

Evidence Behind Treatment of Asymptomatic Hyperuricaemia: A Narrative Review

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Abstract: Background: Asymptomatic hyperuricaemia is frequently detected during assessment of metabolic and kidney disease. Although elevated serum urate is associated with adverse health outcomes, the value of pharmacological treatment in the absence of gout remains uncertain. **Objective:** To critically review the rationale, clinical efficacy, safety, and guideline implications of urate-lowering therapy in adults with asymptomatic hyperuricaemia. **Review approach:** A focused narrative synthesis of selected mechanistic studies, clinical trials, and practice guidelines was undertaken. Evidence was organised by biochemical response, kidney outcomes, cardiovascular outcomes, and prevention of gout. Studies involving established gout or diabetes were considered separately where their applicability to asymptomatic hyperuricaemia was indirect. No quantitative pooling was performed. **Evidence synthesis:** Allopurinol and febuxostat reliably reduce serum urate. However, CKD-FIX, PERL, and FEATHER did not demonstrate overall protection against kidney function decline in their respective populations. Earlier favourable studies largely assessed surrogate outcomes or smaller samples. CARES and FAST provide differing cardiovascular safety findings in patients with gout and do not establish a preventive indication in asymptomatic individuals. Treatment decisions must therefore distinguish laboratory improvement from patient-important benefit. **Conclusion:** Routine pharmacological treatment of isolated asymptomatic hyperuricaemia is not supported by consistent evidence of kidney or cardiovascular benefit. Management should emphasise assessment of underlying causes, established treatment of comorbid disease, and appropriate follow-up. Further trials are needed to define whether carefully selected subgroups benefit from intervention.

Keywords: asymptomatic hyperuricaemia; urate-lowering therapy; allopurinol; febuxostat; chronic kidney disease; cardiovascular safety; narrative review.

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INTRODUCTION

Let's start by explaining what asymptomatic hyperuricemia is: it refers to a condition where the concentration of uric acid in your blood has exceeded the normal standard, yet you have never developed clinically diagnosable gout, nor have you ever experienced any symptoms of a gout attack.

Under the body's normal physiological state, once the uric acid level in the blood rises to approximately 6.8mg/dL, it will reach saturation and precipitate out, forming crystals that deposit in the body. However, some epidemiological research teams use more specific, sex-stratified laboratory thresholds to determine whether uric acid levels exceed the standard.

These two sets of criteria for judging uric acid levels must never be mixed up. The critical threshold defined by biochemical indicators is only used to help us identify people with elevated uric acid, essentially marking an exposure factor that requires attention; but diagnosing gout is an entirely separate matter, which must be

combined with the patient's actual clinical onset, such as a history of episodes of red, swollen, and intensely painful joints, before a diagnosis can be made. Therefore, even if a single elevated uric acid reading is detected, it cannot be directly used as evidence to definitively claim that the patient's inflammatory arthritis or organ damage was caused by uric acid [1,2].

It has now been established that hyperuricemia is associated with hypertension, obesity, diabetes, chronic kidney disease, and cardiovascular diseases. This very association has led many people to consider whether uric acid-lowering interventions could be implemented early to control risks before these conditions worsen.

Hidden behind this is a core clinical question: does lowering uric acid in people who have never had gout really alter the long-term progression of these diseases? To answer this question, merely proving that a certain uric acid-lowering drug can indeed reduce the laboratory indicator of uric acid is far from sufficient—after all, the drug was originally designed to lower uric acid, and

simply fulfilling its intended function does not prove anything more. To definitively settle this question, additional supporting evidence is required [3].

The conceptual differences outlined above will have tangible impacts when applied to the daily clinical scenarios of primary care settings. If a preventive uric acid-lowering drug is casually prescribed to an otherwise healthy person with no physical discomfort, that individual would have to take the medication continuously for several years. During this period, they would bear the risk of potential side effects from the drug, and also have to make extra trips to the hospital for frequent examinations, incurring unnecessary additional costs for medication and tests.

