



## General

### Guideline Title

Medical management of kidney stones: AUA guideline.

### Bibliographic Source(s)

Pearle MS, Goldfarb DS, Assimos DG, Curhan G, Denu-Ciocca CJ, Matlaga BR, Monga M, Penniston KL, Preminger GM, Turk TM, White JR. Medical management of kidney stones: AUA guideline. Linthicum (MD): American Urological Association Education and Research, Inc.; 2014 Mar. 26 p. [156 references]

### 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 body of evidence strength (grade A, B, or C), the strength of the recommendations (Standard, Recommendation, Option), and for statements labeled as Clinical Principle and Expert Opinion are provided at the end of the "Major Recommendations" field.

#### Evaluation

1. A clinician should perform a screening evaluation consisting of a detailed medical and dietary history, serum chemistries and urinalysis on a patient newly diagnosed with kidney or ureteral stones. (*Clinical Principle*)
2. Clinicians should obtain serum intact parathyroid hormone (PTH) level as part of the screening evaluation if primary hyperparathyroidism is suspected. (*Clinical Principle*)
3. When a stone is available, clinicians should obtain a stone analysis at least once. (*Clinical Principle*)
4. Clinicians should obtain or review available imaging studies to quantify stone burden. (*Clinical Principle*)
5. Clinicians should perform additional metabolic testing in high-risk or interested first-time stone formers and recurrent stone formers. (*Standard; Evidence Strength Grade B*)
6. Metabolic testing should consist of one or two 24-hour urine collections obtained on a random diet and analyzed at minimum for total volume, pH, calcium, oxalate, uric acid, citrate, sodium, potassium and creatinine. (*Expert Opinion*)
7. Clinicians should not routinely perform "fast and calcium load" testing to distinguish among types of hypercalciuria. (*Recommendation; Evidence Strength Grade C*)

#### Diet Therapies

8. Clinicians should recommend to all stone formers a fluid intake that will achieve a urine volume of at least 2.5 liters daily. (*Standard; Evidence Strength Grade B*)
9. Clinicians should counsel patients with calcium stones and relatively high urinary calcium to limit sodium intake and consume 1,000-1,200 mg per day of dietary calcium. (*Standard; Evidence Strength Grade B*)
10. Clinicians should counsel patients with calcium oxalate stones and relatively high urinary oxalate to limit intake of oxalate-rich foods and maintain normal calcium consumption. (*Expert Opinion*)
11. Clinicians should encourage patients with calcium stones and relatively low urinary citrate to increase their intake of fruits and vegetables and limit non-dairy animal protein. (*Expert Opinion*)
12. Clinicians should counsel patients with uric acid stones or calcium stones and relatively high urinary uric acid to limit intake of non-dairy animal protein. (*Expert Opinion*)
13. Clinicians should counsel patients with cystine stones to limit sodium and protein intake. (*Expert Opinion*)

#### Pharmacologic Therapies

14. Clinicians should offer thiazide diuretics to patients with high or relatively high urine calcium and recurrent calcium stones. (*Standard; Evidence Strength Grade B*)
15. Clinicians should offer potassium citrate therapy to patients with recurrent calcium stones and low or relatively low urinary citrate. (*Standard; Evidence Strength Grade B*)
16. Clinicians should offer allopurinol to patients with recurrent calcium oxalate stones who have hyperuricosuria and normal urinary calcium. (*Standard; Evidence Strength Grade B*)
17. Clinicians should offer thiazide diuretics and/or potassium citrate to patients with recurrent calcium stones in whom other metabolic abnormalities are absent or have been appropriately addressed and stone formation persists. (*Standard; Evidence Strength Grade B*)
18. Clinicians should offer potassium citrate to patients with uric acid and cystine stones to raise urinary pH to an optimal level. (*Expert Opinion*)
19. Clinicians should not routinely offer allopurinol as first-line therapy to patients with uric acid stones. (*Expert Opinion*)
20. Clinicians should offer cystine-binding thiol drugs, such as alpha-mercaptopropionylglycine (tiopronin), to patients with cystine stones who are unresponsive to dietary modifications and urinary alkalinization, or have large recurrent stone burdens. (*Expert Opinion*)
21. Clinicians may offer acetohydroxamic acid (AHA) to patients with residual or recurrent struvite stones only after surgical options have been exhausted. (*Option; Evidence Strength Grade B*)

