which will then be ordered.) • Unpublished reports will not be considered unless submitted as part of a call for evidence. • Studies must be in English.
Search strategy	A health economic study search will be undertaken using population-specific terms and a health economic study filter – see appendix B below.
Review strategy	Studies not meeting any of the search criteria above will be excluded. Studies published before 2005, abstract-only studies and studies from non-OECD countries or the USA will also be excluded. Each remaining study will be assessed for applicability and methodological limitations using the NICE economic evaluation checklist which can be found in appendix H of Developing NICE guidelines: the manual (2014).[10] **Inclusion and exclusion criteria** • If a study is rated as both 'Directly applicable' and with 'Minor limitations' then it will be included in the guideline. A health economic evidence table will be completed and it will be included in the health economic evidence profile. • If a study is rated as either 'Not applicable' or with 'Very serious limitations' then it will usually be excluded from the guideline. If it is excluded then a health economic evidence table will not be completed and it will not be included in the health economic evidence profile. • If a study is rated as 'Partially applicable', with 'Potentially serious limitations' or both then there is discretion over whether it should be included. **Where there is discretion** The health economist will make a decision based on the relative applicability and quality of the available evidence for that question, in discussion with the guideline committee if required. The ultimate aim is to include health economic studies that are helpful for decision-making in the context of the guideline and the current NHS setting. If several studies are considered of sufficiently high applicability and methodological quality that they could all be included, then the health economist, in discussion with the committee if required, may decide to include only the most applicable studies and to selectively exclude the remaining studies. All studies excluded on the basis of applicability or methodological limitations will be listed with explanation in the excluded health economic studies appendix below. The health economist will be guided by the following hierarchies. *Setting:* • UK NHS (most applicable). • OECD countries with predominantly public health insurance systems (for example, France, Germany, Sweden).

	• OECD countries with predominantly private health insurance systems (for example, Switzerland). • Studies set in non-OECD countries or in the USA will be excluded before being assessed for applicability and methodological limitations. *Health economic study type:* • Cost–utility analysis (most applicable). • Other type of full economic evaluation (cost–benefit analysis, cost-effectiveness analysis, cost–consequences analysis). • Comparative cost analysis. • Non-comparative cost analyses including cost-of-illness studies will be excluded before being assessed for applicability and methodological limitations. *Year of analysis:* • The more recent the study, the more applicable it will be. • Studies published in 2005 or later but that depend on unit costs and resource data entirely or predominantly from before 2005 will be rated as 'Not applicable'. • Studies published before 2005 will be excluded before being assessed for applicability and methodological limitations. *Quality and relevance of effectiveness data used in the health economic analysis:* • The more closely the clinical effectiveness data used in the health economic analysis match with the outcomes of the studies included in the clinical review the more useful the analysis will be for decision-making in the guideline.

Appendix B – Literature search strategies

- What is the optimum frequency of serum urate level monitoring for people continuing on urate-lowering therapies for gout?

The literature searches for this review are detailed below and complied with the methodology outlined in Developing NICE guidelines: the manual.[10]

For more information, please see the Methodology review published as part of the accompanying documents for this guideline.

B.1 Clinical search literature search strategy

Searches were constructed using a PICO framework where population (P) terms were combined with Intervention (I) and in some cases Comparison (C) terms. Outcomes (O) are rarely used in search strategies for interventions as these concepts may not be well described in title, abstract or indexes and therefore difficult to retrieve. Search filters were applied to the search where appropriate.

Table 7: Database date parameters and filters used

Database	Dates searched	Search filter used
Medline (OVID)	1946 – 06 July 2021	Randomised controlled trials Systematic review studies Observational studies Exclusions (animal studies, letters, comments)
Embase (OVID)	1974 – 06 July 2021	Randomised controlled trials Systematic review studies Observational studies Exclusions (animal studies, letters, comments)
The Cochrane Library (Wiley)	Cochrane Reviews to 2021 Issue 7 of 12 CENTRAL to 2021 Issue 7 of 12	None

Medline (Ovid) search terms

1.	exp Gout/
2.	gout*.ti,ab.
3.	toph*.ti,ab.
4.	podagra.ti,ab.
5.	pseudogout.ti,ab.
6.	or/1-5
7.	letter/
8.	editorial/
9.	news/