To put it another way, even if there is only a minor fluctuation in physiological indicators, this can at most indicate that a follow-up re-examination is needed. Based solely on such indicator changes, it is impossible to prove that the benefits of long-term use of the drug will definitely outweigh its harms. This review specifically assesses this balance of pros and cons, and also clarifies why the clinical evidence supporting gout treatment cannot be directly applied to patients with asymptomatic hyperuricemia.

Review Scope and Approach

This article focuses specifically on asymptomatic hyperuricemia in adults, and it is a narrative review, not an original study in which the authors independently conducted clinical research and collected brand-new data from scratch; it only sorts out, integrates, and analyzes and comments on existing relevant research results. This type of asymptomatic hyperuricemia refers to the condition where a patient's blood uric acid level exceeds the standard, but no obvious symptoms related to hyperuricemia have yet appeared, and it has not progressed to the stage of gout attack or other clear complications.

When organizing the content, the authors first selected a number of publicly published studies to analyze one by one; these studies were either directly related to clinical diagnosis and treatment, or focused on the pathogenesis of the disease. In addition, they specifically cross-checked all publicly accessible clinical trial records and clinical guideline documents, relying on these authoritative materials to calibrate all content related to clinical interpretation in their article, to make these analyses more accurate and reliable.

When sorting out the research data at hand, the authors prioritized the conclusions of randomized controlled trials, as this type of trial has higher reference value and stronger result reliability in medical research. At the same time, they also made a clear distinction between two types of trials, and did not confuse them: one type is trials that specifically recruited patients with asymptomatic hyperuricemia directly into the group, and

the other type is trials that only included relevant patient populations. The target populations of the two types of studies are different, and the scope of application of their conclusions is also different.

The landmark core studies used to support the analyses in this article include CKD-FIX, PERL, FEATHER, CARES and FAST.

The entire review carries out discussions around five directions, namely the control of blood uric acid levels, the progression of kidney disease, cardiovascular-related outcomes, the occurrence of new-onset gout, and the safety of treatment, covering several core issues that this type of patient cares about most.

It should be noted that there are several tasks this article did not complete, which is different from the standardized medical research that everyone is familiar with. First, it did not recruit new patients to participate in the study on its own, nor did it conduct personalized analysis at the individual case level, let alone integrate data from various studies to calculate a combined overall effect size. When screening the literature to be included in the analysis, it did not collect all relevant studies completely, nor did it achieve exhaustive inclusion. Throughout the sorting and analysis process, it neither followed a pre-registered systematic review protocol, nor adopted the process of dual independent literature screening to avoid human omissions, let alone conducted formal risk of bias assessments for each included study—all of which are basic tasks that a formal systematic review would complete.

Based on these circumstances, this article should be regarded as a critical narrative comprehensive analysis focusing on a specific direction, and cannot be interpreted as a standard systematic review or meta-analysis.

Biological Rationale and Interpretation of Associations

Uric acid is the final product of purine metabolism in the human body, and it cannot be broken down into other substances once it reaches this stage. It flows throughout the body with the blood circulation, and its concentration in the blood is simultaneously tied to two factors: how much new uric acid the body produces each day, and how much uric acid the body can excrete. Among these, the process by which the kidneys process uric acid is the most critical part of the excretion process. If kidney function declines and the ability to excrete uric acid is impaired, blood uric acid levels may rise. This leads to a situation where when high uric acid and kidney function decline occur together, the underlying relationship between them is difficult to untangle: it may be a consequence that only emerges after the kidneys develop problems, or it may be a contributing factor where excessively high uric acid itself, in turn, damages the kidneys. In addition to this bidirectional interaction, a



host of other factors can affect both uric acid levels and kidney function at the same time, such as whether a person is obese, has high blood pressure, what they eat on a daily basis, and whether they are taking specific medications. When these factors are mixed in, it becomes even more difficult to clarify which is the cause and which is the effect [2,3].