#### Follow-up

22. Clinicians should obtain a single 24-hour urine specimen for stone risk factors within six months of the initiation of treatment to assess response to dietary and/or medical therapy. (*Expert Opinion*)
23. After the initial follow-up, clinicians should obtain a single 24-hour urine specimen annually or with greater frequency, depending on stone activity, to assess patient adherence and metabolic response. (*Expert Opinion*)
24. Clinicians should obtain periodic blood testing to assess for adverse effects in patients on pharmacological therapy. (*Standard; Evidence Strength Grade A*)
25. Clinicians should obtain a repeat stone analysis, when available, especially in patients not responding to treatment. (*Expert Opinion*)
26. Clinicians should monitor patients with struvite stones for reinfection with urease-producing organisms and utilize strategies to prevent such occurrences. (*Expert Opinion*)
27. Clinicians should periodically obtain follow-up imaging studies to assess for stone growth or new stone formation based on stone activity (plain abdominal imaging, renal ultrasonography or low dose computed tomography [CT]). (*Expert Opinion*)

#### Definitions:

##### Body of Evidence Strength

Grade A: Well-conducted and highly-generalizable randomized controlled trials (RCTs) or exceptionally strong observational studies with consistent findings

Grade B: RCTs with some weaknesses of procedure or generalizability or generally strong observational studies with consistent findings

Grade C: Observational studies that are inconsistent, have small sample sizes, or have other problems that potentially confound interpretation of data

Note: By definition, Grade A evidence is evidence about which the Panel has a high level of certainty, Grade B evidence is evidence about which the Panel has a moderate level of certainty, and Grade C evidence is evidence about which the Panel has a low level of certainty.

## American Urological Association (AUA) Nomenclature Linking Statement Type to Evidence Strength

Standard: Directive statement that an action should (benefits outweigh risks/burdens) or should not (risks/burdens outweigh benefits) be taken based on Grade A or B evidence

Recommendation: Directive statement that an action should (benefits outweigh risks/burdens) or should not (risks/burdens outweigh benefits) be taken based on Grade C evidence

Option: Non-directive statement that leaves the decision regarding an action up to the individual clinician and patient because the balance between benefits and risks/burdens appears equal or appears uncertain based on Grade A, B, or C evidence

Clinical Principle: A statement about a component of clinical care that is widely agreed upon by urologists or other clinicians for which there may or may not be evidence in the medical literature

Expert Opinion: A statement, achieved by consensus of the Panel, that is based on members' clinical training, experience, knowledge, and judgment for which there is no evidence

## Clinical Algorithm(s)

None provided

## Scope

### Disease/Condition(s)

Kidney stones

### Guideline Category

Diagnosis

Evaluation

Management

Prevention

Treatment

### Clinical Specialty

Emergency Medicine

Family Practice

Internal Medicine

Nephrology

Nutrition

Surgery

Urology

# Intended Users

Advanced Practice Nurses

Dietitians

Nurses

Physician Assistants

Physicians

# Guideline Objective(s)

To provide a clinical framework for the diagnosis, prevention and follow-up of adult patients with kidney stones based on the best available published literature

# Target Population

Adult patients with kidney stones

# Interventions and Practices Considered

## Diagnosis/Evaluation

1. Detailed medical and dietary history
2. Serum chemistries
3. Urinalysis
4. Serum intact parathyroid hormone (PTH) levels
5. Stone analysis
6. Review of imaging studies
7. Metabolic testing
8. 24-hour urine collection
9. "Fast and calcium load" testing (not routinely recommended)
10. Periodic blood testing

## Management/Treatment

1. Diet based
  - High fluid intake
  - Limiting sodium intake
  - Limiting intake of oxalate-rich foods
  - Increasing intake of fruits and vegetables
  - Limiting non-dairy animal protein
  - Normal calcium intake (recommended daily allowance [RDA])
2. Pharmacological
  - Thiazide diuretics
  - Potassium citrate therapy
  - Allopurinol
  - Cystine-binding thiol drugs (alpha-mercaptopyrionylglycine [tiopronin])
  - Acetohydroxamic acid (AHA)
3. Surgery
4. Follow-up

## Major Outcomes Considered

- Stone recurrence (symptomatic/asymptomatic detection through imaging)
- Clinical aspects of kidney stones:
  - Changes in stone size
  - Residual stone clearance
  - Intermediate biochemical changes in urine or blood
- Quality of life
- Adverse events
- Morbidity related to treatment of recurrent stones

## Methodology

### Methods Used to Collect/Select the Evidence

Searches of Electronic Databases

### Description of Methods Used to Collect/Select the Evidence

The primary source of evidence for this guideline was the systematic review and data extraction conducted as part of the Agency for Healthcare Research and Quality (AHRQ) Comparative Effectiveness Review Number 61 titled *Recurrent Nephrolithiasis in Adults: Comparative Effectiveness of Preventative Medical Strategies* (2012). That report, prepared by the University of Minnesota Evidence-Based Practice Center (EPC), included searches of MEDLINE, the Cochrane Database of Systematic Reviews, Google Scholar, ClinicalTrials.gov and Web of Science for English-language studies published from 1948 through November 2011 relevant to the treatment of recurrent nephrolithiasis in adults.