10.	exp historical article/
11.	Anecdotes as Topic/
12.	comment/
13.	case report/
14.	(letter or comment*).ti.
15.	or/7-14
16.	randomized controlled trial/ or random*.ti,ab.
17.	15 not 16
18.	animals/ not humans/
19.	exp Animals, Laboratory/
20.	exp Animal Experimentation/
21.	exp Models, Animal/
22.	exp Rodentia/
23.	(rat or rats or mouse or mice).ti.
24.	or/17-23
25.	6 not 24
26.	Limit 25 to English language
27.	randomized controlled trial.pt.
28.	controlled clinical trial.pt.
29.	randomi#ed.ti,ab.
30.	placebo.ab.
31.	randomly.ti,ab.
32.	Clinical Trials as topic.sh.
33.	trial.ti.
34.	or/27-33
35.	Meta-Analysis/
36.	exp Meta-Analysis as Topic/
37.	(meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
38.	((systematic* or evidence*) adj3 (review* or overview*)).ti,ab.
39.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
40.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
41.	(search* adj4 literature).ab.
42.	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
43.	cochrane.jw.
44.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
45.	or/35-44
46.	Epidemiologic studies/
47.	Observational study/
48.	exp Cohort studies/
49.	(cohort adj (study or studies or analys* or data)).ti,ab.
50.	((follow up or observational or uncontrolled or non randomi#ed or epidemiologic*) adj (study or studies or data)).ti,ab.

51.	((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys* or cohort* or data)).ti,ab.
52.	Controlled Before-After Studies/
53.	Historically Controlled Study/
54.	Interrupted Time Series Analysis/
55.	(before adj2 after adj2 (study or studies or data)).ti,ab.
56.	exp case control studies/
57.	case control*.ti,ab.
58.	Cross-sectional studies/
59.	(cross sectional and (study or studies or review or analys* or cohort* or data)).ti,ab.
60.	or/46-59
61.	26 and (34 or 45 or 60)

Embase (Ovid) search terms

1.	exp Gout/
2.	gout*.ti,ab.
3.	toph*.ti,ab.
4.	podagra.ti,ab.
5.	pseudogout.ti,ab.
6.	or/1-5
7.	letter.pt. or letter/
8.	note.pt.
9.	editorial.pt.
10.	case report/ or case study/
11.	(letter or comment*).ti.
12.	or/7-11
13.	randomized controlled trial/ or random*.ti,ab.
14.	12 not 13
15.	animal/ not human/
16.	nonhuman/
17.	exp Animal Experiment/
18.	exp Experimental Animal/
19.	animal model/
20.	exp Rodent/
21.	(rat or rats or mouse or mice).ti.
22.	or/14-21
23.	6 not 22
24.	Limit 23 to English language
25.	random*.ti,ab.
26.	factorial*.ti,ab.
27.	(crossover* or cross over*).ti,ab.
28.	((doubl* or singl*) adj blind*).ti,ab.
29.	(assign* or allocat* or volunteer* or placebo*).ti,ab.
30.	crossover procedure/
31.	single blind procedure/

32.	randomized controlled trial/
33.	double blind procedure/
34.	or/25-33
35.	systematic review/
36.	meta-analysis/
37.	(meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
38.	((systematic* or evidence*) adj3 (review* or overview*)).ti,ab.
39.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
40.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
41.	(search* adj4 literature).ab.
42.	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
43.	cochrane.jw.
44.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
45.	or/35-44
46.	Clinical study/
47.	Observational study/
48.	family study/
49.	longitudinal study/
50.	retrospective study/
51.	prospective study/
52.	cohort analysis/
53.	follow-up/
54.	cohort*.ti,ab.
55.	53 and 54
56.	(cohort adj (study or studies or analys* or data)).ti,ab.
57.	((follow up or observational or uncontrolled or non randomi#ed or epidemiologic*) adj (study or studies or data)).ti,ab.
58.	((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys* or cohort* or data)).ti,ab.
59.	(before adj2 after adj2 (study or studies or data)).ti,ab.
60.	exp case control study/
61.	case control*.ti,ab.
62.	cross-sectional study/
63.	(cross sectional and (study or studies or review or analys* or cohort* or data)).ti,ab.
64.	or/46-52,55-63
65.	24 and (34 or 45 or 64)

Cochrane Library (Wiley) search terms

#1.	MeSH descriptor: [Gout] explode all trees
#2.	gout*:ti,ab
#3.	toph*:ti,ab
#4.	podagra:ti,ab
#5.	pseudogout:ti,ab

#6.	(or #1-#5)

B.2 Health Economics literature search strategy

Health economic evidence was identified by conducting a broad search relating to a Gout population in NHS Economic Evaluation Database (NHS EED – this ceased to be updated after March 2015) and the Health Technology Assessment database (HTA – this ceased to be updated after March 2018). NHS EED and HTA databases are hosted by the Centre for Research and Dissemination (CRD). Additional searches were run on Medline and Embase for health economics studies and quality of life studies.

