National Institute for Health and Care Excellence

Final

Renal and ureteric stones: assessment and management

Imaging for follow-up

NICE guideline NG118

Intervention evidence review (J)

January 2019

Final

This evidence review was developed by the National Guideline Centre

NICE accredited
www.nice.org.uk/accreditation

Disclaimer

The recommendations in this guideline represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, professionals are expected to take this guideline fully into account, alongside the individual needs, preferences and values of their patients or service users. The recommendations in this guideline are not mandatory and the guideline does not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and, where appropriate, their carer or guardian.

Local commissioners and providers have a responsibility to enable the guideline to be applied when individual health professionals and their patients or service users wish to use it. They should do so in the context of local and national priorities for funding and developing services, and in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities. Nothing in this guideline should be interpreted in a way that would be inconsistent with compliance with those duties.

NICE guidelines cover health and care in England. Decisions on how they apply in other UK countries are made by ministers in the Welsh Government, Scottish Government, and Northern Ireland Executive. All NICE guidance is subject to regular review and may be updated or withdrawn.

Copyright
© NICE 2019. All rights reserved. Subject to Notice of rights.

ISBN: 978-1-4731-3190-3

Contents

1 Imaging for follow up

1.1 Review question: In people who have or have had renal or ureteric stone, what is the optimum frequency of imaging?

1.2 Introduction

Patients with a history of renal stones do have an increased risk of developing further stones in their lifetime. It is also known that stone fragments remaining following stone treatment are also likely to increase in size with time. These two factors suggest follow-up in stone patients particularly in those at high risk of progression (larger post treatment fragments) or further stones (2 previous episodes) require follow-up. There is wide variation in current clinical opinion on which patient to follow-up, the optimum frequency of imaging and the best imaging modality. The question will endeavour to address this variation.

1.3 PICO table

For full details see the review protocol in appendix A.

Table 1: PICO characteristics of review question

Population	People (adults, children and young people) with suspected (or under investigation for) renal and ureteric stones
Intervention	Monitoring at any of the below frequencies: ○ ≤6 monthly ○ > 6 monthly ○ rapid access/review on request (includes no follow up for asymptomatic people)
Comparison	All of the above frequencies compared with each other
Outcomes	• Stone free • Change in stone size • Stone recurrence • Quality of life • Unplanned admissions • Intervention
Study design	RCTs and SRs of RCTs. Cross-sectional studies, cohort studies will be considered if not enough RCT evidence is found.

1.4 Clinical evidence

1.4.1 Included studies

No relevant clinical studies were identified.

See also the study selection flow chart in appendix C, study evidence tables in appendix D, forest plots in appendix E and GRADE tables in appendix H.

1.4.2 Excluded studies

See the excluded studies list in appendix I.

© NICE 2019. All rights reserved. Subject to Notice of rights.

1.4.3 Summary of clinical studies included in the evidence review

No evidence was identified.

1.4.4 Quality assessment of clinical studies included in the evidence review

No evidence was identified.

1.5 Economic evidence

1.5.1 Included studies

No relevant health economic studies were identified.

1.5.2 Excluded studies

No health economic studies that were relevant to this question were excluded due to assessment of limited applicability or methodological limitations.

See also the health economic study selection flow chart in appendix G.

1.5.3 Unit costs

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

Table 2: UK costs of diagnostic imaging

Diagnostic imaging	Detail	Unit cost
X-ray	Direct access plain film Currency code: DAPF	£29.78
Ultrasound	Ultrasound Scan with duration of less than 20 minutes, without Contrast Currency code: RD40Z	£51.59
Computerised Tomography (CT)	Adults: Computerised Tomography Scan of One Area, without Contrast, 19 years and over Currency code: RD20A	£85.56
	Children: Computerised Tomography Scan of One Area, without Contrast, between 6 and 18 years Currency code: RD20B	£91.67
	Computerised Tomography Scan of One Area, without Contrast, 5 years and under Currency code: RD20C	£94.72

Source: NHS reference costs 2016/17 [14]

Other costs to consider are also the costs of the consultations with a clinician to deliver the results of the imaging. Additionally there may also be unplanned resource use because of follow up that is not frequent enough, such as a GP appointment or hospital attendance.

© NICE 2019. All rights reserved. Subject to Notice of rights.

Table 3: UK costs of other resource use

Resource	Detail	Unit cost
Follow up consultation	HRG code: WF01A Non-Admitted Face-to-Face Attendance, Consultant led follow-up - Urology	£103 (a)
GP appointment	Per consultation	£38 (b)
A&E attendance	HRG code: VB09Z Type 01 non admitted, Emergency Medicine, Category 1 Investigation with Category 1-2 Treatment	£119 (a)

(a) Source: NHS reference costs 2016/17[14]
(b) Including direct care staff costs and qualifications. Source: PSSRU 2017

1.6 Resource costs

The committee has not made any recommendations based on this review. Consequently there is no impact on resources.

1.7 Evidence statements

1.7.1 Clinical evidence statements

- No relevant published evidence was identified.

1.7.2 Health economic evidence statements

- No relevant economic evaluations were identified.

1.8 The committee's discussion of the evidence

1.8.1 Interpreting the evidence

1.8.1.1 The outcomes that matter most

The committee agreed that stone-free state, change in stone size, stone recurrence, quality of life, unplanned admission and intervention were the outcomes that were critical for decision making. No evidence was found, therefore there was no evidence for any of the outcomes.

1.8.1.2 The quality of the evidence

No evidence was found.

1.8.1.3 Benefits and harms

The committee considered that current practice is varied and may depend on a number of patient factors. For instance it was noted that a first time stone former may not need as much follow up as a recurrent stone former, as not all people who develop a stone for the first time will go on to develop a second stone. Recurrent stone formers are more likely to continue to develop future stones. Due to the variation in practice, the committee agreed that a consensus recommendation would not be appropriate as it was felt that there was not sufficient rationale on which to base a recommendation on. Therefore, the committee agreed that further research to investigate the optimum frequency of imaging would be of great benefit.

