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Medical and surgical interventions for the treatment of urinary stones in children (Review)

Barreto L, Jung JH, Abdelrahim A, Ahmed M, Dawkins GPC, Kazmierski M

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Medical and surgical interventions for the treatment of urinary stones in children

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ABSTRACT

Background

Urolithiasis is a condition where crystalline mineral deposits (stones) form within the urinary tract. Urinary stones can be located in any part of the urinary tract. Affected children may present with abdominal pain, blood in the urine or signs of infection. Radiological evaluation is used to confirm the diagnosis, to assess the size of the stone, its location, and the degree of possible urinary obstruction.

Objectives

To assess the effects of different medical and surgical interventions in the treatment of urinary tract stones of the kidney or ureter in children.

Search methods

We searched the Cochrane Register of Controlled Trials (CENTRAL), MEDLINE (Ovid), Embase (Ovid) as well as the World Health Organization International Clinical Trials Registry Platform Search Portal and ClinicalTrials.gov. We searched reference lists of retrieved articles and conducted an electronic search for conference abstracts for the years 2012 to 2017. The date of the last search of all electronic databases was 31 December 2017 and we applied no language restrictions.

Selection criteria

We included all randomised controlled trials (RCTs) and quasi-RCTs looking at interventions for upper urinary tract stones in children. These included shock wave lithotripsy, percutaneous nephrolithotripsy, ureterorenoscopy, open surgery and medical expulsion therapy for upper urinary tract stones in children aged 0 to 18 years.

Data collection and analysis

We used standard methodological procedures according to Cochrane guidance. Two review authors independently searched and assessed studies for eligibility and conducted data extraction. 'Risk of bias' assessments were completed by three review authors independently. We used Review Manager 5 for data synthesis and analysis. We used the GRADE approach to assess the quality of evidence.

Main results

We included 14 studies with a total of 978 randomised participants in our review, informing eight comparisons. The studies contributing to most comparisons were at high or unclear risk of bias for most domains.

Shock wave lithotripsy versus dissolution therapy for intrarenal stones: based on one study (87 participants) and consistently very low quality evidence, we are uncertain about the effects of SWL on stone-free rate (SFR), serious adverse events or complications of treatment and secondary procedures for residual fragments.

Slow shock wave lithotripsy versus rapid shock wave lithotripsy for renal stones: based on one study (60 participants) and consistently very low quality evidence, we are uncertain about the effects of SWL on SFR, serious adverse events or complications of treatment and secondary procedures for residual fragments.

Shock wave lithotripsy versus ureteroscopy with holmium laser or pneumatic lithotripsy for renal and distal ureteric stones: based on three studies (153 participants) and consistently very low quality evidence, we are uncertain about the effects of SWL on SFR, serious adverse events or complications of treatment and secondary procedures.

Shock wave lithotripsy versus mini-percutaneous nephrolithotripsy for renal stones: based on one study (212 participants), SWL likely has a lower SFR (RR 0.88, 95% CI 0.80 to 0.97; moderate quality evidence); this corresponds to 113 fewer stone-free patients per 1000 (189 fewer to 28 more). SWL may reduce severe adverse events (RR 0.13, 95% CI 0.02 to 0.98; low quality evidence); this corresponds to 66 fewer serious adverse events or complications per 1000 (74 fewer to 2 more). Rates of secondary procedures may be higher (RR 2.50, 95% CI 1.01 to 6.20; low-quality evidence); this corresponds to 85 more secondary procedures per 1000 (1 more to 294 more).

Percutaneous nephrolithotripsy versus tubeless percutaneous nephrolithotripsy for renal stones: based on one study (23 participants) and consistently very low quality evidence, we are uncertain about the effects of SWL on SFR, serious adverse events or complications of treatment and secondary procedures.

Percutaneous nephrolithotripsy versus tubeless mini-percutaneous nephrolithotripsy for renal stones: based on one study (70 participants), SFR are likely similar (RR 1.03, 95% CI 0.93 to 1.14; moderate-quality evidence); this corresponds to 28 more per 1,000 (66 fewer to 132 more). We did not find any data relating to serious adverse events. Based on very low quality evidence we are uncertain about secondary procedures.

Alpha-blockers versus placebo with or without analgesics for distal ureteric stones: based on six studies (335 participants), alpha-blockers may increase SFR (RR 1.34, 95% CI 1.16 to 1.54; low quality evidence); this corresponds to 199 more stone-free patients per 1000 (94 more to 317 more). Based on very low quality evidence we are uncertain about serious adverse events or complications and secondary procedures.

Authors' conclusions

Based on mostly very low-quality evidence for most comparisons and outcomes, we are uncertain about the effect of nearly all medical and surgical interventions to treat stone disease in children. Common reasons why we downgraded our assessments of the quality of evidence were: study limitations (risk of bias), indirectness, and imprecision. These issues make it difficult to draw clinical inferences. It is important that affected individuals, clinicians, and policy-makers are aware of these limitations of the evidence. There is a critical need for better quality trials assessing patient-important outcomes in children with stone disease to inform future guidelines on the management of this condition.

PLAIN LANGUAGE SUMMARY

Interventions for treating urinary stones in children

Review question

What is the evidence for treating stones of the kidney or ureter in children?

Background

Urinary stones occur in up to 5 in 100 children in high-income countries. These rates have been noted to be increasing. To treat urinary stones in children, urologists use medications, shock wave therapy, open surgery, and small scopes that are put into the bladder or through the skin. It is not clear how well each of these treatments work and what the side effects are.

Study characteristics

We included 14 studies with a total of 978 randomised children with stones in either the kidney or ureter, which connects the kidney to the bladder. The number of children in the studies varied from 22 to 221 children. There were seven trials of different types of surgery, four trials of medications and one study that compared medication with surgery. The amount of time the trials followed participants for ranged from one week to one year.

Key results

Shock waves versus medication to dissolve stones: we are uncertain about the effect on successful removal of stones, serious complications and the need for a second procedure to treat the stones.

Shock waves given slowly versus shock waves given fast: we are uncertain about the effect of slow shock waves on successful removal of stones. We are also uncertain about the effect on serious complications and the need for other procedures.

Shock waves versus treatment using a scope through the bladder to break up the stone: we are uncertain about the effect of shock waves on successful removal of stones compared to using a scope. We are also uncertain about the effect on serious complications and the need for other procedures.

Shock waves versus treatment using a scope through the skin into the kidney: shock waves are likely less successful in the removal of stones. Shock waves appears to reduce severe adverse events but more often secondary procedures are needed to remove all the stones.

Use of a scope through the kidney with a drainage tube afterwards versus without a drainage tube: we are uncertain about the effect on successful removal of stones, serious complications or the need for more procedures.

Use of a scope through the kidney with a regular versus very small (“mini”) tube through the skin: successful removal of stones are likely similar in both procedures. We did not find any data relating to serious adverse events. We are uncertain about the effect on the need for another procedure.

Alpha-blockers versus placebo with or without ibuprofen: alpha-blockers may increase successful removal of stones. We are uncertain about serious complications and the need for more procedures.

Quality of the evidence.

The quality of evidence for most outcomes was very low. This means that we are very uncertain about most of the review findings.

SUMMARY OF FINDINGS FOR THE MAIN COMPARISON *[Explanation]*

Participants: children with uncomplicated radiolucent renal stone Intervention: SWL (Lithotripter S; total count of 2,000 per session at 12 to 14 kV power and a frequency of 60 to 70 per minute) under general anaesthesia Control: oral potassium sodium hydrogen citrate at a dose of 1 mEq/kg per day in 2 or 3 divided doses after meals					
Outcomes	No. of participants (studies)	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)	
				Risk with Dissolution therapy for renal stones	Risk difference with SWL
Stone-free rate Follow-up: mean 3 months	87 (1 RCT)	⊕○○○ VERY LOW ¹²	RR 1.13 (0.90 to 1.41)	Study population	
				729 per 1,000	95 more per 1,000 (73 fewer to 299 more)
Serious adverse events or complications of treatment Follow-up: mean 3 months	87 (1 RCT)	⊕○○○ VERY LOW ¹²	RR 1.23 (0.08 to 19.05)	Study population	
				21 per 1,000	5 more per 1,000 (19 fewer to 376 more)
Secondary procedures for residual fragments Follow-up: mean 3 months	87 (1 RCT)	⊕○○○ VERY LOW ¹²	RR 0.66 (0.29 to 1.50)	Study population	
				271 per 1,000	92 fewer per 1,000 (192 fewer to 135 more)
Hospital stay - not reported	-	-	-	-	-

***The risk in the intervention group** (and its 95% CI) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval; **RCT:** randomised controlled trial; **RR:** risk ratio; **SWL:** shock wave lithotripsy.