Table 8: Database date parameters and filters used

Database	Dates searched	Search filter used
Medline	Health Economics 1 January 2014 – 14 June 2021 Quality of Life 1946 – 14 June 2021	Health economics studies Quality of life studies Exclusions (animal studies, letters, comments)
Embase	Health Economics 1 January 2014 – 14 June 2021 Quality of Life 1974 – 14 June 2021	Health economics studies Quality of life studies Exclusions (animal studies, letters, comments)
Centre for Research and Dissemination (CRD)	HTA - Inception – 31 March 2018 NHSEED - Inception to March 2015	None

Medline (Ovid) search terms

1.	exp Gout/
2.	gout*.ti,ab.
3.	toph*.ti,ab.
4.	Uric Acid/
5.	uric acids*.ti,ab.
6.	(urate adj (crystal* or sodium or mono sodium)).ti,ab.
7.	hyperuricemia/
8.	(hyperuric* or hyper uric*).ti,ab.
9.	podagra.ti,ab.
10.	or/1-9
11.	letter/
12.	editorial/
13.	news/

14.	exp historical article/
15.	Anecdotes as Topic/
16.	comment/
17.	case report/
18.	(letter or comment*).ti.
19.	or/11-18
20.	randomized controlled trial/ or random*.ti,ab.
21.	19 not 20
22.	animals/ not humans/
23.	exp Animals, Laboratory/
24.	exp Animal Experimentation/
25.	exp Models, Animal/
26.	exp Rodentia/
27.	(rat or rats or mouse or mice).ti.
28.	or/21-27
29.	10 not 28
30.	limit 29 to English language
31.	Economics/
32.	Value of life/
33.	exp "Costs and Cost Analysis"/
34.	exp Economics, Hospital/
35.	exp Economics, Medical/
36.	Economics, Nursing/
37.	Economics, Pharmaceutical/
38.	exp "Fees and Charges"/
39.	exp Budgets/
40.	budget*.ti,ab.
41.	cost*.ti.
42.	(economic* or pharmaco?economic*).ti.
43.	(price* or pricing*).ti,ab.
44.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
45.	(financ* or fee or fees).ti,ab.
46.	(value adj2 (money or monetary)).ti,ab.
47.	or/31-46
48.	quality-adjusted life years/
49.	sickness impact profile/
50.	(quality adj2 (wellbeing or well being)).ti,ab.
51.	sickness impact profile.ti,ab.
52.	disability adjusted life.ti,ab.
53.	(qal* or qtime* or qwb* or daly*).ti,ab.
54.	(euroqol* or eq5d* or eq 5*).ti,ab.

55.	(qol* or hql* or hqol* or h qol* or hrqol* or hr qol*).ti,ab.
56.	(health utility* or utility score* or disutilit* or utility value*).ti,ab.
57.	(hui or hui1 or hui2 or hui3).ti,ab.
58.	(health* year* equivalent* or hye or hyes).ti,ab.
59.	discrete choice*.ti,ab.
60.	rosser.ti,ab.
61.	(willingness to pay or time tradeoff or time trade off or tto or standard gamble*).ti,ab.
62.	(sf36* or sf 36* or short form 36* or shortform 36* or shortform36*).ti,ab.
63.	(sf20 or sf 20 or short form 20 or shortform 20 or shortform20).ti,ab.
64.	(sf12* or sf 12* or short form 12* or shortform 12* or shortform12*).ti,ab.
65.	(sf8* or sf 8* or short form 8* or shortform 8* or shortform8*).ti,ab.
66.	(sf6* or sf 6* or short form 6* or shortform 6* or shortform6*).ti,ab.
67.	or/48-66
68.	30 and (47 or 67)