© NICE 2019. All rights reserved. Subject to Notice of rights.

It was noted that for follow-up imaging, plain abdominal radiograph is commonly used in current UK practice, and that there is a known risk associated with radiation exposure. Therefore when considering the frequency of follow-up imaging, the amount of exposure to radiation would need to be considered.

The committee noted that follow up for children and young people is also varied. Some children and young people receive follow up imaging every year, often regardless of various patient factors, whereas others are discharged with basic fluid and dietary advice upon becoming stone-free and a negative metabolic assessment. Those with residual fragments are followed-up, but the frequency of this can be variable and may depend on multiple patient factors. The committee noted that the type of imaging used for follow-up for children and young people is likely to be ultrasound. The committee discussed whether a research recommendation would be appropriate in this paediatric population, but agreed that randomisation to infrequent follow up may not be ethical in this population.

1.8.2 Cost effectiveness and resource use

No economic evidence was identified for this question.

Different frequencies of imaging have a direct cost of more imaging and consultation costs in the same time period e.g. every 3 months versus every 6 months equals 4 tests per year versus 2 tests per year. The type of imaging may also be important and affects costs, but is generally x-ray.

The indirect impact however, is that monitoring too frequently before changes have a chance to occur incurs the costs of monitoring with limited benefit of picking up changes. Monitoring that is not frequent enough can lead to changes occurring before imaging has a chance to take place, which could result in more unplanned resource use, such as emergency attendances, adverse events because of delayed treatment, or surgical interventions that could have been avoided if other non-invasive treatments (like MET) were provided earlier. Therefore there is a balance to be struck between imaging frequently enough but not too frequently. This is likely to be based partly on the epidemiology of stone formation.

It could also be argued that it is unnecessary to follow people up at all, as they will present when they develop a stone. However, an individual might have a symptomatic stone that could be moving, and monitoring is important to prevent a serious event such as risk of ureteric obstruction, or someone may be asymptomatic but might have a stone that is growing so pre-emptive treatment might be given. So although there might be an argument for waiting and treating people when they develop symptoms, there is a decrement to quality of life in doing so and complications that can be avoided.

Whether someone is followed up in practice is based on a risk assessment taking into account different factors such as patient history. Hence there is large variation in follow up, and is often patient dependent, thus it is difficult to give generic advice. The committee felt they could not make a consensus recommendation, and decided that this area would benefit from further research.

© NICE 2019. All rights reserved. Subject to Notice of rights.

References

1. Beck EM, Riehle RA, Jr. The fate of residual fragments after extracorporeal shock wave lithotripsy monotherapy of infection stones. Journal of Urology. 1991; 145(1):6-9; discussion 9-10

2. Channa NA, Ghangro AB, Soomro AM, Noorani L. Analysis of kidney stones by FTIR spectroscopy. Journal of the Liaquat University of Medical and Health Sciences. 2007; 6(2):66-73

3. Clifford-Mobley O, Sjogren A, Lindner E, Rumsby G. Urine oxalate biological variation in patients with primary hyperoxaluria. Urolithiasis. 2016; 44(4):333-7

4. Da Silva SFR, De Matos DC, Da Silva SL, Daher EDF, Campos HDH, Da Silva CAB. Chemical and morphological analysis of kidney stones: a double-blind comparative study. Acta Cirurgica Brasileira. 2010; 25(5):444-8

5. Dhandapani C, Shibulal JS, Narayanasamy K. Metabolic evaluation of patients with recurrent and multiple renal stones: a prospective study. Asian Journal of Pharmaceutical and Clinical Research. 2016; 9(Suppl 3):212-8

6. Durgawale P, Shariff A, Hendre A, Patil S, Sontakke A. Chemical analysis of stones and its significance in urolithiasis. Biomedical Research. 2010; 21(3):305-10

7. Ferraro PM, Curhan GC, D'Addessi A, Gambaro G. Risk of recurrence of idiopathic calcium kidney stones: analysis of data from the literature. Journal of Nephrology. 2017; 30(2):227-33

8. Gambaro G, Croppi E, Coe F, Lingeman J, Moe O, Worcester E et al. Metabolic diagnosis and medical prevention of calcium nephrolithiasis and its systemic manifestations: a consensus statement. Journal of Nephrology. 2016; 29(6):715-34

9. Hess B. Metabolic syndrome, obesity and kidney stones. Arab Journal of Urology. 2012; 10(3):258-64

10. Krautschick AW. Metabolic evaluation and medical therapy for stone formation. Current Opinion in Urology. 1999; 9(4):335-8

11. Naseri M. Urolithiasis in Asian children: evaluation of metabolic factors. Journal of Pediatric Biochemistry. 2013; 3(4):225-38

12. Naseri M, Varasteh AR, Alamdaran SA. Metabolic factors associated with urinary calculi in children. Iranian Journal of Kidney Diseases. 2010; 4(1):32-8

13. National Institute for Health and Care Excellence. Developing NICE guidelines: the manual. London. National Institute for Health and Care Excellence, 2014. Available from: http://www.nice.org.uk/article/PMG20/chapter/1%20Introduction%20and%20overview

14. NHS Improvement. Reference costs 2016/17: highlights, analysis and introduction to the data. London. 2017. Available from: https://improvement.nhs.uk/resources/reference-costs/

15. Orakzai N, Hanbury DC, Farrington K. Screening for biochemical abnormalities in urolithiasis patients. Journal of Ayub Medical College, Abbottabad. 2004; 16(2):60-3

16. Skolarikos A, Straub M, Knoll T, Sarica K, Seitz C, Petrik A et al. Metabolic evaluation and recurrence prevention for urinary stone patients: EAU guidelines. European Urology. 2015; 67(4):750-63

© NICE 2019. All rights reserved. Subject to Notice of rights.