GRADE Working Group grades of evidence

High certainty: We are very confident that the true effect lies close to that of the estimate of the effect

Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different

Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect

Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

¹ Downgraded by one level for study limitations: unclear or high risk of bias in almost all domains.

² Downgraded by two levels for imprecision: confidence interval is very wide and crosses clinically meaningful threshold.

BACKGROUND

Description of the condition

Urolithiasis or stone disease is a condition where crystalline mineral deposits form within the urinary tract. Metabolic, anatomical factors, iatrogenic and idiopathic causes all contribute to stone formation. In children, urinary tract infections can contribute to stone development.

Formation of the urinary stones is positively enhanced by increased concentrations of uric acid, calcium, oxalate and cystine molecules. Crystallisation inhibitors such as citrate, magnesium, glycosaminoglycans and pyrophosphate play an important role as inhibitors in the formation of the urinary stones and their depletion may be the main cause of the stone formation.

Composition of the stones, their location in the urinary tract and prevalence of the disease varies around the world. The prevalence rate in low- to middle-income countries such as Pakistan and Turkey is 5% to 15% (Shah 1991), compared with 1% to 5% in high-income countries (Elsobky 2000; Yoshida 1990). Overall girls are more susceptible to nephrolithiasis than boys (Novak 2009).

Urinary stones can be located in any part of the urinary tract. Many stones found in children born in low- to middle-income countries are located within the urinary bladder (Rizvi 2002; Rizvi 2003). There is some evidence to suggest that the predominant location of urinary stones has shifted from the bladder to the upper urinary tract over a 13-year period from 1987 to 2000 (Rizvi 2002). Of these cases, 75% to 80% have upper urinary tract stones and 5% are caused by infection (Ozokutan 2000).

The manifestation and clinical presentation of urinary stones in children differs from the adult population and can vary with age. Fifty per cent of children will present with abdominal pain, 33% with haematuria and 11% with infection. Children under the age of five years most commonly present with blood in the urine, while pain is a more common finding in older children. In younger children the localisation of pain is not as typical as in adults and flank pain radiating to the groin is rare (Santos-Victoriano 1998). Pain in children with stones can have a distribution such as appendicitis or gastroenteritis. In infants, the only presenting sign of stone disease might be urinary tract infection.

Diagnosis is confirmed by radiological evaluation which is also used to assess the size of the stone, location and the degree of possible urinary obstruction.

Description of the intervention

The most appropriate management strategy depends on a number of factors, principally the size, location and composition of the stone. Other factors influencing management include the availability of different treatment options, local expertise, as well as

anatomical variations such as in children with congenital abnormalities of the urinary tract.

Shock wave lithotripsy (SWL) involves the use of shock waves focused from outside the body onto the stone. It is a commonly used therapy for children with smaller upper urinary tract stones as long as there is adequate drainage of the urinary system below the level of the stone. SWL can also be used for treatment of ureteric stones. Success rates and complications are significantly affected by the location of the stone and can also depend on the type of machine used.

In children with larger and more complex stone disease percutaneous nephrolithotripsy (PCNL) is widely used, which involves establishing a percutaneous working tract to fragment and remove the stone(s) using ultrasound, laser or pneumatic lithotripsy. This technique is considered in children with large upper tract stones (1.5 cm or larger). Until recently this technique was limited by the availability of appropriately sized instruments however paediatric-size instruments are now available (Desai 2005).

Children with stones within the ureter or collecting system may be treated by ureterorenoscopy, which involves insertion of a ureterorenoscope through the bladder. One limitation is that in smaller children the size of the ureteric orifice may be insufficient to accommodate an ureterorenoscope. Different contact lithotripsy techniques - such as laser, ultrasound, and pneumatic lithotripsy - can be utilised with ureterorenoscopy. This technique is mainly used in children with a stone size from 4 mm where visualisation during SWL has failed or cannot be done.

Open stone surgery may be used in very young children with large stones or in children with a large stone which would require multiple endoscopic procedures. It is also indicated in children with a stone in the presence of congenital anomalies of the urinary system or orthopaedic anomalies where operative positioning is impossible. Open surgery is rarely indicated as first-line treatment in children. It has the advantage of very high primary stone clearance rates but this radical approach has obvious disadvantages and potential complications. Laparoscopic and robotic surgery are becoming more popular in the treatment of various urological conditions requiring a surgical approach, but is not yet commonly used in the treatment of paediatric stones (Dahm 2014).

Medical expulsion therapy is a conservative medication-based method of stone management. It involves the administration of medications to accelerate and facilitate the spontaneous passage of ureteric stones. Corticosteroids, hormones, nonsteroidal anti-inflammatory agents, calcium-channel blockers and alpha-adrenergic blockers have been used in the conservative management of stone disease.

The stone-free rate (SFR) is the measure of success of the intervention. However, there is currently no consensus regarding the size of the fragment to define 'stone-free' for children. Fragments of 3 mm or less are often regarded as insignificant in adult practice. A child's capacity to pass a stone has been shown to be greater than in adults, probably due to higher tissue compliance. Kidney stones

less than 3 mm are likely to pass spontaneously and the chance of passing a ureteric stone less than 5 mm is approximately 70%. The passage rate of stones greater than 5 mm does not depend on age in children older than one year (Pietrow 2002).

How the intervention might work

SWL is thought to be relatively safe and effective. The reported SFR following treatment depends on the location and size of the stone. There is a negative correlation between stone size and effectiveness of stone clearance. The disadvantages of SWL include the need for potential fluoroscopic localisation of some stones and the inability to adequately focus the energy in smaller children, as the machines in use are designed for older patients. The equipment is bulky and cumbersome and difficult to move; in children the technique is typically performed under general anaesthesia, and many patients with kidney stones have significant co-morbidities making this an important consideration when multiple attempts at stone clearance may be required. Complications of SWL can include urosepsis, haematuria, flank pain, and 'steinstrasse'. There is risk of hypertension in SWL application to the kidney (Denburg 2016). All of these complications are less common with second generation lithotrippers (Kroovand 1987). The stone-free range for SWL reported by most centres for moderate sized stones is between 70% and 80% (Picramenos 1996; Van Horn 1995). SWL is the least invasive procedure for the management of most types of stones in children.

PCNL in children was first reported 30 years ago by Woodside and colleagues (Woodside 1985). Initial results were excellent with a reported SFR of 100% and no complications. Subsequent publications have demonstrated a number of potential complications of PCNL including renal scarring (Wilson 1993), bleeding, postoperative infection and persistent urinary leakage. Standard PCNL involves usage of percutaneous tubes to maintain adequate drainage of the kidney post procedure. Due to the belief that the nephrostomy tubes can contribute to postoperative pain, use of small nephrostomy tubes or a 'tubeless' approach via ureteric stents or catheters instead of nephrostomy tubes has been developed. Use of ureteroscopic techniques is similar to those in adults. Complete stone clearance rates of up to 90% have been reported with the use of a semi-rigid ureteroscope (Dogan 2011). The incidence of vesicoureteric reflux disease after ureteroscopy is very low (Thomas 1993).

Alpha-1 adrenergic receptors are located throughout the human ureter. The physiologic response to antagonism of these receptors is decreased contraction, decreased peristaltic frequency, and increased fluid bolus volume transported down the ureter. Alpha-blockers (specifically alpha-1 antagonists) increase the spontaneous expulsion rate of distal ureteric stones, hence reducing the time to stone passage. The rate of spontaneous passage with no medical intervention for a stone of less than 5 mm located in the

proximal ureter is 29% to 98% and in the distal ureter is 71% to 98% (Segura 1997).

Why it is important to do this review

There is a large body of evidence on the management of upper urinary tract stone disease in adults, but significantly less evidence on the management in children. Although urinary stones are less prevalent in children than in adults, they are associated with significant morbidity and there is evidence that the incidence is increasing (Clayton 2011). In addition, recent technological developments in stone management has expanded the treatment choices. While there are existing systematic reviews that assess the effects of medical expulsive therapy and ureteroscopy (Glina 2015; Ishii 2014; Ishii 2015; Tian 2017; Velazquez 2015) the reviews are less rigorous and include non-randomised controlled trials regardless of study design. Furthermore, none apply the GRADE approach or use the same methodology as Cochrane reviews (Guyatt 2008). In this era, with the availability of numerous procedures for the treatment of urinary tract stones in children, the findings of this Cochrane Review will be relevant to policymakers, healthcare providers and patients.

OBJECTIVES

To assess the effects of different medical and surgical interventions in the treatment of urinary tract stones of the kidney or ureter in children.

METHODS

Criteria for considering studies for this review

Types of studies

We included randomised controlled trials (RCTs) and quasi-RCTs (RCTs in which allocation to treatment was obtained by alternation, use of alternate medical records, date of birth or other predictable methods).