Embase (Ovid) search terms

1.	exp gout/
2.	gout*.ti,ab.
3.	toph*.ti,ab.
4.	exp uric acid/
5.	uric acid*.ti,ab.
6.	(urate adj (crystal* or sodium or mono sodium)).ti,ab.
7.	exp hyperuricemia/
8.	(hyperuric* or hyper uric*).ti,ab.
9.	podagra.ti,ab.
10.	or/1-9
11.	letter.pt. or letter/
12.	note.pt.
13.	editorial.pt.
14.	Case report/ or Case study/
15.	(letter or comment*).ti.
16.	or/11-15
17.	randomized controlled trial/ or random*.ti,ab.
18.	16 not 17
19.	animal/ not human/
20.	Nonhuman/
21.	exp Animal Experiment/
22.	exp Experimental animal/
23.	Animal model/
24.	exp Rodent/
25.	(rat or rats or mouse or mice).ti.
26.	or/18-25
27.	10 not 26

28.	limit 27 to English language
29.	health economics/
30.	exp economic evaluation/
31.	exp health care cost/
32.	exp fee/
33.	budget/
34.	funding/
35.	budget*.ti,ab.
36.	cost*.ti.
37.	(economic* or pharmaco?economic*).ti.
38.	(price* or pricing*).ti,ab.
39.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
40.	(financ* or fee or fees).ti,ab.
41.	(value adj2 (money or monetary)).ti,ab.
42.	or/29-41
43.	quality adjusted life year/
44.	"quality of life index"/
45.	short form 12/ or short form 20/ or short form 36/ or short form 8/
46.	sickness impact profile/
47.	(quality adj2 (wellbeing or well being)).ti,ab.
48.	sickness impact profile.ti,ab.
49.	disability adjusted life.ti,ab.
50.	(qal* or qtime* or qwb* or daly*).ti,ab.
51.	(euroqol* or eq5d* or eq 5*).ti,ab.
52.	(qol* or hql* or hqol* or h qol* or hrqol* or hr qol*).ti,ab.
53.	(health utility* or utility score* or disutilit* or utility value*).ti,ab.
54.	(hui or hui1 or hui2 or hui3).ti,ab.
55.	(health* year* equivalent* or hye or hyes).ti,ab.
56.	discrete choice*.ti,ab.
57.	rosser.ti,ab.
58.	(willingness to pay or time tradeoff or time trade off or tto or standard gamble*).ti,ab.
59.	(sf36* or sf 36* or short form 36* or shortform 36* or shortform36*).ti,ab.
60.	(sf20 or sf 20 or short form 20 or shortform 20 or shortform20).ti,ab.
61.	(sf12* or sf 12* or short form 12* or shortform 12* or shortform12*).ti,ab.
62.	(sf8* or sf 8* or short form 8* or shortform 8* or shortform8*).ti,ab.
63.	(sf6* or sf 6* or short form 6* or shortform 6* or shortform6*).ti,ab.
64.	or/43-63
65.	28 and (42 or 64)

