



General

Guideline Title

Dietary and pharmacologic management to prevent recurrent nephrolithiasis in adults: a clinical practice guideline from the American College of Physicians.

Bibliographic Source(s)

Qaseem A, Dallas P, Forcica MA, Starkey M, Denberg TD, Clinical Guidelines Committee of the American College of Physicians. Dietary and pharmacologic management to prevent recurrent nephrolithiasis in adults: a clinical practice guideline from the American College of Physicians. *Ann Intern Med.* 2014 Nov 4;161(9):659-67. [35 references] [PubMed](#)

Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Recommendations

Major Recommendations

Definitions for the overall quality of evidence (high, moderate, low, or insufficient evidence to determine net benefits or risks) and the strength of the recommendations (strong, weak) are provided at the end of the "Major Recommendations" field.

Recommendation 1: The American College of Physicians (ACP) recommends management with increased fluid intake spread throughout the day to achieve at least 2 L of urine per day to prevent recurrent nephrolithiasis. (Grade: weak recommendation, low-quality evidence)

Low-quality evidence showed that increased fluid intake is associated with a reduction in stone recurrence. Evidence also did not show any difference between tap water and a specific brand of mineral water (Fuggi brand oligomineral water). People who already drink recommended amounts of liquids and those in whom increased fluid intake is contraindicated should not be directed to increase their fluid intake further. Although some low-quality evidence shows that a decrease in the consumption of soft drinks is associated with a reduced risk for stone recurrence, this benefit was limited to patients who drank soft drinks acidified by phosphoric acid, such as colas, but not for drinks acidified by citric acid, such as fruit-flavored sodas.

Recommendation 2: ACP recommends pharmacologic monotherapy with a thiazide diuretic, citrate, or allopurinol to prevent recurrent nephrolithiasis in patients with active disease in which increased fluid intake fails to reduce the formation of stones. (Grade: weak recommendation, moderate-quality evidence)

Moderate-quality evidence showed that thiazide diuretics, citrates, and allopurinol reduce the risk for recurrence of composite calcium stones. Combination therapy with these agents was not more beneficial than monotherapy. Although biochemistry and some observational data on stone

recurrence suggest that the choice of treatment could be based on the type of metabolic abnormality, evidence from randomized, controlled trials is lacking to correlate the drug of choice and stone type to the prevention of stone recurrence. Most patients have calcium stones, and evidence showed that thiazide diuretics, citrates, and allopurinol all effectively reduced recurrence of this stone type. Note that the available evidence evaluated higher doses of thiazides (hydrochlorothiazide, 50 mg; chlorthalidone, 25 or 50 mg; indapamide, 2.5 mg) to prevent recurrent nephrolithiasis. The use of lower doses of thiazides is associated with fewer adverse effects, but their effectiveness in preventing stone recurrence compared with higher doses is not known. All of the medications are associated with adverse events, which are summarized in Table 2 in the original guideline document.

Definitions:

Grading of Quality of Evidence

High-Quality Evidence: Evidence is considered high quality when it is obtained from 1 or more well-designed and well-executed randomized, controlled trials (RCTs) that yield consistent and directly applicable results. This also means that further research is very unlikely to change confidence in the estimate of effect.

Moderate-Quality Evidence: Evidence is considered moderate quality when it is obtained from RCTs with important limitations—for example, biased assessment of the treatment effect, large loss to follow-up, lack of blinding, unexplained heterogeneity (even if it is generated from rigorous RCTs), indirect evidence originating from similar (but not identical) populations of interest, and RCTs with a very small number of participants or observed events. In addition, evidence from well-designed controlled trials without randomization, well-designed cohort or case-control analytic studies, and multiple time series with or without intervention are in this category. Moderate-quality evidence also means that further research will probably have an important effect on confidence in the estimate of effect and may change the estimate.

Low-Quality Evidence: Evidence obtained from observational studies would typically be rated as low quality because of the risk for bias. Low-quality evidence means that further research is very likely to have an important effect on confidence in the estimate of effect and will probably change the estimate. However, the quality of evidence may be rated as moderate or even high, depending on circumstances under which evidence is obtained from observational studies. Factors that may contribute to upgrading the quality of evidence include a large magnitude of the observed effect, a dose-response association, or the presence of an observed effect when all plausible confounders would decrease the observed effect.

Insufficient Evidence to Determine Net Benefits or Risks: When the evidence is insufficient to determine for or against routinely providing a service, the recommendation was graded as "insufficient evidence to determine net benefits or risks." Evidence may be conflicting, of poor quality, or lacking, and hence the balance of benefits and harms cannot be determined. Any estimate of effect that is very uncertain as evidence is either unavailable or does not permit a conclusion.