Types of participants

Inclusion criteria

We included children (aged 0 to 18 years) with upper tract urinary stones confirmed by imaging, who required medical or surgical intervention.

Exclusion criteria

We excluded trials of children with lower urinary tract stones such as urinary bladder or urethral stones, active urinary tract infection, urinary tract anomalies, non-functioning kidney, previously diagnosed reflux, voiding dysfunction, and history of ureteral or bladder surgery (or both).

Diagnostic criteria for urinary stone

Stone diagnosis was made by sonography or kidney-ureter-bladder radiography and was confirmed by intravenous urography or computerised tomography (CT) scan.

Types of interventions

The following interventions have been examined and compared.

- Shock wave lithotripsy.
- Percutaneous nephrolithotripsy.
- Ureterorenoscopy (regardless of the type of lithotripsy).
- Open stone surgery.
- Medical expulsive therapy.

Studies comparing surgical and medical management have been included.

Types of outcome measures

Primary outcomes

- Stone-free rate.
- Serious adverse events or complications of treatment.
- Secondary procedures for residual fragments.

Secondary outcomes

- Hospital stay.
- Pain.

Our primary and secondary outcomes were changed after the publication of the protocol. For information on the outcomes we initially planned to assess see: [Differences between protocol and review](#).

Method and timing of outcome measurement

- Stone-free rate: defined as complete stone clearance or clinically insignificant residual fragments measuring less than 4 mm (a commonly used measure of 'success') ([Park 1998](#)).
- Serious adverse events or complications of treatment: defined by a Clavien-Dindo classification of 3 or over ([Dindo 2004](#)). If the authors did not use the Clavien-Dindo system, we will judge the adverse events by severity using the available information described in the studies.

- Secondary procedures for residual fragments measuring 4 mm or more ([Park 1998](#)).
- Hospital stay: measured in hours and days.
- Pain: measured by dose of medication, pain scale (e.g. visual analogue scale), or pain episodes.

We used clinically important differences for the review outcomes to rate the quality of evidence for imprecision in the 'Summary of findings' tables ([Johnston 2013](#)). When the mean difference (MD) or risk ratio (RR) was equal to or larger than the clinically important difference, we assumed that many patients may have gained clinically meaningful improvement from treatment; when the MD lies between 0.5 and 1.0 clinically important difference, an appreciable number of participants have likely achieved a clinically meaningful improvement; and when the MD falls below 0.5 clinically important difference, it is unlikely that an appreciable number of participants achieve clinically meaningful improvement ([Johnston 2013](#)). No threshold was established for the SFR, serious adverse events or complications of treatment and secondary procedures. We considered the clinically important differences of all listed outcomes as a relative risk reduction of at least 25% ([Guyatt 2011a](#)). We used a clinically meaningful threshold of one day for length of hospital stay to assess efficacy and comparative effectiveness. As different measurement methods were used to assess pain related outcomes in the articles, we defined a clinically meaningful threshold for pain based on each measurement method (dose of medication, pain scale, pain episodes, and so on).

Main outcomes for the 'Summary of findings' tables

We assessed the following main outcomes, where available, in the following order of importance for the narrative 'Summary of findings' tables.

- Stone-free rate.
- Serious adverse events or complications of treatment.
- Secondary procedures for residual fragments.
- Hospital stay.

Search methods for identification of studies

Electronic searches

The search strategy was developed with the Cochrane Renal Group's Trials Search Co-ordinator in 2012 and a search of the Cochrane Renal Group's Specialised Register was conducted. The latest search was conducted on 31 December 2017 of the databases detailed below. The search strategy terms used for the different databases are listed in [Appendix 1](#). The search strategy was conducted independently by two authors (LB, AA). The following electronic sources were used to identify relevant studies.

- Cochrane Central Register of Controlled trials (CENTRAL).

- MEDLINE (Ovid).
- Embase (Ovid).

To identify RCTs and quasi-RCTs we applied the Cochrane Highly Sensitive Search Strategy outlined in the *Cochrane Handbook of Systematic Reviews of Interventions* (Higgins 2011). No language limitations were applied. See [Appendix 1](#) for search terms used in strategies for this review.

Searching other resources

We also searched the references of full articles retrieved for our review to identify any additional studies. To identify unpublished trials or trials in progress, we searched the following sources: ClinicalTrials.gov, the World Health Organization International Clinical Trials Registry Platform Search Portal (apps.who.int/trialsearch/) and the International Standard Randomised Controlled Trial Number registry ([controlled-trials.com](https://www.controlled-trials.com)). We conducted a search of abstract proceedings of major urological and paediatric urology meetings, covering the years 2012 to 2017 ([Appendix 2](#)). We contacted the authors of studies identified as potentially eligible to obtain clarification on missing data.

Data collection and analysis

Selection of studies

We used the search strategy described above to obtain titles and abstracts of studies that were relevant to the review. The titles and abstracts were screened independently by two review authors (LB, AA) on the basis of our inclusion and exclusion criteria. The two authors independently screened and assessed retrieved abstracts and discarded studies that were not applicable. The conflict resolution was performed by a third author (MK) independently. If resolution of a disagreement was not possible, we assigned the study as 'awaiting classification' and contacted study authors for clarification. We documented reasons for exclusion of studies that may have reasonably been expected to be included in the review in a [Characteristics of excluded studies](#) table. We presented an adapted PRISMA flow diagram showing the process of study selection ([Liberati 2009](#)).

Data extraction and management

Data extraction was carried out independently by two authors (LB, MK) using modified data extraction forms created in Microsoft Excel. We extracted the following information, where available, which we provided in the [Characteristics of included studies](#) table.

- Study design.
- Study dates (if dates were not available then this was reported as such).
- Study settings and country.

- Participant inclusion and exclusion criteria.
- Participant details, baseline demographics.
- The number of participants by study and by study arm.
- Details of relevant experimental and comparator interventions such as SWL device.
- Definitions of relevant outcomes, method and timing of outcome measurement as well as any relevant subgroups.
- Study funding sources.
- Declarations of interest by primary investigators.

We resolved any disagreements by discussion or, if required, by consultation with a third review author (AA).

We attempted to contact authors of included studies to obtain important missing data as needed.

Dealing with duplicate and companion publications

In the event of duplicate publications, companion documents or multiple reports of a primary study, we obtained the maximum yield of information by mapping all publications to unique studies and collating all available data. The most complete data set aggregated across all known publications was used and in case of doubt, priority was given to the publication reporting the longest follow-up associated with our primary or secondary outcomes.

Assessment of risk of bias in included studies

We assessed the risk of bias in the included studies for the following domains, in accordance with the Cochrane 'Risk of bias' tool ([Higgins 2011](#); [Appendix 3](#)).

- Was there adequate sequence generation (selection bias)?
- Was allocation adequately concealed (selection bias)?
- Was knowledge of the allocated interventions adequately prevented during the study (detection bias)?
 - Participants and personnel
 - Outcome assessors
- Were incomplete outcome data adequately addressed (attrition bias)?
 - Are reports of the study free of suggestion of selective outcome reporting (reporting bias)?
 - Was the study apparently free of other problems that could put it at a risk of bias?

We judged risk of bias domains as 'low risk', 'high risk', or 'unclear risk' and evaluated individual bias items as described in the *Cochrane Handbook for Systematic Reviews of Interventions* ([Higgins 2011](#)). We presented a 'Risk of bias' summary figure to illustrate these findings.

For selection bias (random sequence generation and allocation concealment), we have evaluated risk of bias at the trial level.

We considered all outcomes as equally susceptible to performance bias (blinding of participants and personnel) and assessed them in one group.

For detection bias (blinding of outcome assessment), we grouped outcomes as being either susceptible to detection bias (subjective outcomes) or not susceptible to detection bias (objective outcomes).

We defined the following endpoints as subjective outcomes:

- stone-free rate;
- serious adverse events or complications of treatment;
- pain.

We defined the following endpoints as objective outcomes:

- secondary procedures for residual fragments;
- hospital stay.

We also assessed attrition bias (incomplete outcome data) on an outcome-specific basis, but created groups of outcomes based on similar reporting characteristics.

For reporting bias (selective reporting), we evaluated risk of bias at the trial level. In the absence of an available protocol, we rated the risk of selective reporting as unclear.

We further summarised the risk of bias across domains for each outcome in each included study, as well as across studies and domains for each outcome, in accordance with the approach for summary assessments of the risk of bias presented in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011).

Measures of treatment effect

We combined data from individual studies for meta-analysis where interventions were similar enough. We expressed dichotomous outcome results (SFR, adverse events and complications after treatment, number of second procedures for residual fragments measuring 4 mm or more as RRs with 95% confidence intervals (CIs). We used the MD where continuous scales of measurement are used to assess the effects of treatment (mean hospital stay, pain scale, pain medication).