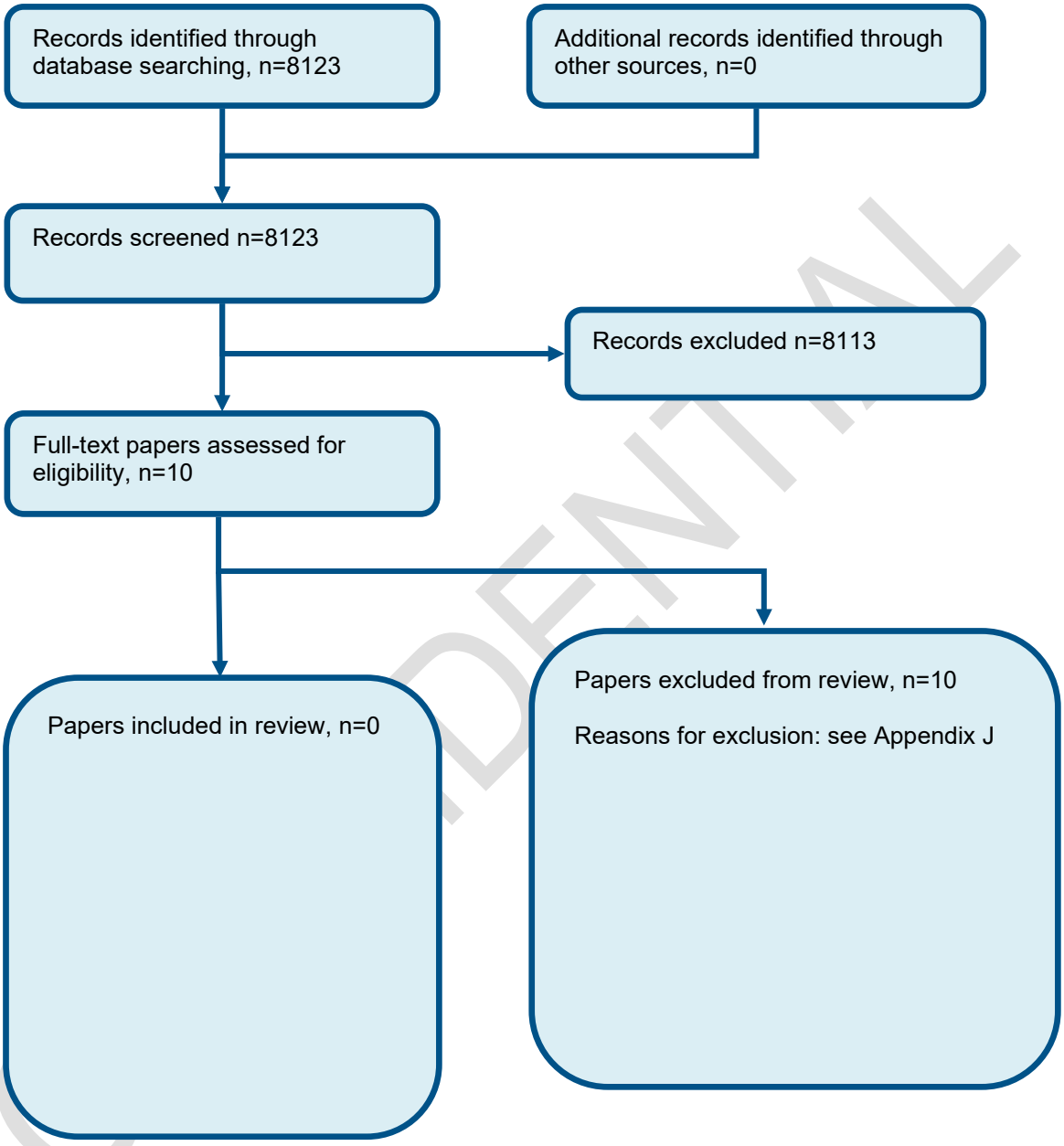
NHS EED and HTA (CRD) search terms

#1.	MeSH DESCRIPTOR Gout EXPLODE ALL TREES
#2.	(gout*)
#3.	(toph*)
#4.	MeSH DESCRIPTOR Uric Acid EXPLODE ALL TREES

#5.	(uric acid*)
#6.	((urate near (crystal* or sodium or mono sodium)))
#7.	MeSH DESCRIPTOR Hyperuricemia EXPLODE ALL TREES
#8.	((hyperuric* or hyper uric*))
#9.	(podagra)
#10.	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9

Appendix C – Effectiveness evidence study selection

Figure 1: Flow chart of clinical study selection for the review of optimum frequency of serum urate level monitoring for people continuing on urate-lowering therapies for gout



Appendix D – Effectiveness evidence

No studies were included.