17. Tiselius HG, Daudon M, Thomas K, Seitz C. Metabolic work-up of patients with urolithiasis: indications and diagnostic algorithm. European Urology Focus. 2017; 3(1):62-71

18. Weizer AZ, Auge BK, Silverstein AD, Delvecchio FC, Brizuela RM, Dahm P et al. Routine postoperative imaging is important after ureteroscopic stone manipulation. Journal of Urology. 2002; 168(1):46-50

19. Worster A, Haines T. Does replacing intravenous pyelography with noncontrast helical computed tomography benefit patients with suspected acute urolithiasis? Canadian Association of Radiologists Journal. 2002; 53(3):144-8

© NICE 2019. All rights reserved. Subject to Notice of rights.

Appendices

Appendix A: Review protocols

Table 4: Review protocol: imaging for follow up

Field	Content
Review question	In people who have or have had renal or ureteric stone, what is the optimum frequency of imaging?
Type of review question	Intervention review A review of health economic evidence related to the same review question was conducted in parallel with this review. For details see the health economic review protocol for this NICE guideline.
Objective of the review	The aim of this review is to identify how often repeated imaging should be performed
Eligibility criteria – population / disease / condition / issue / domain	People (adults, children and young people) with suspected (or under investigation for) renal and ureteric stones
Eligibility criteria – intervention(s) / exposure(s) / prognostic factor(s)	Monitoring at any of the below frequencies: • ≤6 monthly • 6 monthly • rapid access/review on request (includes no follow up for asymptomatic people)
Eligibility criteria – comparator(s) / control or reference (gold) standard	All of the above frequencies compared with each other
Outcomes and prioritisation	• Stone free • Change in stone size • Stone recurrence • Quality of life • Unplanned admissions • Intervention
Eligibility criteria – study design	RCTs and SRs of RCTs. Cross-sectional studies, cohort studies will be considered if not enough RCT evidence is found.
Other exclusion criteria	Bladder stones Open surgery for renal (kidney and ureteric) stones Laparoscopic nephrolithotomy and pyelolithotomy Non-English language studies

Proposed sensitivity / subgroup analysis, or meta-regression	Strata:
	• Population
	  ○ Adults (≥16 years)
	  ○ Children and young people (<16 years)
	• Symptomatic/asymptomatic
	• Previous intervention
	• Stone composition:
	  ○ Calcium
	  ○ Struvite
	  ○ Uric acid

© NICE 2019. All rights reserved. Subject to Notice of rights.

Field	Content
	○ Cystine • Recurrent stone • Current stone free status
Selection process – duplicate screening / selection / analysis	Studies are sifted by title and abstract. Potentially significant publications obtained in full text are then assessed against the inclusion criteria specified in this protocol.
Data management (software)	Pairwise meta-analyses performed using Cochrane Review Manager (RevMan5). GRADEpro used to assess the quality of evidence for each outcome Endnote for bibliography, citations, sifting and reference management Data extractions performed using EviBase, a platform designed and maintained by the National Guideline Centre (NGC)
Information sources – databases and dates	Clinical search databases to be used: Medline, Embase, Cochrane Library Date: all years Health economics search databases to be used: Medline, Embase, NHSEED, HTA Date: Medline, Embase from 2014 NHSEED, HTA – all years Language: Restrict to English only Supplementary search techniques: backward citation searching Key papers: Not known
Identify if an update	Not applicable
Author contacts	https://www.nice.org.uk/guidance/indevelopment/gid-ng10033
Highlight if amendment to previous protocol	For details please see section 4.5 of Developing NICE guidelines: the manual.
Search strategy – for one database	For details please see appendix B
Data collection process – forms / duplicate	A standardised evidence table format will be used, and published as appendix D of the evidence report.
Data items – define all variables to be collected	For details please see evidence tables in Appendix D (clinical evidence tables) or H (health economic evidence tables).
Methods for assessing bias at outcome / study level	Standard study checklists are used to critically appraise individual studies. For details please see section 6.2 of Developing NICE guidelines: the manual. The risk of bias is evaluated for each outcome on a study using the QUADAS-2 checklist.
Criteria for quantitative synthesis	For details please see section 6.4 of Developing NICE guidelines: the manual.
Methods for quantitative analysis – combining studies and exploring (in)consistency	For details please see the separate Methods report for this guideline.
Meta-bias assessment – publication bias, selective reporting bias	For details please see section 6.2 of Developing NICE guidelines: the manual.
Confidence in cumulative evidence	For details please see sections 6.4 and 9.1 of Developing NICE guidelines: the manual.

© NICE 2019. All rights reserved. Subject to Notice of rights.

Field	Content
Rationale / context – what is known	For details please see the introduction to the evidence review.
Describe contributions of authors and guarantor	A multidisciplinary committee developed the evidence review. The committee was convened by the National Guideline Centre (NGC) and chaired by Andrew Dickinson in line with section 3 of Developing NICE guidelines: the manual. Staff from NGC undertook systematic literature searches, appraised the evidence, conducted meta-analysis and cost-effectiveness analysis where appropriate, and drafted the evidence review in collaboration with the committee. For details please see Developing NICE guidelines: the manual.
Sources of funding / support	NGC is funded by NICE and hosted by the Royal College of Physicians.
Name of sponsor	NGC is funded by NICE and hosted by the Royal College of Physicians.
Roles of sponsor	NICE funds NGC to develop guidelines for those working in the NHS, public health and social care in England.
PROSPERO registration number	Not registered

Table 5: Health economic review protocol

Review question	All questions – health economic evidence
Objectives	To identify economic studies relevant to any of the review questions.
Search criteria	• Populations, interventions and comparators must be as specified in the individual review protocol above. • Studies must be of a relevant 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 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	An economic study search will be undertaken using population-specific terms and an economic study filter – see Appendix G *[in the Full guideline]*.
Review strategy	Studies not meeting any of the search criteria above will be excluded. Studies published before 2002, 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 G of the 2014 NICE guidelines manual.[13] **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. An economic evidence table will be completed and it will be included in the 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 an economic evidence table will not be completed and it will not be included in the economic evidence profile.