Unit of analysis issues

The unit of analysis was the individual participant. In the event that we identified cross-over trials, cluster-randomised trials, or trials with more than two intervention groups for inclusion in the review, we handled these in accordance with guidance provided in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011).

Dealing with missing data

We sought to obtain missing data from study authors and performed intention-to-treat analyses if data were available; we otherwise performed available case analyses. We investigated attrition rates, e.g. dropouts, losses to follow-up and withdrawals, and critically appraised issues of missing data. We did not impute missing data.

Assessment of heterogeneity

Heterogeneity was analysed using a χ^2 test on $N-1$ degrees of freedom with an alpha of 0.05 used for statistical significance and with the I^2 test (Higgins 2003). I^2 values of 25%, 50% and 75% generally correspond to low, medium and high levels of heterogeneity. However, this was interpreted in the given clinical context and also assessed for clinical significance.

When we encountered heterogeneity, we attempted to determine possible reasons for it by examining individual study and subgroup characteristics. In the event of excessive heterogeneity unexplained by subgroup analyses, we planned not to report outcome results as the pooled effect estimate in a meta-analysis but to provide a narrative description of the results of each study.

Assessment of reporting biases

We attempted to obtain study protocols to assess for selective outcome reporting.

If we had included 10 studies or more investigating a particular outcome, we would have used funnel plots to assess small-study effects. Several explanations can be offered for the asymmetry of a funnel plot, including true heterogeneity of effect with respect to trial size, poor methodological design (and hence bias of small trials) and publication bias. For these reasons, should we be able to create a funnel plot in future versions of this review, we will interpret it carefully.

Data synthesis

We summarised data using a random-effects model. We interpreted random-effects meta-analyses with due consideration of the whole distribution of effects. We performed statistical analyses according to the statistical guidelines contained in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). For dichotomous outcomes, we used the Mantel-Haenszel method; for continuous outcomes, we used the inverse variance method. We used Review Manager 5 software (RevMan 2014) to perform all analyses.

Subgroup analysis and investigation of heterogeneity

We expected the following characteristics to introduce clinical heterogeneity, and we planned to carry out subgroup analyses with investigation of interactions.

- Size of the kidney stone (less than 10 mm versus 10 mm or more).
- Location of the stone (renal pelvis versus ureter).

These subgroup analyses are based on the following observations and European Association of Urology guidelines (uroweb.org/guideline/urolithiasis/).

- The selection of the procedure differs depending on the size of the stone (more than 20 mm: 1. PCNL, 2. retrograde renal

surgery or SWL; 10 mm to 20 mm: SWL or endourology; less than 10 mm: 1. SWL or retrograde renal surgery, 2. PCNL).

- The selection of the procedure differs depending on the location of the stone (renal pelvis: PCNL, retrograde renal surgery or SWL; proximal ureter: SWL, ante- or retrograde ureteroscopy; distal ureter: ureteroscopy or SWL).

Sensitivity analysis

We planned to perform sensitivity analyses in order to explore the influence of the following factors (when applicable) on effect sizes.

- Restricting the analysis by taking into account risk of bias, by excluding studies at 'high risk' or 'unclear risk'.

'Summary of findings' table

We presented the overall quality of the evidence for each outcome according to the GRADE approach, which takes into account five criteria not only related to internal validity (risk of bias, inconsistency, imprecision, publication bias), but also to external validity, such as directness of results (Guyatt 2008). For each comparison, two review authors (LB, JHJ) independently rated the quality of evidence (QoE) for each outcome as 'high', 'moderate', 'low', or 'very low' using [GRADEpro GDT](#). We resolved any discrepancies by consensus, or, if needed, by arbitration by a third review author (AA). For each comparison, we presented a summary of the evidence for the main outcomes in a 'Summary of findings' table,

which provides key information about the best estimate of the magnitude of the effect in relative terms and absolute differences for each relevant comparison of alternative management strategies; numbers of participants and studies addressing each important outcome; and the rating of the overall confidence in effect estimates for each outcome (Guyatt 2011b; Schünemann 2011).

RESULTS

Description of studies

For a detailed description of studies see [Table 1, Characteristics of included studies](#) and [Characteristics of excluded studies](#).

Results of the search

We identified a total of 700 references from all searches; after removing duplicates, we screened 617 titles. After screening titles we excluded a further 541 references; we then reviewed the abstracts of 76 references. This led to us excluding a further 55 references and retrieving full-text articles for 21 studies. After review of the full-text articles, we excluded seven studies. A total of 14 studies were included in the final review. The flow of studies identified to be included in the review is summarised in a flow chart ([Figure 1](#)).

Figure 1. Flow diagram.

Included studies

A detailed description of the characteristics of included studies is presented elsewhere (see [Characteristics of included studies](#)). The following is a succinct overview.

Source of data

The data presented in the review are obtained from published literature. We identified 14 trials as eligible for inclusion. Surgical and medical interventions are assessed in the various studies (see [Table 1](#)).

Comparisons

Seven of the trials compared surgical interventions ([Aghamir 2012](#); [Basiri 2010](#); [De Domenicis 2005](#); [Gamal 2017](#); [Kumar 2015](#); [Salem 2014](#); [Song 2015](#)). Six trials compared medical intervention ([Aldaquadossi 2015](#); [Aydogdu 2009](#); [Elgalaly 2017](#); [Erturhan 2013](#); [Fahmy 2017](#); [Mokhless 2012](#)) and one trial compared medical versus surgical intervention ([Elderwy 2014](#)) (see [Table 2](#)).

Overview of trial populations

The 14 studies included a total of 978 participants. Individual sample sizes ranged from 22 to 221 participants.

The seven trials of surgical interventions included a total of 535 participants ([Aghamir 2012](#); [Basiri 2010](#); [De Domenicis 2005](#); [Gamal 2017](#); [Kumar 2015](#); [Salem 2014](#); [Song 2015](#)). Two groups of 263 and 272 surgical patients were compared.

The six trials of medical interventions included a total of 347 participants ([Aldaquadossi 2015](#); [Aydogdu 2009](#); [Elgalaly 2017](#); [Erturhan 2013](#); [Fahmy 2017](#); [Mokhless 2012](#)). There was a total of 158 participants in the intervention arm and 189 in the control arm. Five participants did not complete one of the trials and were not included in their group analysis ([Erturhan 2013](#)).

The medical versus surgical group included 96 participants and 87 completed the study ([Elderwy 2014](#)). The medical intervention group had 48 participants and the surgical intervention group 39 participants.

Trial design

Thirteen studies were RCTs and one had a quasi-randomised design ([Elderwy 2014](#)). Trials were performed in the years ranging from July 2002 until 2017. The number of study centres in all studies ranged from a single centre to six. Two of the 14 trials were Multicentre ([Basiri 2010](#); [Erturhan 2013](#)), one surgical (which took place in seven centres) and one medical intervention study

(not detailed). Only one out of the four medical therapy trials included a placebo. All surgical-only trials included a two-arm study group with a surgical intervention as comparator. Duration of follow-up ranged from one week to one year.

Settings

Ten trials were conducted in the hospital setting ([Aghamir 2012](#); [Aldaquadossi 2015](#); [Basiri 2010](#); [De Domenicis 2005](#); [Elderwy 2014](#); [Elgalaly 2017](#); [Fahmy 2017](#); [Gamal 2017](#); [Salem 2014](#); [Song 2015](#)), one in the hospital outpatient setting ([Aydogdu 2009](#)), and three in a mixed hospital and outpatient setting ([Erturhan 2013](#); [Kumar 2015](#); [Mokhless 2012](#)).

Participants

The mean age of trial participants ranged from 20.3 months to 11.1 years (with an age range of 0.5 to 17 years). Ethnic groups were not described, however two studies were conducted in Turkey ([Aydogdu 2009](#); [Erturhan 2013](#)), seven studies in Egypt ([Aldaquadossi 2015](#); [Elderwy 2014](#); [Elgalaly 2017](#); [Fahmy 2017](#); [Gamal 2017](#); [Mokhless 2012](#); [Salem 2014](#)), two studies in Iran ([Aghamir 2012](#); [Basiri 2010](#)), one in India ([Kumar 2015](#)), one in China ([Song 2015](#)), and one in Italy ([De Domenicis 2005](#)). Major exclusion criteria were renal abnormalities and coagulopathy; individual exclusion criteria are detailed in the [Characteristics of included studies](#) table. Inclusion criteria related to stone size and age. In the surgical group, stone size range was 5 mm to 45 mm ([Aghamir 2012](#); [Basiri 2010](#); [De Domenicis 2005](#); [Gamal 2017](#); [Kumar 2015](#); [Salem 2014](#); [Song 2015](#)). In the medical therapy group, stone size ranged from 2 mm to 12 mm ([Aydogdu 2009](#); [Elgalaly 2017](#); [Erturhan 2013](#); [Fahmy 2017](#); [Mokhless 2012](#)), and less than 1 cm in [Aldaquadossi 2015](#). In the medical and surgical intervention group the median stone size was 12 mm (10 mm to 16 mm) ([Elderwy 2014](#)).