The American College of Physicians Guideline Grading System*		
Quality of Evidence	Strength of Recommendation	
	Benefits Clearly Outweigh Risks and Burden or Risks and Burden Clearly Outweigh Benefits	Benefits Finely Balanced With Risks and Burden
High	Strong	Weak
Moderate	Strong	Weak
Low	Strong	Weak
Insufficient evidence to determine net benefits or risks		

* Adopted from the classification developed by the GRADE (Grading of Recommendations Assessment, Development, and Evaluation) Workgroup.

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

Recurrent nephrolithiasis (kidney stones)

Guideline Category

Management

Prevention

Clinical Specialty

Family Practice

Internal Medicine

Nephrology

Preventive Medicine

Urology

Intended Users

Advanced Practice Nurses

Nurses

Physician Assistants

Physicians

Guideline Objective(s)

To present the available evidence on the comparative effectiveness and safety of preventive dietary and pharmacologic management for recurrent nephrolithiasis

Target Population

All adults with recurrent nephrolithiasis (≥ 1 prior kidney stone episode)

Interventions and Practices Considered

1. Increased fluid (tap or mineral water) intake spread throughout the day
2. Pharmacological monotherapy (thiazide diuretic, citrate or allopurinol)

Major Outcomes Considered

- Symptomatic stone recurrence
- Radiographic and composite stone recurrence
- Pain
- Urinary tract obstruction with acute renal impairment
- Infection
- Procedure-related morbidity

- Emergency department visits
- Hospitalizations
- Quality of life
- End-stage renal disease
- Adverse effects/withdrawal rates associated with dietary and pharmacologic interventions

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

The literature search included English-language trials identified by using MEDLINE, the Cochrane Database of Systematic Reviews (January 1948 to September 2012), Google Scholar, ClinicalTrials.gov, and Web of Science. The literature search was updated in March 2014, and no additional studies met the inclusion or exclusion criteria. Dietary interventions that were evaluated included intake of fluids, calcium, animal protein, sodium, fruit and fiber, purine, oxalate, potassium, soft drinks, citrus, or multicomponent diets. We also included empirical dietary interventions and those tailored according to patient demographics, comorbid conditions, baseline diet, baseline urine or blood biochemical testing, and/or stone type. Pharmacologic agents evaluated include medications approved by the U.S. Food and Drug Administration and available in the United States for prescription (for example, hydrochlorothiazide, chlorthalidone, indapamide, potassium citrate, potassium-magnesium citrate, sodium citrate, allopurinol, magnesium hydroxide, or acetohydroxamic acid [AHA]). For key questions 1, 2, 4, and 6, we considered final clinical health outcomes as the most important measures of treatment benefit, including symptomatic stone recurrence, pain, urinary tract obstruction with acute renal failure, infection, morbidity related to treatment of a recurrent stone, emergency department visits or hospitalizations for treatment of recurrent stones (for example, for renal colic or acute renal failure), quality of life (general or urologic), and end-stage renal disease. The next most important measures of treatment considered for key questions 1, 2, 4, and 6 were intermediate stone outcomes, including composite recurrence (combination of symptomatic or radiographically detected recurrence), recurrence detected only by scheduled radiographic imaging, and change in stone size. Evidence suggests that stones identified with imaging are associated with symptomatic recurrence. For key questions 3 and 5, adverse effects included any reported by eligible trials (for example, nausea, diarrhea, hypokalemia, weight change, hyperlipidemia, and hyperglycemia). Measures of treatment adherence were those reported by the individual trials (for example, self-report questionnaire, pill count, or as estimated by follow-up urine biochemical measures). Further details about the methods and inclusion and exclusion criteria applied in the evidence review are available in the full Agency for Healthcare Research and Quality (AHRQ) report (see the "Availability of Companion Documents" field).

Number of Source Documents

28 English-language randomized, controlled trials that studied treatments to prevent recurrent kidney stones and reported stone outcomes were included.

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Grading of Quality of Evidence

High-Quality Evidence: Evidence is considered high quality when it is obtained from 1 or more well-designed and well-executed randomized,

controlled trials (RCTs) that yield consistent and directly applicable results. This also means that further research is very unlikely to change confidence in the estimate of effect.

Moderate-Quality Evidence: Evidence is considered moderate quality when it is obtained from RCTs with important limitations—for example, biased assessment of the treatment effect, large loss to follow-up, lack of blinding, unexplained heterogeneity (even if it is generated from rigorous RCTs), indirect evidence originating from similar (but not identical) populations of interest, and RCTs with a very small number of participants or observed events. In addition, evidence from well-designed controlled trials without randomization, well-designed cohort or case-control analytic studies, and multiple time series with or without intervention are in this category. Moderate-quality evidence also means that further research will probably have an important effect on confidence in the estimate of effect and may change the estimate.