Previous experimental studies have also found that the physiological pathways related to uric acid in the human body can trigger a series of bodily abnormalities—including oxidative stress, endothelial cell dysfunction, activation of the renin-angiotensin system, and vascular damage. The associations observed in these experiments happen to form a coherent logic that explains why, in addition to its well-known impact on joints (such as triggering the joint pain of gout), uric acid can also affect parts of the body beyond the joints. However, the models used in these experiments ultimately cannot replicate the real conditions in living humans: they cannot simulate the actual uric acid levels people experience in daily life, the state of a person living with multiple concurrent diseases, or the real course of a disease that lingers for several years or even decades in an individual. There is also another easily confused point: the drugs used to lower uric acid that inhibit xanthine oxidase do not only reduce serum uric acid levels—they also directly alter the oxidative pathways in the body. As a result, not all of the physiological changes observed after using these drugs can be attributed solely to "reduced uric acid"; it is impossible to determine which changes stemmed from lowering uric acid and which stemmed from the altered oxidative pathways [3].

When all the limitations and confounding factors in these experiments are stacked together, it means that to verify the causal hypothesis that "lowering uric acid can treat diseases", we cannot rely on inferences from laboratory results—we must conduct direct clinical trials. Those studies that are based solely on observing populations, even if researchers make various corrections and adjustments to eliminate all confounding interference factors, cannot fully erase all unaccounted-for residual interference. To put it another way, even if an association is actually observed between uric acid levels and the progression and prognosis of a condition, that does not mean that lowering this uric acid indicator will definitely lead to an improvement in the condition. To conduct truly reliable clinical trials, two completely distinct scenarios must also be separated: one is to use uric acid-lowering interventions for prevention when an organ has only just developed early-stage damage, before it develops structural organic problems, to prevent the condition from worsening; the other is to use uric acid-lowering methods for treatment when an organ has already developed clear structural lesions. Even if a negative result is eventually obtained in a group of patients whose conditions have progressed to an advanced stage—that is, the conclusion that no benefit of lowering uric acid was found—this result cannot answer

all biological questions related to uric acid, and it remains critically important for prescribing medications to the real populations that participated in the study.

Biochemical Effects and Surrogate Outcomes

Drugs classified as xanthine oxidase inhibitors can effectively reduce the body's production of uric acid. The fact that allopurinol and febuxostat are able to lower blood uric acid levels has long been recognized by the medical community. However, one issue has never reached a consensus: if a person has not yet developed gout, only elevated uric acid, is there any tangible clinical benefit to lowering their uric acid for their health? This remains controversial at present. The uric acid control targets set for patients already diagnosed with gout are designed to help them dissolve existing uric acid crystals that have formed in the body, so this value cannot be directly adopted as a preventive target that all asymptomatic hyperuricemia populations must adhere to [2,4].

Some small-scale intervention studies, that is, studies where uric acid-lowering measures are administered to subjects to observe changes, have previously reported that after uric acid reduction, the human body exhibits some physiological changes that develop in a positive direction. Kambey and his colleagues conducted such a study: they selected subjects who all had high uric acid but no gout symptoms and completely normal renal function. After administering allopurinol to these subjects, it was found that the subjects' endothelial function, which is the function of endothelial cells in blood vessels that maintain vascular health, improved, and the estimated glomerular filtration rate, an indicator used to assess renal function, also increased. Additionally, Taqueer and his colleagues also recorded that after uric acid was lowered, patients' insulin resistance, the state where the body cannot properly utilize insulin, and various indicators reflecting systemic inflammation levels all showed improvement [5,6]. However, the findings of these small-scale studies only support conducting more in-depth relevant research; they cannot directly prove that lowering uric acid can truly reduce the incidence of myocardial infarction or renal failure, or extend people's lifespan.