Eligible studies included randomized controlled trials (RCTs) and large prospective observational trials of patient populations limited to adults aged 18 years or older with a history of one or more past kidney stone episodes. Studies addressing acute pain management and treatment to promote expulsion of stones were excluded. Full details of the AHRQ search strategies and inclusion/exclusion criteria can be found in the original report.

To augment and broaden the body of evidence provided in the AHRQ report, the American Urological Association Education and Research, Inc. (AUA) conducted additional supplementary searches of PubMed and EMBASE for relevant articles published between January 2007 and November 2012, which were systematically reviewed using a methodology developed *a priori*. Study populations were limited to adults 18 years or older with one or more past kidney stone episodes. No limitations on study design were set, however the search protocol prioritized RCTs, controlled clinical trials (CCTs) and prospective studies with a comparison group. A total of 3,760 abstracts were obtained, from which 24 articles were selected for full-text review. All dietary and pharmacologic therapies were acceptable, with the exception of interventions addressing acute pain management for urolithiasis, treatment to promote expulsion of ureteral stones, pharmacological agents not approved by the U.S. Food and Drug Administration (FDA) for use in the United States, and finally imaging for suspected acute renal colic.

### Number of Source Documents

Overall, the supplementary review identified 18 studies to complement the 28 randomized controlled trials (RCTs) identified by the Agency for Healthcare Research and Quality (AHRQ) report.

### 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

Body of Evidence Strength

Grade A: Well-conducted and highly-generalizable randomized controlled trials (RCTs) or exceptionally strong observational studies with consistent findings

Grade B: RCTs with some weaknesses of procedure or generalizability or generally strong observational studies with consistent findings

Grade C: Observational studies that are inconsistent, have small sample sizes, or have other problems that potentially confound interpretation of data

Note: By definition, Grade A evidence is evidence about which the Panel has a high level of certainty, Grade B evidence is evidence about which the Panel has a moderate level of certainty, and Grade C evidence is evidence about which the Panel has a low level of certainty.

## Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review

## Description of the Methods Used to Analyze the Evidence

Data on study design, treatment parameters (e.g., dose, administration protocols, follow-up durations), patient characteristics (i.e., age, gender, race, stone composition), adverse events, and primary outcomes (as defined by study authors) were extracted to evidence tables for analysis and synthesis by the methodologist.

Quality of Studies and Determination of Evidence Strength

Quality of individual studies was rated as high, moderate, or low based on instruments tailored to specific study designs. Randomized controlled trials (RCTs) were assessed using the Cochrane Risk of Bias instrument. Conventional diagnostic cohort studies, diagnostic case-control studies, or diagnostic case series that presented data on diagnostic test characteristics were evaluated using the Quality Assessment of Diagnostic Accuracy Studies (QUADAS-2) tool that evaluates the quality of diagnostic accuracy studies. Cohort studies with a comparison of interest were evaluated with the Newcastle-Ottawa scale.

The categorization of evidence strength is conceptually distinct from the quality of individual studies. Evidence strength refers to the body of evidence available for a particular question and includes consideration of study design, individual study quality, consistency of findings across studies, adequacy of sample sizes, and generalizability of samples, settings and treatments for the purposes of the guideline.

Limitations of the Literature

The Panel proceeded with full awareness of the limitations of the kidney stone literature. These limitations include heterogeneous patient groups, small sample sizes, lack of studies with diagnostic accuracy data, lack of RCTs or controlled studies with patient outcome data, and use of a variety of outcome measures. Overall, these difficulties precluded use of meta-analytic procedures or other quantitative analyses. Instead, narrative syntheses were used to summarize the evidence for the questions of interest.

## Methods Used to Formulate the Recommendations

Expert Consensus

Expert Consensus (Delphi)

## Description of Methods Used to Formulate the Recommendations

The Panel was created by the American Urological Association Education and Research, Inc. (AUA). The Practice Guidelines Committee (PGC) of the AUA selected the Panel Chair and Vice Chair who in turn appointed the additional panel members, all of whom have specific expertise with regard to the guideline subject.

Linking Statement Type to Evidence Strength

The AUA nomenclature system explicitly links statement type to body of evidence strength and the Panel's judgment regarding the balance

between benefits and risks/burdens (see the "Rating Scheme for the Strength of the Recommendations" field).