Low-Quality Evidence: Evidence obtained from observational studies would typically be rated as low quality because of the risk for bias. Low-quality evidence means that further research is very likely to have an important effect on confidence in the estimate of effect and will probably change the estimate. However, the quality of evidence may be rated as moderate or even high, depending on circumstances under which evidence is obtained from observational studies. Factors that may contribute to upgrading the quality of evidence include a large magnitude of the observed effect, a dose-response association, or the presence of an observed effect when all plausible confounders would decrease the observed effect.

Insufficient Evidence to Determine Net Benefits or Risks: When the evidence is insufficient to determine for or against routinely providing a service, the recommendation was graded as "insufficient evidence to determine net benefits or risks." Evidence may be conflicting, of poor quality, or lacking, and hence the balance of benefits and harms cannot be determined. Any estimate of effect that is very uncertain as evidence is either unavailable or does not permit a conclusion.

Methods Used to Analyze the Evidence

Meta-Analysis

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Note from the National Guideline Clearinghouse: A systematic evidence review was prepared by the Minnesota Evidence-based Practice Center (EPC) (see the "Availability of Companion Documents" field).

Data Extraction and Quality Assessment

For each article, 1 reviewer extracted details on study design, participant characteristics, outcomes, and adverse events, and a second reviewer checked accuracy. Using criteria developed by the Cochrane Collaboration, 2 reviewers rated individual study quality as good, fair, or poor on the basis of adequacy of allocation concealment, blinding, reporting reasons for attrition, and how analyses accounted for incomplete data (Appendix Table 3 in the systematic evidence review). Following methods developed by the Agency for Healthcare Research and Quality's (AHRQ) Effective Health Care Program, 2 reviewers graded the strength of evidence (SOE) for the efficacy of each treatment comparison in preventing stone recurrence on the basis of risk of bias, consistency, directness, and precision (see Appendix Tables 4 to 6 in the systematic evidence review). Discrepancies in quality ratings and SOE grades were resolved by discussion and consensus.

Data Synthesis and Analysis

Reviewers pooled results if clinical heterogeneity of patient populations, interventions, and outcomes was minimal. Data were analyzed in Review Manager, version 5.1 (The Nordic Cochrane Center, Copenhagen, Denmark). Random-effects models were used to generate pooled estimates of relative risks (RRs) and 95% confidence intervals (CIs), and statistical heterogeneity was summarized using the I^2 statistic. When there were few randomized controlled trials (RCTs) for a given treatment and no overlap of reported outcomes, reviewers synthesized data qualitatively. For analyses of pharmacologic treatments, reviewers evaluated results by drug class and individual agent. Where data allowed, treatment efficacy was explored according to patient characteristics, stone characteristics, baseline and follow-up biochemical measures, and study duration.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

This guideline is based on a systematic evidence review that addressed the following key questions in adults with a history of nephrolithiasis:

1. Do results of baseline stone composition and blood and urine chemistries predict the effectiveness of diet and/or pharmacologic treatment on final health outcomes and intermediate stone outcomes, as well as reduce adverse effects?
2. Do results of follow-up blood and urine biochemistry measurements predict final health outcomes and intermediate stone outcomes in adults being treated to prevent recurrence?
3. What is the effectiveness and comparative effectiveness of different dietary therapies on final health outcomes and intermediate stone outcomes?
4. What is the evidence that dietary therapies to reduce risk for recurrent stone episodes are associated with adverse effects?
5. What is the effectiveness and comparative effectiveness of different pharmacologic therapies on final health outcomes and intermediate stone outcomes?
6. What is the evidence that pharmacologic therapies to reduce risk for recurrent stone episodes are associated with adverse effects?

This guideline rates the evidence and recommendations by using the American College of Physicians' (ACP's) guideline grading system (see the "Rating Scheme for the Strength of the Evidence" and "Rating Scheme for the Strength of the Recommendations" fields). Details of the guideline development process can be found in the summary of methods paper (see the "Availability of Companion Documents" field).

Rating Scheme for the Strength of the Recommendations

The American College of Physicians Guideline Grading System*		
Quality of Evidence	Strength of Recommendation	
	Benefits Clearly Outweigh Risks and Burden or Risks and Burden Clearly Outweigh Benefits	Benefits Finely Balanced With Risks and Burden
High	Strong	Weak
Moderate	Strong	Weak
Low	Strong	Weak
Insufficient evidence to determine net benefits or risks		

* Adopted from the classification developed by the GRADE (Grading of Recommendations Assessment, Development, and Evaluation) Workgroup.

Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

Internal Peer Review

Description of Method of Guideline Validation

This guideline was approved by the American College of Physicians (ACP) Board of Regents on November 23, 2013.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Decreased kidney stone recurrence

Refer to the "Benefits of Dietary Therapies" and "Benefits of Pharmacologic Therapies" sections in the original guideline document for additional information concerning efficacy of specific interventions.