It is important to note that the indicators used in the aforementioned studies, such as endothelial function and estimated glomerular filtration rate, are all surrogate endpoints—they are not actual clinical outcomes, only substitute indicators used to replace true hard clinical endpoints. These types of surrogate endpoint indicators are particularly susceptible to interference from many factors: whether the study duration is long enough, whether there are measurement errors, whether subjects received other concurrent treatments during the trial, and differences in the baseline physical conditions of different subjects before the trial began, all can affect the final measured results. If an improvement in estimated glomerular filtration rate or a certain inflammatory



indicator is only observed over a very short period of time, this change may not be sustained, let alone indicate that it can truly bring tangible clinical benefits. If conclusions drawn from the surrogate indicators of small studies conflict with the results of larger trials that observe true clinically meaningful hard endpoints, when formulating treatment decisions for patients, the conclusions of those large trials must be given greater weight and used as the core reference.

Evidence for Kidney Protection

Allopurinol in chronic kidney disease

The CKD-FIX trial conducted a set of controlled tests, administering allopurinol and a placebo to eligible adult patients respectively. All these patients had stage 3 or 4 chronic kidney disease, had never suffered from gout, and faced a very high risk of kidney disease progression—put simply, their kidneys had already sustained damage, and there was a high probability that their kidney function would continue to deteriorate. A total of 369 participants were randomly recruited for the trial, and data from 363 of them was ultimately included in the core outcome analysis. The remaining 6 participants failed to complete the full follow-up period for various reasons, so their data was not used in the most critical final statistics. The entire follow-up period lasted 104 weeks, which is exactly two years. Over these two years, researchers continuously tracked and recorded changes in kidney function in both groups. The core indicator used to measure kidney function was the estimated glomerular filtration rate; the rate at which this value declines represents the speed of kidney function deterioration. According to the final statistics, there was almost no difference in the annual decline rate of the estimated glomerular filtration rate between the two groups: the group taking allopurinol had an average annual decline of $3.33\text{mL/min/1.73m}^2$, while the placebo group had an average annual decline of $3.23\text{mL/min/1.73m}^2$, a difference of only 0.1, a gap so small it can almost be ignored. More critically, the 95% confidence interval for this between-group difference was -1.18 to 0.97 [7], and this range of fluctuation indicates there is no statistically significant difference between the effects of the two groups, meaning it cannot be proven that allopurinol can actually slow the decline of kidney function.

These results provide no evidence to support the routine use of allopurinol as a kidney-protective treatment regimen for this type of patient. When the trial's recruitment period ended, the pre-determined sample size was not met, a flaw that reduces the precision of the study's findings. Put simply, researchers originally planned to recruit more participants to make the conclusion more reliable, but the final number of participants was insufficient, which undermines the credibility of the results. But even setting aside this flaw, the currently observed results lack sufficient persuasive power to support doctors widely prescribing this drug to this type of patient to slow the progression of kidney

disease. The conclusions of this study are most suitable for reference in populations with similar characteristics to the patients enrolled in this trial, and are not applicable to all people with only mildly elevated uric acid levels [7]. In other words, one cannot use the findings of this study to judge whether allopurinol is effective just because a physical examination reveals slightly elevated uric acid; this study's findings can only serve as a reference for people whose baseline conditions fully match those of the patients who participated in this trial.

Allopurinol in type 1 diabetes

PERL evaluated allopurinol in people with type 1 diabetes and early-to-moderate diabetic kidney disease. Despite lowering serum urate, treatment did not produce a clinically meaningful improvement in kidney outcomes [8]. This trial is informative about a proposed urate-mediated mechanism in diabetic kidney disease, but its population should not be described as identical to an unselected asymptomatic hyperuricaemia cohort. Its entry criteria and diabetes-specific setting limit direct extrapolation.