Appendix E – Forest plots

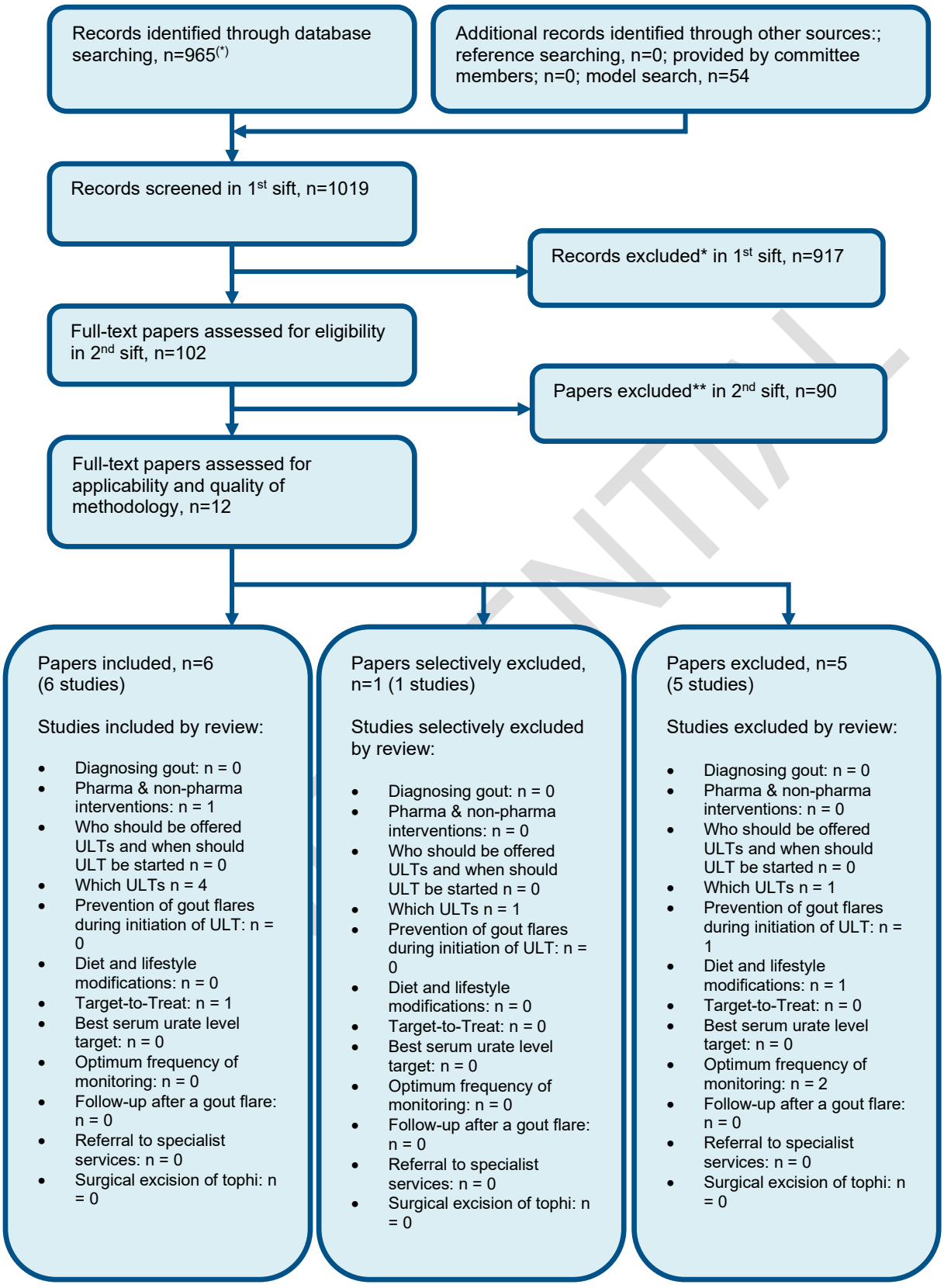
No studies were included.

Appendix F – GRADE tables

No studies were included.

Appendix G – Economic evidence study selection

Figure 1: Flow chart of health economic study selection for the guideline



* excludes conference abstracts (n=280)

**Non-relevant population, intervention, comparison, design or setting; non-English language

Appendix H – Economic evidence tables

None.

Appendix I – Health economic model

No original economic modelling was undertaken for this review question.

Appendix J – Excluded studies

Clinical studies

Table 9: Studies excluded from the clinical review

Study	Exclusion reason
Alvarado-de la Barrera 2020[1]	Incorrect analysis/comparison - study aimed to determine proportion of patients achieving target urate level for patients with non-severe and severe gout, as well as remission after 5 years of follow-up, before and after study, no adjusted multivariate analysis
Bai 2020[2]	Incorrect study design- cross-sectional study, study analysed risk factors for frequency of flares
Edwards 2011[5]	Incorrect analysis - study analysed correlations between flares, SF-36 and daily reported activity loss measures
Harrold 2010[7]	Incorrect analysis/comparison - study aimed to determine factors associated with resuming therapy
McLachlan 2011[9]	Incorrect analysis/incorrect comparison - cohort study assessed cardiovascular disease risk management intervention
Perez-Ruiz 2011[12]	Incorrect analysis/incorrect comparison - study analysed risk factors for crystal proven recurrence of gout
Raebel 2006[13]	Incorrect analysis/comparison - adjusted analysis of factors associated with lack of serum creatinine monitoring during Allopurinol therapy
Shoji 2004[15]	Incorrect analysis/incorrect comparison - retrospective study analysed risk factors (serum urate levels) for recurrence of acute gouty attacks
Wall 2010[16]	Incorrect analysis/incorrect comparison - study compared two different general internal medicine practices in terms of compliance to guidelines for treatment of gout
Yeo 2019[17]	Incorrect study design- cross-sectional study, study assessed point prevalence of gout, gout treatment and achievement of target SU among adults treated with long-term dialysis.