In some instances, the review revealed insufficient publications to address certain questions from an evidence basis; therefore, some statements are provided as *Clinical Principles* or as *Expert Opinions* with consensus achieved using a modified Delphi technique if differences of opinion emerged. A *Clinical Principle* is a statement about a component of clinical care that is widely agreed upon by urologists or other clinicians for which there may or may not be evidence in the medical literature. *Expert Opinion* refers to a statement, achieved by consensus of the Panel, that is based on members' clinical training, experience, knowledge and judgment and for which there is no evidence. In the case of this guideline, such statement types were not included.

## Rating Scheme for the Strength of the Recommendations

American Urological Association (AUA) Nomenclature Linking Statement Type to Evidence Strength

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## Cost Analysis

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

## Method of Guideline Validation

Peer Review

## Description of Method of Guideline Validation

The American Urological Association Education and Research, Inc. (AUA) conducted an extensive peer review process. The initial draft of this Guideline was distributed to 107 peer reviewers of varying backgrounds; 40 responded with comments. The panel reviewed and discussed all submitted comments and revised the draft as needed. Once finalized, the Guideline was submitted for approval to the Practice Guidelines Committee (PGC). It was then submitted to the AUA Board of Directors for final approval. The Guideline was approved by the AUA Board of Directors in March 2014.

## 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).

Where evidence was lacking, recommendations are supported by expert opinion or consensus.

# Benefits/Harms of Implementing the Guideline Recommendations

## Potential Benefits

Appropriate management of patients with kidney stones

## Potential Harms

The majority of medications prescribed for stone prevention are associated with potential adverse effects, some of which can be detected with blood testing. For example, thiazide therapy may promote hypokalemia and glucose intolerance; allopurinol and tiopronin may cause an elevation in liver enzymes; acetohydroxamic acid (AHA) and tiopronin may induce anemia and other hematologic abnormalities; potassium citrate may result in hyperkalemia. Such monitoring may also allow the clinician to detect other metabolic abnormalities; for example patients with undiagnosed primary hyperparathyroidism may develop hypercalcemia after initiation of thiazide therapy. The type and frequency of testing should be tailored to the patient's comorbidities and medications.

## Qualifying Statements

### Qualifying Statements

- While these guidelines do not necessarily establish the standard of care, American Urological Association Education and Research, Inc. (AUA) seeks to recommend and to encourage compliance by practitioners with current best practices related to the condition being treated. As medical knowledge expands and technology advances, the guidelines will change. Today these evidence-based guidelines statements represent not absolute mandates but provisional proposals for treatment under the specific conditions described in each document. For all these reasons, the guidelines do not pre-empt physician judgment in individual cases.
- Treating physicians must take into account variations in resources, and patient tolerances, needs, and preferences. Conformance with any clinical guideline does not guarantee a successful outcome. The guideline text may include information or recommendations about certain drug uses ("off label") that are not approved by the U.S Food and Drug Administration (FDA), or about medications or substances not subject to the FDA approval process. AUA urges strict compliance with all government regulations and protocols for prescription and use of these substances. The physician is encouraged to carefully follow all available prescribing information about indications, contraindications, precautions and warnings. These guidelines and best practice statements are not in-tended to provide legal advice about use and misuse of these substances.
- Although guidelines are intended to encourage best practices and potentially encompass available technologies with sufficient data as of close of the literature review, they are necessarily time-limited. Guidelines cannot include evaluation of all data on emerging technologies or management, including those that are FDA-approved, which may immediately come to represent accepted clinical practices.
- For this reason, the AUA does not regard technologies or management which are too new to be addressed by this guideline as necessarily experimental or investigational.

## Implementation of the Guideline

### Description of Implementation Strategy

An implementation strategy was not provided.

## Institute of Medicine (IOM) National Healthcare Quality Report Categories

### IOM Care Need



Getting Better

Living with Illness

## IOM Domain

Effectiveness

Patient-centeredness

## Identifying Information and Availability

### Bibliographic Source(s)

Pearle MS, Goldfarb DS, Assimos DG, Curhan G, Denu-Ciocca CJ, Matlaga BR, Monga M, Penniston KL, Preminger GM, Turk TM, White JR. Medical management of kidney stones: AUA guideline. *Linthicum (MD): American Urological Association Education and Research, Inc.*; 2014 Mar. 26 p. [156 references]

### Adaptation

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

### Date Released

2014 Mar

### Guideline Developer(s)

American Urological Association Education and Research, Inc. - Medical Specialty Society

### Source(s) of Funding

Funding of the committee was provided by the American Urological Association, Inc. (AUA). Committee members received no remuneration for their work.