© NICE 2019. All rights reserved. Subject to Notice of rights.

- 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 Committee if required. The ultimate aim is to include 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 as excluded economic studies in Appendix M.

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 have been excluded before being assessed for applicability and methodological limitations.

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 have been 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 2002 or later but that depend on unit costs and resource data entirely or predominantly from before 2002 will be rated as 'Not applicable'.
- Studies published before 2002 will have been excluded before being assessed for applicability and methodological limitations.

Quality and relevance of effectiveness data used in the economic analysis:

- The more closely the clinical effectiveness data used in the economic analysis matches 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

The literature searches for this review are detailed below and complied with the methodology outlined in Developing NICE guidelines: the manual 2014, updated 2017 https://www.nice.org.uk/guidance/pmg20/resources/developing-nice-guidelines-the-manual-pdf-72286708700869

For more detailed information, please see the Methodology Review. [Add cross reference]

© NICE 2019. All rights reserved. Subject to Notice of rights.

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 6: Database date parameters and filters used

Database	Dates searched	Search filter used
Medline (OVID)	1946 – 29 November 2017	Exclusions Randomised controlled trials Systematic review studies Observational studies Diagnostic tests studies
Embase (OVID)	1974 – 29 November 2017	Exclusions Randomised controlled trials Systematic review studies Observational studies Diagnostic tests studies
The Cochrane Library (Wiley)	Cochrane Reviews to 2017 Issue 11 of 12 CENTRAL to 2017 Issue 10 of 12 DARE, and NHSEED to 2015 Issue 2 of 4 HTA to 2016 Issue 4 of 4	None

Medline (Ovid) search terms

1.	exp urolithiasis/
2.	(nephrolitiasis or nephrolith or nephroliths or urolithias?s or ureterolithias?s).ti,ab.
3.	((renal or kidney* or urinary or ureter* or urethra*) adj3 (stone* or calculi or calculus or calculosis or lithiasis or c?olic*)).ti,ab.
4.	stone disease*.ti,ab.
5.	((calculi or calculus or calcium oxalate or cystine) adj3 (crystal* or stone* or lithiasis)).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/

© NICE 2019. All rights reserved. Subject to Notice of rights.

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.	exp Tomography/
28.	tomograph*.ti,ab.
29.	(NCCT or CT or UHCT).ti,ab.
30.	((CAT or body) adj2 scan*).ti,ab.
31.	or/27-30
32.	Radiography/
33.	Radiography, Abdominal/
34.	Urography/
35.	(radiograph* or x ray* or xray* KUB or urograph*).ti,ab.
36.	or/32-35
37.	Ultrasonography/
38.	(ultrasonograph* or ultrasound or ultrasonic or sonograph* or echograph* or echotomograph*).ti,ab.
39.	(ultra adj2 (sound or sonic)).ti,ab.
40.	(sound* adj2 (wave* or frequenc*)).ti,ab.
41.	(US adj3 imag*).ti,ab.
42.	or/37-41
43.	Magnetic Resonance Imaging/
44.	((magnetic or nuclear) adj2 resonance adj3 imag*).ti,ab.
45.	(MRI or NMR or NMRI or fMRI or MR).ti,ab.
46.	or/43-45
47.	31 or 36 or 42 or 46
48.	26 and 47
49.	exp "sensitivity and specificity"/
50.	(sensitivity or specificity).ti,ab.
51.	((pre test or pretest or post test) adj probability).ti,ab.
52.	(predictive value* or PPV or NPV).ti,ab.
53.	likelihood ratio*.ti,ab.
54.	likelihood function/
55.	((area under adj4 curve) or AUC).ti,ab.
56.	(receive* operat* characteristic* or receive* operat* curve* or ROC curve*).ti,ab.
57.	(diagnos* adj3 (performance* or accurac* or utilit* or value* or efficien* or effectiveness)).ti,ab.
58.	gold standard.ab.
59.	or/49-58
60.	randomized controlled trial.pt.
61.	controlled clinical trial.pt.
62.	randomi#ed.ti,ab.
63.	placebo.ab.

© NICE 2019. All rights reserved. Subject to Notice of rights.

64.	randomly.ti,ab.
65.	Clinical Trials as topic.sh.
66.	trial.ti.
67.	or/60-66
68.	Meta-Analysis/
69.	exp Meta-Analysis as Topic/
70.	(meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
71.	((systematic* or evidence*) adj3 (review* or overview*)).ti,ab.
72.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
73.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
74.	(search* adj4 literature).ab.
75.	(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.
76.	cochrane.jw.
77.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
78.	or/68-77
79.	Epidemiologic studies/
80.	Observational study/
81.	exp Cohort studies/
82.	(cohort adj (study or studies or analys* or data)).ti,ab.
83.	((follow up or observational or uncontrolled or non randomi#ed or epidemiologic*) adj (study or studies or data)).ti,ab.
84.	((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys* or cohort* or data)).ti,ab.
85.	Controlled Before-After Studies/
86.	Historically Controlled Study/
87.	Interrupted Time Series Analysis/
88.	(before adj2 after adj2 (study or studies or data)).ti,ab.
89.	or/79-88
90.	exp case control study/
91.	case control*.ti,ab.
92.	or/90-91
93.	89 or 92
94.	Cross-sectional studies/
95.	(cross sectional and (study or studies or review or analys* or cohort* or data)).ti,ab.
96.	or/94-95
97.	89 or 96
98.	89 or 92 or 96
99.	59 or 67 or 78 or 98
100.	48 and 99

Embase (Ovid) search terms

1.	exp urolithiasis/
2.	(nephrolitiasis or nephrolith or nephroliths or urolithias?s or ureterolithias?s).ti,ab.