Diagnosis

Imaging (kidneys ureters bladder ultrasound, kidneys ureters bladder radiograph and/or CT scan) was the modality of choice for confirming the diagnosis and clearance of renal stones in all studies.

Interventions

In the surgical group, interventions were SWL, retrograde ureteroscopy, PCNL, mini-PCNL, tubeless PCNL, and tubeless mini-PCNL, mini-PCNL ([Aghamir 2012](#); [Basiri 2010](#); [De Domenicis 2005](#); [Gamal 2017](#); [Kumar 2015](#); [Salem 2014](#); [Song 2015](#)).

In the study comparing medical with surgical intervention, potassium sodium hydrogen citrate (at a dose of 1 mEq/kg per day) was administered orally for one to three months to the medical group whilst the surgical group were treated with the Lithotripter S (Dornier Medtech, Kennesaw, Georgia) under general anaesthesia (Elderwy 2014).

In the medical group the intervention was the use of an alpha blocker: doxazosin (0.03 mg/Kg) in two studies, tamsulosin (0.4 mg in those over four years of age and 0.2 mg in those under two years of age) in two studies, and silodosin (8 mg) (Aldaquadossi 2015; Aydogdu 2009; Elgalaly 2017; Erturhan 2013; Fahmy 2017; Mokhless 2012). Two of these studies included a placebo (Fahmy 2017; Mokhless 2012). One of these studies (Fahmy 2017) compared two interventions (tamsulosin and silodosin) and placebo.

Outcomes

The most commonly defined outcome in the publications was SFR. There were different definitions of SFR across the studies. Two studies considered SFR as fragments less than or equal to 4 mm (Aghamir 2012; Song 2015), and one as fragments less than 3 mm (Salem 2014). All other studies defined SFR as complete clearance of stones. All included studies were assessed for adverse events and the need for second procedures. Complications were reported in seven studies (Aghamir 2012; Basiri 2010; De Domenicis 2005; Elderwy 2014; Gamal 2017; Kumar 2015; Song 2015). The rate of secondary procedures was reported in eight studies (Aghamir 2012; Basiri 2010; De Domenicis 2005; Elderwy 2014; Gamal 2017; Kumar 2015; Salem 2014; Song 2015). Hospital stay was

included in five studies (Aghamir 2012; Basiri 2010; Gamal 2017; Kumar 2015; Song 2015). Pain requiring analgesia or being documented as 'pain episodes' was included in three studies (Aghamir 2012; Elgalaly 2017; Mokhless 2012).

While all studies reported SFRs, only seven studies reported serious adverse events or complications of treatments. This limits the application of the information at the point of care or in clinical practice guidelines.

Funding source and conflicts of interests

Three studies declared no conflict of interest (Aldaquadossi 2015; Elgalaly 2017; Mokhless 2012). No funding source was reported in five studies (Aldaquadossi 2015; Elgalaly 2017; Gamal 2017; Kumar 2015; Mokhless 2012).

Excluded studies

We excluded four of five trials after evaluation of the full publication. The main reasons for exclusion are detailed in the tables of [Characteristics of excluded studies](#).

Studies awaiting classification and ongoing trials

We did not identify any studies as awaiting classification, nor did we identify any ongoing trials.

Risk of bias in included studies

Assessments of risk of bias are summarised in [Figure 2](#) and [Figure 3](#). Judgement of individual domains are discussed below.

Figure 2. 'Risk of bias' graph: review authors' judgements about each 'Risk of bias' item presented as percentages across all included studies.

Figure 3. 'Risk of bias' summary: review authors' judgements about each 'Risk of bias' item for each included study.

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias): Subjective outcomes	Blinding of outcome assessment (detection bias): Objective outcomes	Incomplete outcome data (attrition bias): Stone free rate	Incomplete outcome data (attrition bias): Serious adverse events or complications of treatment	Incomplete outcome data (attrition bias): Secondary procedures	Incomplete outcome data (attrition bias): Hospital stay	Incomplete outcome data (attrition bias): Pain	Selective reporting (reporting bias)	Other bias
Aghamir 2012	?	?	+	?	+	+	+	+	+	+	+	?
Aldaquadosi 2015	?	?	+	?	+	+	+	?	?	+	?	+
Aydogdu 2009	?	?	?	?	+	+	?	+	?	?	+	+
Basiri 2010	+	?	?	?	+	+	+	+	+	?	+	+
De Domenicis 2005	+	+	?	?	+	+	+	+	+	?	+	+
Elderwy 2014	+	?	?	+	+	?	?	?	?	?	?	+
Elgalaly 2017	+	?	?	?	+	+	+	?	?	+	?	+
Erturhan 2013	+	?	+	+	+	+	?	?	?	+	+	+
Fahmy 2017	?	?	+	+	+	+	+	?	?	?	?	?
Gamal 2017	?	?	?	?	+	?	?	?	?	?	?	?
Kumar 2015	+	?	?	?	+	+	+	+	+	?	?	+
Mokhless 2012	?	?	?	?	+	+	+	+	+	?	?	+
Salem 2014	?	?	?	?	+	+	+	+	?	?	?	+
Song 2015	+	?	?	?	+	?	?	?	?	?	?	+

Allocation

Random sequence generation

Six of the 14 studies describe randomisation with adequate sequence generation (Basiri 2010; De Domenicis 2005; Elgalaly 2017; Erturhan 2013; Kumar 2015; Song 2015), leading to a low risk of bias. We judged one study, which employed quasi-randomisation by month of presentation, as having a high risk of bias (Elderwy 2014). The remaining studies did not provide information on sequence generation, leading to an unclear risk of bias.

Allocation concealment

We judged only one study, which used opaque, sealed and numbered envelopes, as having a low risk of bias (De Domenicis 2005). Other trials did not describe an adequate method of allocation concealment and we judged them as having unclear risk of bias in this domain.

Blinding

Blinding of participants and personnel

We rated one study as 'low risk of bias' and three studies as 'high risk of bias' (Aghamir 2012; Aldaquadossi 2015; Erturhan 2013). Other trials did not describe an adequate method for blinding participants and personnel and we judged them as having an unclear risk of bias.

Blinding of outcome assessment

- Blinding of subjective outcomes (SFR, serious adverse events or complications of treatment, pain): we judged two studies as having low risk of bias (Elderwy 2014; Fahmy 2017) and one study as having high risk of bias (Erturhan 2013). Other trials did not describe an adequate method and we judged them as having unclear risk of bias.
- Blinding of objective outcomes (secondary procedures for residual fragments, hospital stay): we rated all trials as 'low risk of bias' due to the objective nature of the outcomes.

Incomplete outcome data

- SFR: we rated nine studies as 'low risk of bias' (Aghamir 2012; Aldaquadossi 2015; Aydogdu 2009; Basiri 2010; De Domenicis 2005; Elgalaly 2017; Kumar 2015; Mokhless 2012; Salem 2014) and two studies as 'high risk of bias' (Erturhan 2013; Fahmy 2017). The remaining studies were rated as 'unclear risk of bias'.
- Serious adverse events or complications of treatment: we rated eight studies as 'low risk of bias' (Aghamir 2012; Aldaquadossi 2015; Basiri 2010; De Domenicis 2005; Elgalaly 2017; Kumar 2015; Mokhless 2012; Salem 2014) and one study as 'high risk of bias' (Fahmy 2017). The remaining studies were rated as 'unclear risk of bias'.
- Secondary procedures for residual fragments: we rated seven studies as 'low risk of bias' (Aghamir 2012; Aydogdu 2009; Basiri 2010; De Domenicis 2005; Kumar 2015; Mokhless 2012; Salem 2014). The remaining studies were rated as 'unclear risk of bias'.
- Hospital stay: we rated five studies as 'low risk of bias' (Aghamir 2012; Basiri 2010; De Domenicis 2005; Kumar 2015; Mokhless 2012). The remaining studies were rated as 'unclear risk of bias'.
- Pain: we rated three studies as 'low risk of bias' (Aghamir 2012; Aldaquadossi 2015; Elgalaly 2017) and one study as 'high risk of bias' (Erturhan 2013). The remaining were rated as 'unclear risk of bias'.