Febuxostat in asymptomatic hyperuricaemia

There was a trial called FEATHER that specifically recruited patients meeting two criteria simultaneously to test the efficacy of febuxostat. These patients had stage 3 chronic kidney disease and also suffered from asymptomatic hyperuricemia, meaning they had elevated uric acid levels but experienced no related discomfort symptoms. The official primary report of the trial records that a total of 443 subjects were initially enrolled through random grouping. When the data was compiled for analysis at the end, 2 people could not be included in the statistics, leaving a total of 441 people whose data was ultimately used to calculate the results.

The study specifically calculated a core indicator reflecting kidney function: the annual change slope of the estimated glomerular filtration rate. This slope can directly show whether kidney function declines or remains stable year by year. The calculated result was that in the group taking febuxostat, the value of this slope was $0.70\text{ mL/min/1.73m}^2$ higher than that of the other group. Looking at this difference alone, it seemed that patients who used febuxostat maintained better kidney function, a result that favored febuxostat. However, the 95% confidence interval used to judge whether this result was truly reliable spanned 0, with a range from -0.21 to 1.62 . The fact that this interval included 0 meant that the previously mentioned difference of 0.70 might only be a false impression caused by random error, and febuxostat might not actually have this advantage. Therefore, the core comparative result of this trial did not have statistical significance [9].

In addition to the overall analysis, the study also conducted exploratory subgroup analyses, which meant dividing patients into smaller groups to explore patterns. Even if some potential signals were found in these small



groups, they must be interpreted in combination with the neutral overall result of the entire trial, and it was not allowed to cite the subgroup results in isolation from the main premise. The potential patterns discovered in these subgroups could only be used to propose research hypotheses for subsequent new trials, and could not serve as a basis for prescribing the drug for any specific subgroup. It was not permitted to directly claim that a small group of patients could definitely use this medication.

When summarizing the results of all these important studies, even if medication could significantly lower patients' uric acid levels, this effect could not be stably converted into preserved kidney function. Lowering uric acid did not prevent kidney function decline in all studies, and there was no inevitable, consistently valid correlation between lowering uric acid and protecting kidney function. Table 1 in the original text compiles all research evidence related to the kidneys and the real-world application scenarios of this evidence.

Table 1. Selected randomised trials evaluating kidney outcomes

Trial	Population and comparison	Main interpretation
CKD-FIX [7]	Stage 3–4 CKD without gout; allopurinol versus placebo; 104 weeks	No slowing of eGFR decline; directly relevant to progressive CKD without gout.
PERL [8]	Type 1 diabetes with kidney disease; allopurinol versus placebo	No clinically meaningful kidney benefit; indirect evidence for general asymptomatic hyperuricaemia.
FEATHER [9]	Stage 3 CKD with asymptomatic hyperuricaemia; febuxostat versus placebo; 108 weeks	No significant overall improvement in eGFR slope; subgroup findings require confirmation.

Abbreviations: CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate.

Cardiovascular Outcomes and Drug Safety

When it comes to urate-lowering issues related to cardiovascular health, two entirely unrelated core issues must first be disentangled; they must never be discussed as a single matter. The first is whether reducing uric acid itself can prevent cardiovascular diseases, and the second is whether the safety profiles of different urate-lowering drugs available on the market are identical. Only by discussing these two issues separately can we avoid confusion.

If a study simply recruits a group of gout patients and conducts a head-to-head comparison between two drugs that both have confirmed urate-lowering effects, the primary function of this trial is nothing more than to determine which of the two drugs has a better safety profile. It cannot draw any further conclusions: for people who only have elevated serum uric acid detected in physical examinations, who have never experienced a gout attack and have no other related symptoms, taking any urate-lowering drug is better for their health than not taking any such drug at all. Trials that only compare two effective drugs against each other are fundamentally incapable of proving this claim.