© NICE 2019. All rights reserved. Subject to Notice of rights.

3.	((renal or kidney* or urinary or ureter* or urethra*) adj3 (stone* or calculi or calculus or calculosis or lithiasis or c?olic*)).ti,ab.
4.	stone disease*.ti,ab.
5.	((calculi or calculus or calcium oxalate or cystine) adj3 (crystal* or stone* or lithiasis)).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.	exp *tomography/
26.	tomograph*.ti,ab.
27.	(NCCT or CT or UHCT).ti,ab.
28.	((CAT or body) adj2 scan*).ti,ab.
29.	or/25-28
30.	*radiography/
31.	*abdominal radiography/
32.	*urography/
33.	(radiograph* or x ray* or xray* KUB or urograph*).ti,ab.
34.	or/30-33
35.	*echography/
36.	(ultrasonograph* or ultrasound or ultrasonic or sonograph* or echograph* or echotomograph*).ti,ab.
37.	(ultra adj2 (sound or sonic)).ti,ab.
38.	(sound* adj2 (wave* or frequenc*)).ti,ab.
39.	(US adj3 imag*).ti,ab.
40.	or/35-39
41.	*nuclear magnetic resonance imaging/
42.	((magnetic or nuclear) adj2 resonance adj3 imag*).ti,ab.
43.	(MRI or NMR or NMRI or fMRI or MR).ti,ab.
44.	or/41-43
45.	29 or 34 or 40 or 44

© NICE 2019. All rights reserved. Subject to Notice of rights.

46.	24 and 45
47.	exp "sensitivity and specificity"/
48.	(sensitivity or specificity).ti,ab.
49.	((pre test or pretest or post test) adj probability).ti,ab.
50.	(predictive value* or PPV or NPV).ti,ab.
51.	likelihood ratio*.ti,ab.
52.	((area under adj4 curve) or AUC).ti,ab.
53.	(receive* operat* characteristic* or receive* operat* curve* or ROC curve*).ti,ab.
54.	(diagnos* adj3 (performance* or accurac* or utilit* or value* or efficien* or effectiveness)).ti,ab.
55.	diagnostic accuracy/
56.	diagnostic test accuracy study/
57.	gold standard.ab.
58.	or/47-57
59.	random*.ti,ab.
60.	factorial*.ti,ab.
61.	(crossover* or cross over*).ti,ab.
62.	((doubl* or singl*) adj blind*).ti,ab.
63.	(assign* or allocat* or volunteer* or placebo*).ti,ab.
64.	crossover procedure/
65.	single blind procedure/
66.	randomized controlled trial/
67.	double blind procedure/
68.	or/59-67
69.	systematic review/
70.	meta-analysis/
71.	(meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
72.	((systematic* or evidence*) adj3 (review* or overview*)).ti,ab.
73.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
74.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
75.	(search* adj4 literature).ab.
76.	(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.
77.	cochrane.jw.
78.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
79.	or/69-78
80.	Clinical study/
81.	Observational study/
82.	family study/
83.	longitudinal study/
84.	retrospective study/
85.	prospective study/
86.	cohort analysis/
87.	follow-up/

© NICE 2019. All rights reserved. Subject to Notice of rights.

88.	cohort*.ti,ab.
89.	87 and 88
90.	(cohort adj (study or studies or analys* or data)).ti,ab.
91.	((follow up or observational or uncontrolled or non randomi#ed or epidemiologic*) adj (study or studies or data)).ti,ab.
92.	((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys* or cohort* or data)).ti,ab.
93.	(before adj2 after adj2 (study or studies or data)).ti,ab.
94.	or/80-86,89-93
95.	exp case control study/
96.	case control*.ti,ab.
97.	or/95-96
98.	94 or 97
99.	cross-sectional study/
100.	(cross sectional and (study or studies or review or analys* or cohort* or data)).ti,ab.
101.	or/99-100
102.	94 or 101
103.	94 or 97 or 101
104.	58 or 68 or 79 or 103
105.	46 and 104

Cochrane Library (Wiley) search terms

#1.	MeSH descriptor: [Urolithiasis] explode all trees
#2.	(nephrolitiasis or nephrolith or nephroliths or urolithias?s or ureterolithias?s):ti,ab
#3.	((renal or kidney* or urinary or ureter* or urethra*) near/3 (stone* or calculi or calculus or calculosis or lithiasis or c?olic*)):ti,ab
#4.	stone disease*:ti,ab
#5.	((calculi or calculus or calcium oxalate or cystine) near/3 (crystal* or stone* or lithiasis)):ti,ab
#6.	(or #1-#5)
#7.	MeSH descriptor: [Tomography] explode all trees
#8.	tomograph*:ti,ab
#9.	(NCCT or CT or UHCT):ti,ab
#10.	((CAT or body) near/2 scan*):ti,ab
#11.	(or #7-#10)
#12.	MeSH descriptor: [Radiography] this term only
#13.	MeSH descriptor: [Radiography, Abdominal] this term only
#14.	MeSH descriptor: [Urography] explode all trees
#15.	(radiograph* or x ray* or xray or KUB or urograph*):ti,ab
#16.	(or #12-#15)
#17.	MeSH descriptor: [Ultrasonography] this term only
#18.	(ultrasonograph* or ultrasound or ultrasonic or sonograph* or echograph* or echotomograph*):ti,ab
#19.	(ultra near/2 (sound or sonic)):ti,ab
#20.	(sound* near/2 (wave* or frequenc*)):ti,ab
#21.	(US near/3 imag*):ti,ab
#22.	(or #17-#21)

© NICE 2019. All rights reserved. Subject to Notice of rights.