Potential Harms

- Adverse effects associated with thiazides include orthostasis, gastrointestinal upset, erectile dysfunction, fatigue, and muscle symptoms.
- Adverse effects associated with citrate therapy include gastrointestinal symptoms.
- Adverse effects associated with allopurinol include rash, acute gout, and leukopenia.

Refer to the "Harms of Dietary Therapies" and "Harms of Pharmacologic Therapies" sections in the original guideline document for additional information on harms associated with specific interventions.

Contraindications

Contraindications

People who already drink recommended amounts of liquids and those in whom increased fluid intake is contraindicated should not be directed to increase their fluid intake further.

Qualifying Statements

Qualifying Statements

- Clinical practice guidelines are "guides" only and may not apply to all patients and all clinical situations. Thus, they are not intended to override clinicians' judgment. All American College of Physicians (ACP) clinical practice guidelines are considered automatically withdrawn or invalid 5 years after publication, or once an update has been issued.
- The authors of this article are responsible for its contents, including any clinical or treatment recommendations.

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Implementation Tools

Mobile Device Resources

Patient Resources

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Staying Healthy

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

Qaseem A, Dallas P, Forcica MA, Starkey M, Denberg TD, Clinical Guidelines Committee of the American College of Physicians. Dietary and pharmacologic management to prevent recurrent nephrolithiasis in adults: a clinical practice guideline from the American College of Physicians. *Ann Intern Med.* 2014 Nov 4;161(9):659-67. [35 references] [PubMed](#)

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2014 Nov 4

Guideline Developer(s)

American College of Physicians - Medical Specialty Society

Source(s) of Funding

Financial support for the development of this guideline comes exclusively from the American College of Physicians (ACP) operating budget.

Guideline Committee

Clinical Guidelines Committee of the American College of Physicians

Composition of Group That Authored the Guideline

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Financial Disclosures/Conflicts of Interest

Disclosures

Authors followed the policy regarding conflicts of interest described at www.annals.org/article.aspx?articleid=745942 . Disclosures can be viewed at www.acponline.org/authors/icmje/ConflictOfInterestForms.do?msNum=M13-2908 . Any financial and nonfinancial conflicts of interest of the group members were declared, discussed, and resolved. A record of conflicts of interest is kept for each Clinical Guidelines Committee meeting and conference call and can be viewed at www.acponline.org/clinical_information/guidelines/guidelines/conflicts_cgc.htm .

Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Guideline Availability

Available from the [Annals of Internal Medicine Web site](#) .

Print copies: Available from the American College of Physicians (ACP), 190 N. Independence Mall West, Philadelphia PA 19106-1572.

Availability of Companion Documents

The following are available:

- Fink HA, Wilt TJ, Eidman KE, Garimella PS, MacDonald R, Rutks IR, Brasure M, Kane RL, Ouellette J, Monga M. Medical management to prevent recurrent nephrolithiasis in adults: a systematic review for an American College of Physicians clinical guideline. *Ann Intern Med.* 2013 Apr 2;158(7):535-543. Available from the [Annals of Internal Medicine Web site](#) .
- Fink HA, Wilt TJ, Eidman KE, Garimella PS, MacDonald R, Rutks IR, Brasure M, Kane RL, Monga M. Recurrent nephrolithiasis in adults: comparative effectiveness of preventive medical strategies review no. 61. (Prepared by the Minnesota Evidence-based Practice Center under Contract No. 290-02-0009.) AHRQ Publication No. 12-EHC049-EF. Rockville (MD): Agency for Healthcare Research and Quality (AHRQ); 2012 Jul. 232 p. Available from the [AHRQ Web site](#) .
- Qaseem A, Snow V, Owens DK, Shekelle P. The development of clinical practice guidelines and guidance statements of the American College of Physicians: summary of methods. *Ann Intern Med.* 2010 Aug 3;153(3):194-199. Available from the [Annals of Internal Medicine Web site](#) .

Print copies: Available from the American College of Physicians (ACP), 190 N. Independence Mall West, Philadelphia PA 19106-1572.

A collection of Recommendation Summaries for all current American College of Physicians Clinical Guidelines is now available for mobile devices from the [American College of Physicians \(ACP\) Web site](#) .

A continuing medical education (CME) activity is available from the [Annals of Internal Medicine Web site](#) .

Patient Resources

The following is available:

- Summaries for patients. Prevention of repeated episodes of kidney stones in adults: a clinical practice guideline from the American College of Physicians. *Ann Intern Med* 2014 Nov 4;161(9):1-24. Electronic copies: Available from the [Annals of Internal Medicine Web site](#)



Print copies: Available from the American College of Physicians (ACP), 190 N. Independence Mall West, Philadelphia PA 19106-1572.

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC Status

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