A trial called CARES specifically compared two commonly used urate-lowering drugs, febuxostat and allopurinol. All subjects recruited for this trial had both gout and a confirmed diagnosis of cardiovascular disease, meeting the trial's eligibility criteria. The trial pre-specified a composite primary cardiovascular endpoint that combined multiple adverse cardiovascular events, and the results for this endpoint met the non-inferiority criteria set before the trial. Simply put, febuxostat was not inferior to allopurinol on this composite indicator. However, what was unusual was

that among patients in the febuxostat group, the mortality rate from cardiovascular causes, as well as the all-cause mortality rate from any cause, were both significantly higher than those in the allopurinol group [10]. There were many complexities in interpreting the results of this trial afterward: many enrolled participants stopped taking their medication on their own mid-trial, and others were completely unreachable during follow-up, a situation commonly referred to as loss to follow-up. These factors all combined to make the results not immediately straightforward. But even with these confounding factors, the finding of higher mortality in the febuxostat group observed in the trial has tangible practical reference value for clinical practice. We cannot simply set aside the elevated mortality rate and pretend it was never observed, just because the composite endpoint yielded a neutral, neither-better-nor-worse result.

After the CARES trial, another trial called FAST also compared these two drugs. The subjects in this trial were elderly gout patients who were already taking allopurinol when they enrolled in the trial, and who had at least one additional cardiovascular risk factor beyond hyperuricemia and gout, such as hypertension or hyperlipidemia. When analyzing the data, the trial specifically calculated statistics for the population that consistently took medication as required, which is an analysis based on actual medication use. The results showed that febuxostat also met the non-inferiority criteria for the primary cardiovascular endpoint, with an adjusted hazard ratio of 0.85 and a corresponding 95% confidence interval of 0.70–1.03. Unlike the CARES trial, this trial did not find that the risk of death was higher in the febuxostat group than in the allopurinol group [11]. It is actually quite normal that these two trials



reached different mortality outcomes, as they differed completely in their patient eligibility criteria, participants' medication histories before enrollment, the follow-up protocols for tracking patients, and the analytical frameworks used for the final data analysis. It is extremely difficult to directly align and compare the results of CARES and FAST, and it is impossible to simply judge which trial's results are correct and which are wrong.

Overall, if a patient meets the clinical indications and truly needs to start urate-lowering therapy, the combined results of these two trials provide critical reference for

clinicians when selecting medications. However, they cannot support another common hypothesis: that people without any hyperuricemia-related symptoms should start taking urate-lowering drugs casually solely to reduce cardiovascular risk. This clear line that must be drawn is particularly important when a patient has multiple cardiovascular risk factors. Even if a person's risk of developing cardiovascular disease is already elevated due to multiple underlying conditions, this fact alone cannot prove that prescribing urate-lowering drugs will actually reduce their risk, nor can it prove that urate-lowering is a reliable and effective intervention.

Table 2. Interpretation of the major cardiovascular safety trials

Trial	Clinical setting	Finding and limit
CARES [10]	Gout with established cardiovascular disease	Primary composite met non-inferiority; higher cardiovascular and all-cause mortality with febuxostat.
FAST [11]	Older adults with gout, prior allopurinol use, and cardiovascular risk	Febuxostat met non-inferiority without excess mortality; eligibility differed from CARES.

Both trials compare active treatment in gout. Neither establishes benefit from initiating urate-lowering therapy in isolated asymptomatic hyperuricaemia.

Prevention of Gout and Other Clinical Indications

Progression from hyperuricaemia to gout is possible but not inevitable. The 2020 American College of Rheumatology guideline conditionally recommends against starting pharmacological urate-lowering therapy in asymptomatic hyperuricaemia. Its evidence assessment estimated that approximately 24 people would need treatment for three years to prevent one first gout flare [4].

A history of gout changes the clinical question. Infrequent symptoms between flares do not make established gout equivalent to asymptomatic hyperuricaemia. Urinary stone disease and acute high urate production in oncological settings also require separate assessment; they should not be used as general arguments for treating an incidental serum urate elevation [2].

Guideline Implications

KDIGO 2024 suggests against using urate-lowering agents solely to delay chronic kidney disease progression in people with chronic kidney disease and asymptomatic hyperuricaemia. This recommendation concerns disease modification and does not remove established indications for treatment of symptomatic urate disease [12].