Selective reporting

We rated five studies as 'high risk of bias' due to inappropriate exclusion of participants with adverse events (Aghamir 2012; Erturhan 2013) and no prespecification of study outcomes with no available protocols (Aydogdu 2009; Basiri 2010; De Domenicis 2005). The others were rated as 'unclear risk of bias' due to there being no available protocols.

Other potential sources of bias

We considered the risk of reporting bias to be low in 10 studies (Aldaquadossi 2015; Aydogdu 2009; Basiri 2010; De Domenicis 2005; Elderwy 2014; Elgalaly 2017; Erturhan 2013; Kumar 2015; Mokhless 2012; Song 2015). We judged Salem 2014 to be at high risk of bias due to baseline imbalance. The other trials appeared to have an unclear risk of bias due to the possibility of difference in follow-up (Aghamir 2012) and insufficient information (abstract only: Fahmy 2017; Gamal 2017).

Effects of interventions

See: [Summary of findings for the main comparison](#) Shock wave lithotripsy versus dissolution therapy for renal stones; [Summary of findings 2](#) Slow shock wave lithotripsy versus rapid shock wave lithotripsy for renal stones; [Summary of findings 3](#) Shock wave lithotripsy versus ureteroscopy with holmium laser or pneumatic lithotripsy for renal and distal ureteric stones; [Summary of findings 4](#) Shock wave lithotripsy versus mini-percutaneous nephrolithotripsy for renal stones; [Summary of findings 5](#) Percutaneous nephrolithotripsy versus tubeless percutaneous nephrolithotripsy for renal stones; [Summary of findings 6](#) Percutaneous nephrolithotripsy versus tubeless mini-percutaneous nephrolithotripsy for renal stones; [Summary of findings 7](#) Alpha-blockers versus placebo with/without analgesics

1. Shock wave lithotripsy versus dissolution therapy for intrarenal stones

We found a single study with 87 participants (39 randomised to SWL and 48 to oral citrate) ([Elderwy 2014](#)). The follow-up period was three months. See [Summary of findings for the main comparison](#).

Primary outcomes

1.1 Stone-free rate

We are uncertain about the effects of SWL on SFR (RR 1.13, 95% CI 0.90 to 1.41; very low-quality evidence). We downgraded for study limitations and very serious imprecision.

1.2 Serious adverse events or complications of treatment

We are uncertain about the effects of SWL on serious adverse events (RR 1.23, 95% CI 0.08 to 19.05; very low-quality evidence). We downgraded for study limitations and very serious imprecision.

1.3 Secondary procedures for residual fragments

We are uncertain about the effects of SWL on secondary procedures for residual fragments (RR 0.66, 95% CI 0.29 to 1.50; very low-quality evidence). We downgraded for study limitations and very serious imprecision.

Secondary outcomes

1.4 Hospital stay

We did not find data related to hospital stay.

1.5 Pain

We did not find data related to pain.

Subgroup analysis and sensitivity analysis

We were unable to produce any preplanned secondary analyses due to the lack of suitable data.

2. Slow shock wave lithotripsy versus rapid shock wave lithotripsy for renal stones

We found a single study with 60 participants (30 randomised to slow SWL and 30 randomised to rapid SWL) ([Salem 2014](#)). The follow-up period was a minimum of one month. See [Summary of findings 2](#).

Primary outcomes

2.1 Stone-free rate

We are uncertain about the effects of slow SWL on SFR (RR 2.25, 95% CI 1.16 to 4.36; very low-quality evidence). We downgraded for study limitations and very serious imprecision.

2.2 Serious adverse events or complications of treatment

We could not estimate the risk of serious adverse events or complications of treatment due to there being no reported events.

2.3 Secondary procedures for residual fragments

We are uncertain about the effects of slow SWL on secondary procedures for residual fragments (RR 0.38, 95% CI 0.11 to 1.28; very low-quality evidence). We downgraded for study limitations and very serious imprecision.

Secondary outcomes

2.4 Hospital stay

We did not find data related to hospital stay.

2.5 Pain

We did not find data related to pain.

Subgroup analysis and sensitivity analysis

We were unable to conduct any preplanned secondary analyses due to the lack of suitable data.

3. Shock wave lithotripsy versus ureteroscopy with holmium laser or pneumatic lithotripsy for renal and distal ureteric stones

We found three studies with 153 participants (75 randomised to SWL and 78 randomised to ureteroscopy) (Basiri 2010; De Domenicis 2005; Gamal 2017). All studies were included in the analyses, except for the outcome 'hospital stay' which included data from Basiri 2010 and Gamal 2017. While two studies reported the follow-up period (two weeks to eight months) (Basiri 2010; De Domenicis 2005), one (Gamal 2017) did not report the period. See [Summary of findings 3](#).

Primary outcomes

3.1 Stone-free rate

We are uncertain about the effects of SWL on SFR (RR 0.62, 95% CI 0.43 to 0.88; very low-quality evidence). We downgraded for study limitations, indirectness, and imprecision.

3.2 Serious adverse events or complications of treatment

We are uncertain about the effects of SWL on severe adverse events (RR 0.56, 95% CI 0.12 to 2.58; very low-quality evidence). We downgraded for study limitations, indirectness, and imprecision.

3.3 Secondary procedures for residual fragments

We are uncertain about the effects of SWL on secondary procedures (RR 3.47, 95% CI 1.32 to 9.15; very low-quality evidence). We downgraded for study limitations, indirectness, and imprecision.

Secondary outcomes

3.4 Hospital stay (hours)

We are uncertain about the effects of SWL on hospital stay (MD -10.71, 95% CI -34.09 to 12.67; very low-quality evidence). We downgraded for study limitations, indirectness, and imprecision.

3.5 Pain

We did not find any data related to pain.

Subgroup analysis and sensitivity analysis

1. Size of the kidney stone (less than 10 mm versus 10 mm or more)

We were unable to conduct any preplanned secondary analyses due to the lack of suitable data.

2. Location of the stone (renal pelvis versus ureter)

- SFR: we found a RR of 0.50 (95% CI 0.25 to 0.98) in the participants with renal stones (Gamal 2017) versus a RR of 0.63 (95% CI 0.39 to 1.03) in the participants with distal ureteral stone (Basiri 2010; De Domenicis 2005). The test for interaction was not significant ($P = 0.57$, $I^2 = 0\%$).

- Serious adverse events or complications of treatment: we found a RR of 0.33 (95% CI 0.02 to 7.39) in the participants with renal stones (Gamal 2017) versus a RR of 0.67 (95% CI 0.12 to 3.82) in the participants with distal ureteral stones (Basiri 2010; De Domenicis 2005). The test for interaction was not significant ($P = 0.70$, $I^2 = 0\%$).

- Secondary procedures for residual fragments: we found a RR of 6.00 (95% CI 0.86 to 41.96) in the participants with renal stones (Gamal 2017) versus a RR of 3.46 (95% CI 0.82 to 14.58) in the participants with distal ureteral stones (Basiri 2010; De Domenicis 2005). The test for interaction was not significant ($P = 0.66$, $I^2 = 0\%$).

- Hospital stay (hours): we found an MD of 0.00 (95% CI -1.07 to 1.07) in the participants with renal stones (Gamal 2017) versus an MD of -24.00 (95% CI -39.45 to -8.55) in the participants with distal ureteral stones (Basiri 2010). The test for interaction was significant ($P = 0.002$, $I^2 = 89.2\%$).

4. Shock wave lithotripsy versus mini-percutaneous nephrolithotripsy for renal stones

We found a single study with 221 participants (110 randomised to SWL and 111 randomised to mini-PCNL) (Kumar 2015). The follow-up period was three months. See [Summary of findings 4](#).

Primary outcomes

4.1 Stone-free rate

SWL likely has lower SFR (RR 0.88, 95% CI 0.80 to 0.97), but this may not represent a clinically important difference and is based on moderate-quality evidence. SWL would result in 113 fewer stone-free patients per 1000 (189 fewer to 28 fewer). We downgraded for study limitations.

4.2 Serious adverse events or complications of treatment

SWL may reduce severe adverse events (RR 0.13, 95% CI 0.02 to 0.98; low-quality evidence). This corresponds to 66 fewer serious adverse events or complications per 1000 (74 fewer to 2 fewer). We downgraded for study limitations and imprecision.

4.3 Secondary procedures for residual fragments

SWL may increase the need of secondary procedures (RR 2.50, 95% CI 1.01 to 6.20; low-quality evidence). SWL would result in 85 more secondary procedures per 1000 (1 more to 294 more). We downgraded for study limitations and imprecision.

Secondary outcomes

4.4 Hospital stay (days)

SWL likely reduces hospital stay (MD -3.40, 95% CI -5.43 to -1.37; moderate-quality evidence). We downgraded for study limitations.