### Guideline Committee

Medical Management of Kidney Stones Guidelines Panel

### Composition of Group That Authored the Guideline

*Panel Members:* Margaret Sue Pearle, MD, PhD (*Chair*), Professor, Urology and Internal Medicine, Utah Southwestern Medical Center, Dallas, TX; David S. Goldfarb, MD (*Vice Chair*), Director, Kidney Stone Prevention Programs, New York VA Med Ctr., Nephrology Section, New York, NY; Dean George Assimos, MD, Chief of Urology, UAB School of Medicine, Birmingham, AL; Gary Curhan, MD, Professor, Harvard Medical School, Brigham and Women's Hospital, Boston, MA; Cynthia J Denu-Ciocca, MD, Assistant Professor of Medicine, UNC School of Medicine, Chapel Hill, NC; Brian R. Matlaga, MD, Associate Professor, Johns Hopkins Medical Institutions, Baltimore, MD; Manoj Monga, MD, Director, Center for Endourology and Stone Disease, The Cleveland Clinic, Cleveland, OH; Kristina Lea Penniston, PhD, Associate

Scientist, Department of Urology, UW School of Medicine and Public Health, Madison, WI; Glenn M. Preminger, MD, Director, Comprehensive Kidney Stone Center & Professor of Urologic Surgery, Duke University Medical Center Department Of Urology, Durham, NC; Thomas M.T. Turk, MD, Professor, Department of Urology, Loyola University Medical Center, Maywood, IL

## Financial Disclosures/Conflicts of Interest

### Conflict of Interest (COI) Disclosures

All panel members completed COI disclosures. Relationships that have expired (more than one year old) since the panel's initial meeting, are listed. Those marked with (C) indicate that compensation was received; relationships designated by (U) indicate no compensation was received.

Consultant/Advisor: Dean G. Assimos, Oxalosis and Hyperoxaluria Foundation (OHF) (U); Gary Curhan, MD, Allena Pharmaceuticals (C); David S. Goldfarb, MD, Takeda (C), Astra Zeneca (C); Brian R. Matlaga, MD, Boston Scientific (C); Manoj Monga, MD, Bard (C), Coloplast (C), Histosonics (C), Olympus (C), US Endoscopy (C) (Expired); Glenn M. Preminger, MD, Boston Scientific (C), Mission Pharmacal (C)

Health Publishing: Dean George Assimos, MD, Med Review in Urology (C), Urology Times (C); Gary Curhan, MD, Manoj Monga, MD, Brazilian Journal of Urology (U), Indian Journal of Urology (U), Journal of Endourology (U), Practical Reviews in Urology (C), Glenn M. Preminger, MD, UpToDate (C)

Leadership Position: Gary Curhan, MD, American Society of Nephrology (C); Manoj Monga, MD, CMS SCIP (U), Endourology Society (U), Glenn M. Preminger, MD, Endourological Society (C); Margaret Sue Pearle, MD, Endourological Society (U), American Board of Urology (U)

Meeting Participant or Lecturer: David S. Goldfarb, MD, Quintiles (C) (Expired); Manoj Monga, MD, Cook Urological (C), Mission Pharmacal (C) (expired); Glenn M. Preminger, MD, Olympus (C)

Scientific Study or Trial: Dean George Assimos, MD, National Institute of Health (NIH) (C); Manoj Monga, MD, Taris Biomedical (C) (Expired), Xenolith (C) (Expired)

Owner, Product Development: David S. Goldfarb, MD, The Ravine Group (C)

Other: Dean George Assimos, MD, Piedmont Stone (C) (Expired); Gary Curhan, MD, UpToDate (C); Manoj Monga, MD, Fortec (C)

## Guideline Status

This is the current release of the guideline.

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

## Guideline Availability

Electronic copies: Available from the [American Urological Association, Inc. Web site](#) .

## Availability of Companion Documents

The following is available:

- Fink HA, Wilt TJ, Eidman KE, Garimella P, MacDonald R, Rutks I, Brasure M, Kane RL, Monga M: Recurrent nephrolithiasis in adults: comparative effectiveness of preventive medical strategies. Comparative Effectiveness Review No. 61. AHRQ Publication No. 12-EHC049-EF. Rockville (MD): Agency for Healthcare Research and Quality; 2012. 232 p. Electronic copies: Available from the [Agency for Healthcare Research and Quality Web site](#) .

## Patient Resources

None available

## NGC Status

This NGC summary was completed by ECRI Institute on September 8, 2014. The information was verified by the guideline developer on September 22, 2014.

## Copyright Statement

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