Gout guidelines also have a defined scope. The 2016 updated EULAR recommendations discuss urate-lowering treatment and targets for patients with gout; those targets should not be applied indiscriminately to people who have never had gout [13]. Differences in guideline scope, outcome priorities, and publication date

must be considered before describing recommendations as contradictory.

A practical synthesis is to identify the disease being treated and the outcome being sought before selecting a drug. Pharmacological success at lowering urate is insufficient justification when the intended goal is prevention of kidney failure or cardiovascular events and that benefit has not been established.

Clinical Assessment and Conservative Management

Assessment begins by confirming that hyperuricaemia is persistent and genuinely asymptomatic. A history should address previous episodes of acute inflammatory arthritis, tophi, stones, medication exposure, and relevant comorbidities. Clinical examination and available kidney investigations help distinguish an incidental biochemical finding from a separate condition requiring treatment. Markedly elevated or unexplained values warrant evaluation of their cause rather than an automatic prescription.

Nonpharmacological care can be incorporated into management of the overall metabolic risk profile. Advice should be realistic and compatible with kidney function and nutritional needs. Weight management, avoidance of excessive alcohol, and moderation of high-fructose drinks and excessive meat intake may be appropriate. Their role should not be overstated as a guaranteed substitute for medication in established gout or as proven prevention of kidney failure through urate reduction [2,12].

Blood pressure, diabetes, lipids, and kidney disease should receive treatments with established indications.



The presence of hyperuricaemia should not distract from those priorities. In Qatar and other primary care settings serving diverse populations, culturally suitable dietary advice and continuity of follow-up can make this approach more practical. Local prevalence or prescribing patterns alone cannot establish that preventive urate lowering improves outcomes.

If pharmacological treatment is considered for a separate accepted indication, its risks require attention. Allopurinol may cause hypersensitivity, while febuxostat selection requires consideration of cardiovascular history and relevant prescribing guidance. Kidney function, concomitant drugs, prior reactions, and monitoring requirements affect the treatment plan. The absence of proven preventive benefit makes even uncommon harms relevant in an otherwise asymptomatic population [4,10,11].

Limitations of the Evidence and Research Priorities

The literature includes heterogeneous populations, urate thresholds, treatment regimens, and outcomes. Trials in gout, diabetic kidney disease, and asymptomatic hyperuricaemia answer related but different questions. Short studies may detect biochemical effects while missing delayed clinical benefit or harm, whereas small samples cannot reliably estimate rare adverse events. Observational treatment comparisons remain vulnerable to confounding by indication and differences in access to care.

This narrative review has additional limitations. Selection of studies was purposive, no formal risk-of-bias instrument was applied, and inaccessible source material restricted some checks to trial records and guideline summaries. It therefore cannot claim exhaustive coverage or a newly graded estimate of certainty. These limitations do not negate the major trial findings, but they should temper claims about all possible patient subgroups.

Future trials should define asymptomatic status consistently and prespecify clinically plausible subgroups, including baseline urate concentration, kidney function, albuminuria, and metabolic risk. Patient-important endpoints should include incident gout, sustained kidney function loss, kidney failure, cardiovascular events, mortality, and treatment burden. Adequate follow-up and representation of diverse populations are needed. Exploratory subgroup results should lead to confirmatory research before becoming routine treatment criteria.

CONCLUSION

Urate-lowering therapy produces clear biochemical effects, but a consistent kidney or cardiovascular benefit has not been demonstrated for routine treatment of asymptomatic hyperuricaemia. Large kidney trials have weakened the case for prescribing solely to preserve renal function, and comparative cardiovascular safety

trials in gout do not establish a preventive indication in asymptomatic individuals. Clinical care should focus on accurate classification, underlying causes, established management of comorbidity, and reassessment if symptoms develop. Treatment for a separate recognised indication should be distinguished from treatment of an isolated laboratory abnormality.

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