#23.	MeSH descriptor: [Magnetic Resonance Imaging] this term only
#24.	((magnetic or nuclear) near/2 resonance near/3 imag*):ti,ab
#25.	(MRI or NMR or NMRI or fMRI or MR):ti,ab
#26.	(or #23-#25)
#27.	#11 or #16 or #22 or #26
#28.	#6 and #27

B.2 Health Economics literature search strategy

Health economic evidence was identified by conducting a broad search relating to renal and ureteric stones population in NHS Economic Evaluation Database (NHS EED – this ceased to be updated after March 2015) and the Health Technology Assessment database (HTA) with no date restrictions. 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.

Table 7: Database date parameters and filters used

Database	Dates searched	Search filter used
Medline	2014 – 9 March 2018	Exclusions Health economics studies
Embase	2014 – 9 March 2018	Exclusions Health economics studies
Centre for Research and Dissemination (CRD)	HTA - Inception – 9 March 2018 NHSEED - Inception to March 2015	None

Medline (Ovid) search terms

1.	exp urolithiasis/
2.	(nephrolitiasis or nephrolith or nephroliths or urolithias?s or ureterolithias?s).ti,ab.
3.	((renal or kidney* or urinary or ureter* or urethra*) adj3 (stone* or calculi or calculus or calculosis or lithiasis or c?olic*)).ti,ab.
4.	stone disease*.ti,ab.
5.	((calculi or calculus or calcium oxalate or cystine) adj3 (crystal* or stone* or lithiasis)).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/

© NICE 2019. All rights reserved. Subject to Notice of rights.

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.	Economics/
28.	Value of life/
29.	exp "Costs and Cost Analysis"/
30.	exp Economics, Hospital/
31.	exp Economics, Medical/
32.	Economics, Nursing/
33.	Economics, Pharmaceutical/
34.	exp "Fees and Charges"/
35.	exp Budgets/
36.	budget*.ti,ab.
37.	cost*.ti.
38.	(economic* or pharmaco?economic*).ti.
39.	(price* or pricing*).ti,ab.
40.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
41.	(financ* or fee or fees).ti,ab.
42.	(value adj2 (money or monetary)).ti,ab.
43.	or/27-42
44.	26 and 43

Embase (Ovid) search terms

1.	exp urolithiasis/
2.	(nephrolitiasis or nephrolith or nephroliths or urolithias?s or ureterolithias?s).ti,ab.
3.	((renal or kidney* or urinary or ureter* or urethra*) adj3 (stone* or calculi or calculus or calculosis or lithiasis or c?olic*)).ti,ab.
4.	stone disease*.ti,ab.
5.	((calculi or calculus or calcium oxalate or cystine) adj3 (crystal* or stone* or lithiasis)).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

© NICE 2019. All rights reserved. Subject to Notice of rights.

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.	health economics/
26.	exp economic evaluation/
27.	exp health care cost/
28.	exp fee/
29.	budget/
30.	funding/
31.	budget*.ti,ab.
32.	cost*.ti.
33.	(economic* or pharmaco?economic*).ti.
34.	(price* or pricing*).ti,ab.
35.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
36.	(financ* or fee or fees).ti,ab.
37.	(value adj2 (money or monetary)).ti,ab.
38.	or/25-37
39.	24 and 38