4.5 Pain

We did not find any data related to pain.

Subgroup analysis and sensitivity analysis

We were unable to conduct any preplanned secondary analyses due to the lack of suitable data.

5. Percutaneous nephrolithotripsy versus tubeless percutaneous nephrolithotripsy for renal stones

We found a single study with 23 participants (10 randomised to PCNL and 13 randomised to tubeless PCNL) (Aghamir 2012). The follow-up period was one month. See [Summary of findings 5](#).

Primary outcomes

5.1 Stone-free rate

We are uncertain about the effect of PCNL in SFR (RR 1.16, 95% CI 0.88 to 1.53; very low-quality evidence). We downgraded for study limitations and very serious imprecision.

5.2 Serious adverse events or complications of treatment

We are uncertain about the effect of PCNL on serious adverse events (RR 0.42, 95% CI 0.02 to 9.43; very low quality evidence). We downgraded for study limitations and very serious imprecision.

5.3 Secondary procedures for residual fragments

We are uncertain about the effect of PCNL on secondary procedures (RR 0.42, 95% CI 0.02 to 9.43; very low-quality evidence). We downgraded for study limitations and very serious imprecision.

Secondary outcomes

5.4 Hospital stay (hours)

PCNL may increase hospital stay (MD 19.16, 95% CI 10.24 to 28.08; low-quality evidence). We downgraded for study limitations and serious imprecision.

5.5 Pain (dose of morphine: mg/kg)

PCNL likely requires larger doses of morphine (MD 0.08, 95% CI 0.05 to 0.11; moderate-quality evidence). We downgraded for study limitations.

Subgroup analysis and sensitivity analysis

We were unable to conduct any preplanned secondary analyses due to the lack of suitable data.

6. Percutaneous nephrolithotripsy versus tubeless mini-percutaneous nephrolithotripsy for renal stones

We found a single study with 78 participants (38 randomised to PCNL and 40 randomised to tubeless mini-PCNL) (Song 2015). The follow-up period was 12 months. See [Summary of findings 6](#).

Primary outcomes

6.1 Stone-free rate

PCNL likely results in no difference in SFR (RR 1.03, 95% CI 0.93 to 1.14; moderate-quality evidence). PCNL would result in 28 more stone-free patients per 1,000 (66 fewer to 132 more). We downgraded for study limitations.

6.2 Serious adverse events or complications of treatment

We did not find any data related to serious adverse events.

6.3 Secondary procedures for residual fragments

We were unable to estimate the risk of secondary procedures due to there being no reported events.

Secondary outcomes

6.4 Hospital stay (days)

PCNL likely increases hospital stay (MD 3.14, 95% CI 2.78 to 3.50; moderate-quality evidence). We downgraded for study limitations.

6.5 Pain

We did not find any data related to pain.

Subgroup analysis and sensitivity analysis

We were unable to conduct any preplanned secondary analyses due to the lack of suitable data.

7. Alpha-blockers versus placebo with/without analgesics for distal ureteric stones

We found six studies with a different number of participants in each analysis ([Aldaquadossi 2015](#); [Aydogdu 2009](#); [Elgalaly 2017](#); [Erturhan 2013](#); [Fahmy 2017](#); [Mokhless 2012](#)). The follow-up period ranged from three to four weeks. See [Summary of findings 7](#).

Primary outcomes

7.1 Stone-free rate

We included six studies with 335 participants (alpha-blocker 185, placebo with/without analgesics 150) in the analysis for SFR ([Aldaquadossi 2015](#); [Aydogdu 2009](#); [Elgalaly 2017](#); [Erturhan 2013](#); [Fahmy 2017](#); [Mokhless 2012](#)). Alpha-blockers may increase SFR (RR 1.34, 95% CI 1.16 to 1.54; low-quality evidence). This

corresponds to 199 more stone-free patients per 1,000 (94 more to 317 more). We downgraded for study limitations and imprecision.

7.2 Serious adverse events or complications of treatment

There were no serious adverse events or complications in either group.

7.3 Secondary procedures for residual fragments

We included one study with 39 participants (alpha-blocker 19, placebo with/without analgesics 20) ([Aydogdu 2009](#)). We are uncertain about the effect of alpha-blockers on secondary procedures (RR 0.53, 95% CI 0.15 to 1.81; very low-quality evidence). We downgraded for study limitations and very serious imprecision.

Secondary outcomes

7.4 Hospital stay

We did not find any data related to hospital stay.

7.5 Pain

We included two studies with 98 participants (alpha-blocker 51, placebo with/without analgesics 47) ([Elgalaly 2017](#); [Mokhless 2012](#)). We are uncertain about the effect of alpha-blockers on pain episodes (MD -1.49, 95% CI -3.04 to 0.06; very low-quality evidence). We downgraded for study limitations and very serious imprecision.

Subgroup analysis and sensitivity analysis

We were unable to conduct any preplanned secondary analyses due to the lack of suitable data.

ADDITIONAL SUMMARY OF FINDINGS *[Explanation]*

Participants: children with solitary radiopaque renal stone Intervention: SWL (Dornier Lithotripter S; total count of 2,500 per session at 14 to 24 kV power) at 80 shock waves per minute Control: SWL (Dornier Lithotripter S; total count of 2,500 per session at 14 to 24 kV power) at 120 shock waves per minute					
Outcomes	No. of participants (studies)	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)	
				Risk with rapid SWL for renal stones	Risk difference with slow SWL
Stone-free rate Follow-up: mean 1 month	60 (1 RCT)	⊕○○○ VERY LOW ¹²	RR 2.25 (1.16 to 4.36)	Study population	
				267 per 1,000	333 more per 1,000 (43 more to 896 more)
Serious adverse events or complications of treatment Follow-up: mean 1 month	60 (1 RCT)	⊕○○○ VERY LOW ¹³	not estimable	Study population	
				-	-
Secondary procedures Follow-up: not reported (minimum 1 month)	60 (1 RCT)	⊕○○○ VERY LOW ¹²	RR 0.38 (0.11 to 1.28)	Study population	
				267 per 1,000	165 fewer per 1,000 (237 fewer to 75 more)
Hospital stay - not reported	-	-	-	-	-

* **The risk in the intervention group** (and its 95% CI) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval; **RCT:** randomised controlled trial; **RR:** risk ratio; **SWL:** shock wave lithotripsy.

GRADE Working Group grades of evidence

High certainty: We are very confident that the true effect lies close to that of the estimate of the effect

Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different

Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect

Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

- ¹ Downgraded by one level for study limitations: unclear risk of bias in half or more domains.
- ² Downgraded by two levels for imprecision: confidence interval is very wide and crosses clinical meaningful threshold.
- ³ Downgraded by two levels for imprecision: very rare event in either group.

Participants: children with renal or distal ureteric stones Intervention: SWL (Compact Delta II with 1,250 to 2,400 (mean 1,530) shockwave and power ranged from 11 to 13 kV, EDAP-Sonolith 4000 with 2500 shock waves (1900-3500) and 450 KJ (330-694)) Control: lithotripsy with holmium laser and/or pneumatic lithotripter					
Outcomes	No. of participants (studies)	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)	
				Risk with Ureteroscopy with Holmium laser or Pneumatic lithotripsy for distal ureteric stones	Risk difference with SWL
Stone-free rate Follow-up: range 2 weeks to 8 months	153 (3 RCTs)	⊕○○○ VERY LOW ¹²³	RR 0.62 (0.43 to 0.88)	Study population	
				859 per 1,000	326 fewer per 1,000 (490 fewer to 103 fewer)
Serious adverse events or complications of treatment Follow-up: range 2 weeks to 8 months	153 (3 RCTs)	⊕○○○ VERY LOW ¹²³	RR 0.56 (0.12 to 2.58)	Study population	
				51 per 1,000	23 fewer per 1,000 (45 fewer to 81 more)
Second procedures Follow-up: range 2 weeks to 8 months	131 (3 RCTs)	⊕○○○ VERY LOW ¹²³	RR 3.47 (1.32 to 9.15)	Study population	
				149 per 1,000	369 more per 1,000 (48 more to 1,216 more)
Hospital stay assessed with: hours Follow-up: range 2 weeks to 3 months ⁵	122 (2 RCT)	⊕○○○ VERY LOW ¹²⁴	-	The mean hospital stay ranged from 4 to 36 hours	MD 10.71 hours lower (34.09 lower to 12.67 higher)
*The risk in the intervention group (and its 95% CI) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).					
CI: confidence interval; MD: mean difference; RCT: randomised controlled trial; RR: risk ratio; SWL: shock wave lithotripsy.					