Health Economic studies

Published health economic studies that met the inclusion criteria (relevant population, comparators, economic study design, published 2005 or later and not from non-OECD country or USA) but that were excluded following appraisal of applicability and methodological quality are listed below. See the health economic protocol for more details.

Table 10: Studies excluded from the health economic review

Reference	Reason for exclusion
Hill-McManus 2018 [8]	Excluded as rated not applicable. The study did not compare different monitoring strategies but compared the cost effectiveness of different ULT strategies and modelled their effectiveness based on medication adherence.
Robinson 2018 [14]	Excluded as rated very serious limitations. The studies main data inputs and assumptions concerning the efficacy of strategies were based on non-RCT evidence and estimates. Unreliable ICERs were reported whereby the incremental values reported did not equate to the overall ICER. In addition, the majority of values used in the sensitivity analysis were estimates. Also rated partially applicable, reasons include: Australian setting may not reflect current NHS context and SF-36 values were used to obtain QALYs.

Appendix K – Research recommendations – full details

K.1.1 Research recommendation

In people with gout (including people with gout and chronic kidney disease), what is the most clinically and cost effective frequency of serum urate level monitoring when target serum urate level is reached?

K.1.2 Why this is important

Gout is a lifelong condition typically requiring long term medication. Currently there is high variability in serum urate monitoring in GP practices in people who have achieved target serum urate level, ranging from annual to no monitoring at all. Serum urate levels can change over time due to various factors such as adherence, increasing age, weight, medication changes, and changes in patients' comorbidities and preferences. It is currently unknown what the optimum frequency of serum urate level monitoring is in people who have achieved a target serum urate level. Knowing this would allow us to ensure gout treatment remains clinically and cost-effective by enabling adjustments to treatment to be made, if required, to optimise management and prevent gout flares and hospital admissions. It would also provide the opportunity for patients to discuss their ongoing expectations, concerns and needs regarding treatment, to enhance concordance with taking long term medication.

K.1.3 Rationale for research recommendation

Importance to 'patients' or the population	Patients' outcomes could be optimised, and adverse consequences and harm from ineffective/inappropriate treatment minimised. Patients would know if treatment was effective or whether adjustments to medication were required to prevent gout flares. Patients would have the opportunity to engage in shared decision making and discuss any concerns regarding remaining on long term medication.
Relevance to NICE guidance	The frequency of serum urate monitoring has been considered in the guidance and no studies were identified. Research in this area would support a future update of the guideline.
Relevance to the NHS	Monitoring serum urate levels could result in increased clinical and cost-effectiveness of treatment, improved quality of life and fewer hospital admissions
National priorities	High- gout is an area of concern identified by NICE as having high variability and needing guidance to improve patient outcomes and standards of care. These aspects have relevance to NHSE 10 Year Plan aims of removing inequalities and variation in care.
Current evidence base	None
Equality considerations	This research recommendation does not address equality issues. We did not identify specific ethnicities or other groups that should be investigated in a different way, or prioritised.

K.1.4 Modified PICO table

Population	People with gout (including people with gout and CKD) who have achieved target serum urate levels
Intervention	To provide **6, 12, or 24 month monitoring** for people who have achieved optimum serum urate levels.
Comparator	Current care (no monitoring) Different time points
Outcome	• serum urate level • serum measures of safety (U&Es) • health related quality of life measures (Gout assessment questionnaire and the Gout impact scale) • pain (VAS) • frequency of flares • joint swelling • patient global assessment of treatment success (VAS) • adverse events (cardiovascular, renal, GI) • admissions (hospital, A&E, urgent care) and GP visits • adherence • costs
Study design	RCT or large cohort study with adjustment for key confounders.
Timeframe	2 to 5 years
Additional information	High: the research is essential to inform future updates of key recommendations in the guideline.