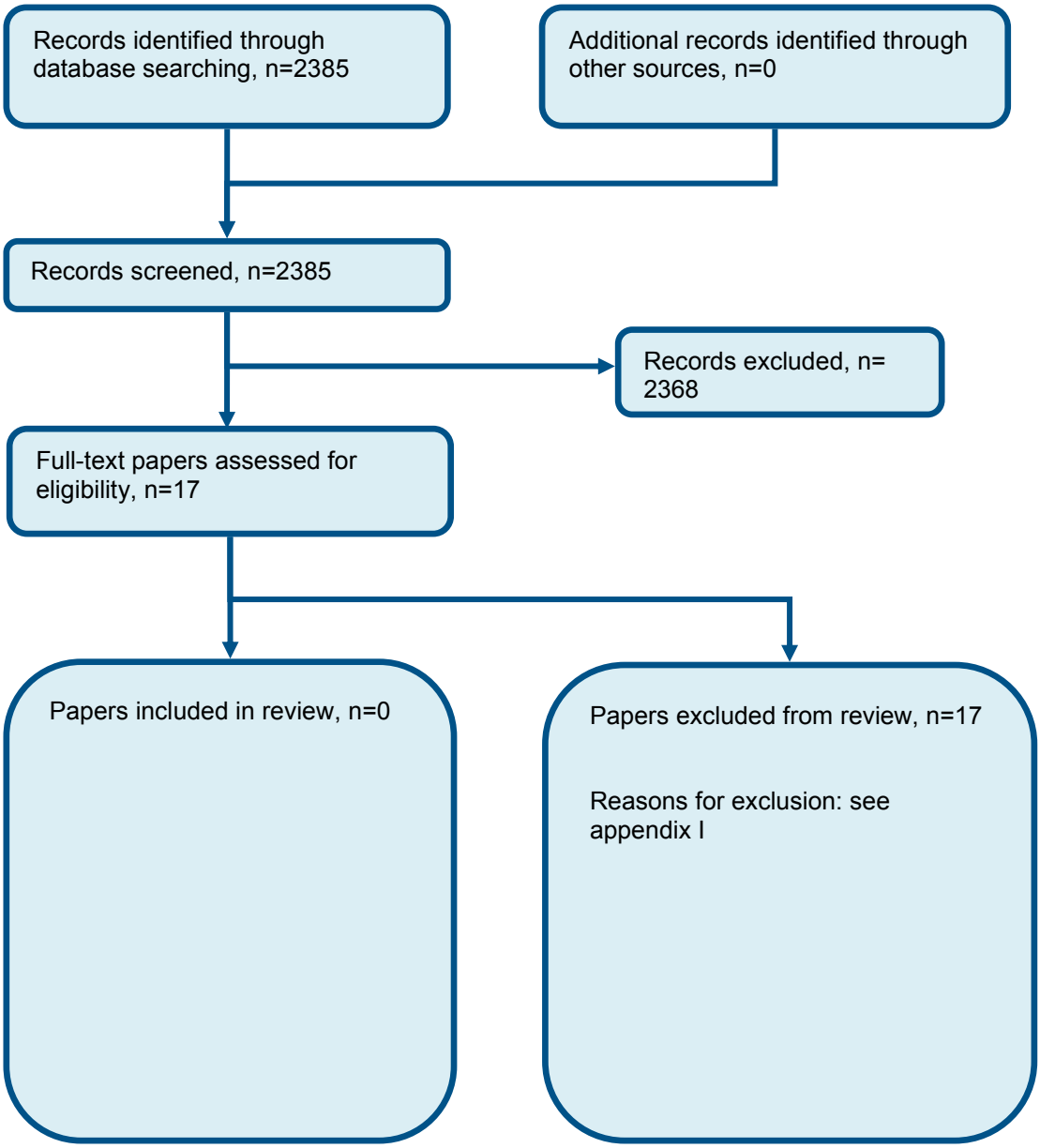
NHS EED and HTA (CRD) search terms

#1.	MeSH DESCRIPTOR urolithiasis EXPLODE ALL TREES
#2.	(((nephrolitiasis or nephrolith or urolithiasis)))
#3.	((((renal or kidney or urinary or ureteric or ureteral or ureter or urethra*) adj2 (stone* or calculi or calculus or calculosis or lithiasis or colic))))
#4.	((stone disease*))
#5.	((((calculi or calculus) adj2 (stone* or lithiasis))))
#6.	(#1 OR #2 OR #3 OR #4 OR #5)

© NICE 2019. All rights reserved. Subject to Notice of rights.

Appendix C: Clinical evidence selection

Figure 1: Flow chart of clinical study selection for the review of imaging for follow up



© NICE 2019. All rights reserved. Subject to Notice of rights.

Appendix D: Clinical evidence tables

No evidence was identified.

Appendix E: Forest plots

No evidence was identified.

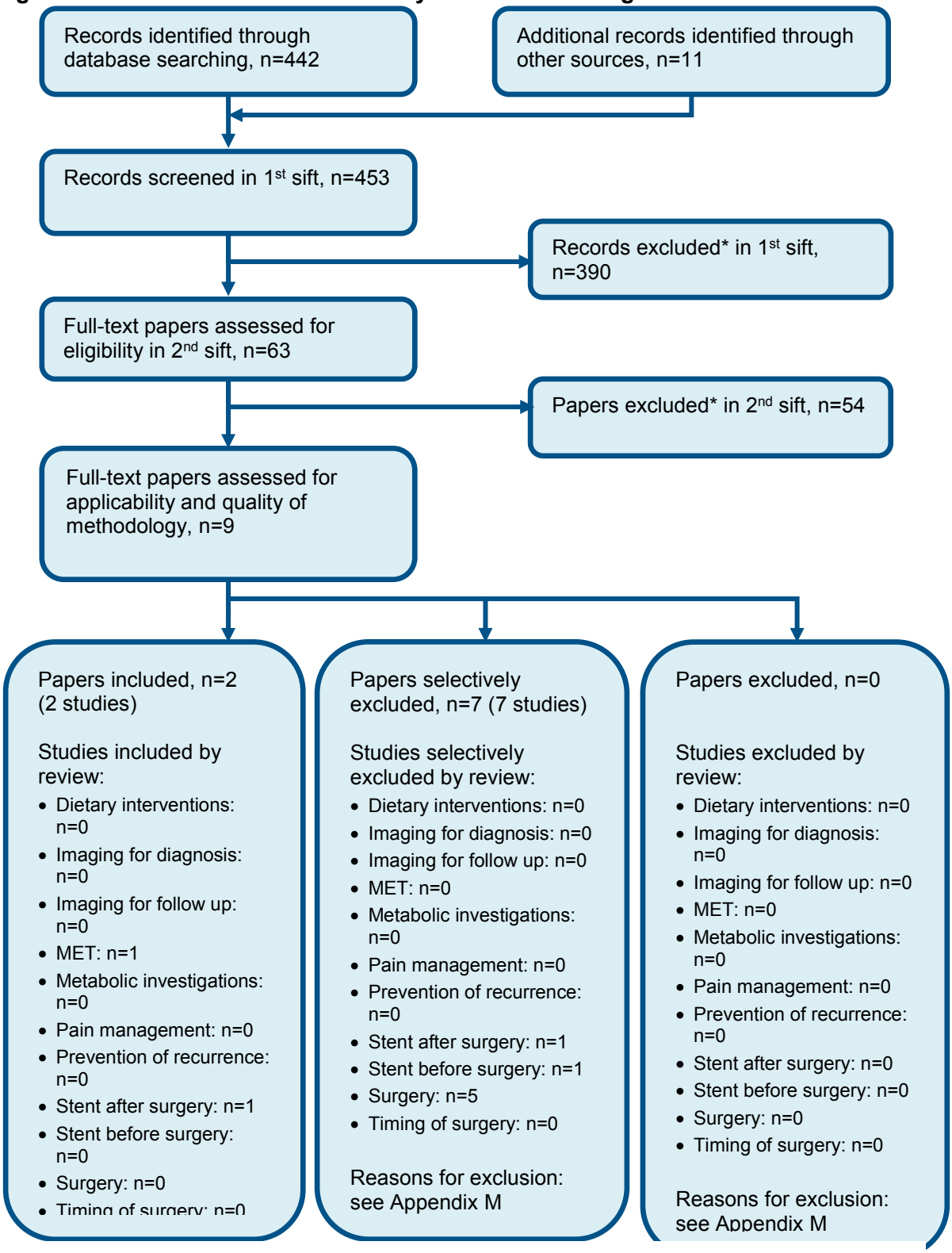
Appendix F: GRADE tables

No evidence was identified.

© NICE 2019. All rights reserved. Subject to Notice of rights.

Appendix G: Health economic evidence selection

Figure 2: Flow chart of economic study selection for the guideline



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

© NICE 2019. All rights reserved. Subject to Notice of rights.

Appendix H: Health economic evidence tables

None

Appendix I: Excluded studies

I.1 Excluded clinical studies

Table 8: Studies excluded from the clinical review

Study	Exclusion reason
Beck 1991[1]	Incorrect study design – no comparison of imaging frequencies
Bugg 2002[2]	Incorrect study design – no comparison of imaging frequencies
Burgher 2004[3]	Incorrect study design – no comparison of imaging frequencies
Chen 1996[4]	Incorrect study design – no comparison of imaging frequencies
Fine 1995[5]	Incorrect study design – no comparison of imaging frequencies
Henriksson 1993[6]	Incorrect study design – no comparison of imaging frequencies
Inci 2007[7]	Incorrect study design – no comparison of imaging frequencies
Karadag 2008[8]	Incorrect study design – no comparison of imaging frequencies
Karod 1999[9]	Incorrect study design – no comparison of imaging frequencies
Lindqvist 2006[10]	Incorrect study design – no comparison of imaging frequencies
Masterson 2017[12]	Incorrect study design – no comparison of imaging frequencies
Michaels 1992[11]	Incorrect study design – no comparison of imaging frequencies
Patel 2000[15]	Incorrect study design – no comparison of imaging frequencies
Ravindra 2017[16]	Incorrect study design – no comparison of imaging frequencies
Villa 2016[17]	Incorrect study design – no comparison of imaging frequencies
Weizer 2002[18]	Incorrect study design – no comparison of imaging frequencies
Worster 2002[19]	Incorrect study design – no comparison of imaging frequencies

I.2 Excluded health economic studies

None

© NICE 2019. All rights reserved. Subject to Notice of rights.

Appendix J: Research recommendations

J.1 Follow up imaging

Research question: What is the clinical and cost effectiveness of 6-monthly imaging for 3 years for people with recurrent calcium renal or ureteric stones?

Why this is important:

Once a patient has had one recurrence of urinary stone they are at increased likelihood of a further recurrence at a later date. If stones are detected earlier, before they become symptomatic, they may be more easily treatable and lead to less morbidity. However imaging patients who are asymptomatic more frequently is costly and also exposes them to ionising radiation. Given that about 50% of patients with a single recurrence will have a further recurrence within 5 years, it is useful to estimate whether it is better to screen patients every 6 months for 3 years. *[do we need a reference for the recurrence rate here ?]*

Criteria for selecting high-priority research recommendations

PICO question	**Population:** People with at least one recurrence of calcium based renal or ureteric stone, who are stone free on entry into trial. **Intervention:** X-ray or US imaging at 6 monthly intervals **Comparison:** No routine surveillance imaging follow up (both groups to also receive baseline CT) **Outcomes:** Primary outcomes; Stone related events (including flank pain, infections, need for interventions, emergency admissions), stones present on CT at 3 years (both groups will have a low dose non-contrast CT at 3 years) Secondary outcomes**:** quality of life (EQ-5D-3L). Cost per QALY as a secondary outcome. **Exclusion:** Children or young people <18 years old
Importance to patients or the population	The importance to patients would be determining the optimal frequency of scanning, to balance the risk of missing stone recurrence with the cost of more frequent imaging. Imaging too infrequently can result in stone formation that is symptomatic and distressing to the patient, as well as the probability of risk such as obstruction. Additionally there may be silent stone formation that clinicians may wish to intervene in because the benefits outweigh the risks. Whereas imaging too frequently can lead to use of resources with limited benefit if stone formation is slower than the rate of imagine.
Relevance to NICE guidance	An answer to this question would change NICE guidance in that there would be clearer evidence for the optimal frequency of follow up imaging in recurrent stone formers- currently no national guidelines are available.
Relevance to the NHS	An answer to this question might save NHS resources if the frequency of rescanning is reduced but conversely it might increase it frequency of rescanning is increased.

© NICE 2019. All rights reserved. Subject to Notice of rights.

National priorities	This would help to reduce patients attending in emergency situations when an asymptomatic stone becomes symptomatic, and may also help reduced unnecessary ionising radiation dose. Recurrent kidney stones are often linked to lifestyle related health problems including obesity and diabetes and limiting the impact of these conditions is one of the NHS top research priorities.
Current evidence base	There are no randomised trials testing different follow up regimens for recurrent kidney stones.
Equality	No issues.
Study design	The study design would involve seeing patients in one arm with routine surveillance imaging every 6 months compared with not routine surveillance. X-ray imaging would be performed where the patient's previous stones were radio-opaque and US if the previous stones were radiolucent. Patients from both arms would be seen at the end of the trial with a low dose non-contrast CT scan.
Feasibility	Stone recurrence has a high enough prevalence to design a suitably powered study to assess follow up scanning in a 3 year time period.
Other comments	
Importance	High: the research is essential to inform future updates of key recommendations in the guideline.

© NICE 2019. All rights reserved. Subject to Notice of rights.