GRADE Working Group grades of evidence

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Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different

Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect

Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

- ¹ Downgraded by one level for study limitations: unclear of high risk of bias in half or more domains among the included studies.
- ² Downgraded by one level for indirectness: discrepancies in inclusion criterion ([Gamal 2017](#) included only participants with a solitary kidney) and baseline stone size among included studies. In addition, stones were in different locations (renal and distal ureter) among included studies.
- ³ Downgraded by two levels for imprecision: confidence interval is very wide and crosses clinically meaningful threshold.
- ⁴ Downgraded by one level for imprecision: confidence interval crosses clinically meaningful threshold.
- ⁵ [Gamal 2017](#) did not report the follow-up period.

Participants: age < 15 years and single radio-opaque lower calyceal calculus 1-2cm Intervention: SWL as an outpatient procedure (Dornier Alpha Compact system; maximum 2,500 per session and a frequency of 90 per minute) Control: mini-PCNL under general anaesthesia					
Outcomes	No. of participants (studies)	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)	
				Risk with Mini-PCNL for re- nal stones	Risk difference with SWL
Stone-free rate Follow-up: mean 3 months	212 (1 RCT)	⊕⊕⊕○ MODERATE ¹	RR 0.88 (0.80 to 0.97)	Study population	
				943 per 1,000	113 fewer per 1,000 (189 fewer to 28 fewer)
Serious adverse events or complications of treatment Follow-up: mean 3 months	212 (1 RCT)	⊕⊕○○ LOW ¹²	RR 0.13 (0.02 to 0.98)	Study population	
				75 per 1,000	66 fewer per 1,000 (74 fewer to 2 fewer)
Secondary procedures Follow-up: mean 3 months	212 (1 RCT)	⊕⊕○○ LOW ¹²	RR 2.50 (1.01 to 6.20)	Study population	
				57 per 1,000	85 more per 1,000 (1 more to 294 more)
Hospital stay assessed with: days Follow-up: mean 3 months	212 (1 RCT)	⊕⊕⊕○ MODERATE ¹	-	The mean hospital stay was 3.7 days	MD 3.4 days lower (5.43 lower to 1.37 lower)

* **The risk in the intervention group** (and its 95% CI) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval; **MD:** mean difference; **PCNL:** percutaneous nephrolithotomy; **RCT:** randomised controlled trial; **RR:** risk ratio; **SWL:** shock wave lithotripsy.

GRADE Working Group grades of evidence

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Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different

Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

¹ Downgraded by one level for study limitations: unclear of high risk of bias in half or more domains.

² Downgraded by one level for imprecision: confidence interval crosses clinically meaningful threshold.

Participants: age < 14 years, presence of renal stone larger than 2.5 cm or renal stone with lesser diameter, and extracorporeal shockwave lithotripsy failure Intervention: PCNL under general anaesthesia Control: tubeless PCNL under general anaesthesia					
Outcomes	No. of participants (studies)	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)	
				Risk with Tubeless PCNL for renal stones	Risk difference with PCNL
Stone-free rate Follow-up: mean 1 months	23 (1 RCT)	⊕○○○ VERY LOW ¹²	RR 1.16 (0.88 to 1.53)	Study population	
				846 per 1,000	135 more per 1,000 (102 fewer to 448 more)
Serious adverse events or complications of treatments Follow-up: mean 1 months	23 (1 RCT)	⊕○○○ VERY LOW ¹²	RR 0.42 (0.02 to 9.43)	Study population	
				77 per 1,000	45 fewer per 1,000 (75 fewer to 648 more)
Secondary procedures Follow-up: mean 1 months	23 (1 RCT)	⊕○○○ VERY LOW ¹²	RR 0.42 (0.02 to 9.43)	Study population	
				77 per 1,000	45 fewer per 1,000 (75 fewer to 648 more)
Hospital stay assessed with: hours Follow-up: mean 1 months	23 (1 RCT)	⊕⊕○○ LOW ¹³	-	The mean hospital stay was 39.5 hours	MD 19.2 hours more (10.2 more to 28.08 more)
*The risk in the intervention group (and its 95% CI) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI). CI: confidence interval; MD: mean difference; PCNL: percutaneous nephrolithotomy; RCT: randomised controlled trial; RR: risk ratio.					

GRADE Working Group grades of evidence

High certainty: We are very confident that the true effect lies close to that of the estimate of the effect

Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different

Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect

Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

¹ Downgraded by one level for study limitations: unclear or high risk of bias in half or more domains.

² Downgraded by two levels for imprecision: confidence interval is very wide and crosses clinically meaningful threshold.

³ Downgraded by one level for imprecision: confidence interval crosses clinically meaningful threshold.

Participants: preschool children under 3 years with renal calculi Intervention: PCNL under general anaesthesia Control: mini-PCNL under general anaesthesia					
Outcomes	No. of participants (studies)	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)	
				Risk with Mini-PCNL for re-nal stones	Risk difference with PCNL
Stone-free rate Follow-up: mean 12 months	70 (1 RCT)	⊕⊕⊕○ MODERATE ¹	RR 1.03 (0.93 to 1.14)	Study population 943 per 1,000	28 more per 1,000 (66 fewer to 132 more)
Serious adverse events or complications of treatment - not reported	-	-	-	-	-
Secondary procedures Follow-up: mean 12 months	70 (1 RCT)	⊕○○○ VERY LOW ¹²	not estimable	Study population -	-
Hospital stay assessed with: days Follow-up: mean 12 months	70 (1 RCT)	⊕⊕⊕○ MODERATE ¹	-	The mean hospital stay was 4.6 days	MD 3.14 days more (2.78 more to 3.5 more)

* **The risk in the intervention group** (and its 95% CI) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval; **MD:** mean difference; **PCNL:** percutaneous nephrolithotomy; **RCT:** randomised controlled trial; **RR:** risk ratio.

GRADE Working Group grades of evidence

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Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect

Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

-
- ¹ Downgraded by one level for study limitations: unclear risk of bias in almost all domains.
- ² Downgraded by two levels for imprecision: very rare event in either group.

Participants: children with radiopaque lower ureteral stones Intervention: alpha blockers (doxazosin, tamsulosin, or silodosin) Control: placebo with/without analgesics					
Outcomes	No. of participants (studies)	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)	
				Risk with placebo with/without analgesics	Risk difference with alpha-blockers
Stone-free rate Follow-up: range 3 weeks to 4 weeks	335 (6 RCTs)	⊕⊕○○ LOW ¹²	RR 1.34 (1.16 to 1.54)	Study population 587 per 1,000	199 more per 1,000 (94 more to 317 more)
Serious adverse events or complications of treatment Follow-up: mean 4 weeks	63 (1 RCT)	⊕○○○ VERY LOW ¹³	not estimable	Study population -	-
Secondary procedures for residual fragments Follow-up: mean 3 weeks	39 (1 RCT)	⊕○○○ VERY LOW ¹⁴	RR 0.53 (0.15 to 1.81)	Study population 300 per 1,000	141 fewer per 1,000 (255 fewer to 243 more)
Hospital stay - not reported	-	-	-	-	-

*The risk in the intervention group (and its 95% CI) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval; RCT: randomised controlled trial; RR: risk ratio.

GRADE Working Group grades of evidence

High certainty: We are very confident that the true effect lies close to that of the estimate of the effect

Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different

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- ¹ Downgraded by one level for study limitations: unclear or high risk of bias in one or more domains.
- ² Downgraded by one levels for imprecision: confidence interval is crosses clinically meaningful threshold.
- ³ Downgraded by two levels for imprecision: very rare event in either group.
- ⁴ Downgraded by two levels for imprecision: confidence interval is very wide and crosses clinically meaningful threshold.

DISCUSSION

Summary of main results

We included 14 studies with a total of 978 participants in our review. The studies compared surgical and medical interventions for the treatment of upper tract stone disease in children; the data from these studies informed eight separate comparisons. The mean age of trial participants ranged from 20.3 months to 11.1 years (with an age range of 0.5 to 17 years). In the surgical group the stone size range was 5 mm to 45 mm. In the medical therapy group, stone size ranged from 2 mm to 12 mm, and in the medical and surgical intervention group the median stone size was 12 mm (10 mm to 16 mm).

Shock wave lithotripsy versus dissolution therapy for intrarenal stones

We are uncertain about the effects of SWL on SFR, serious adverse events or complications of treatment, and secondary procedures for residual fragments.

Slow shock wave lithotripsy versus rapid shock wave lithotripsy for renal stones

We are uncertain about the effects of slow SWL on SFR, serious adverse events or complications of treatment, and about the effects of slow SWL on secondary procedures for residual fragments.

Shock wave lithotripsy versus ureteroscopy with holmium laser or pneumatic lithotripsy for renal and distal ureteric stones

We are uncertain about the effects of SWL on SFR, serious adverse events or complications of treatment, and secondary procedures for residual fragments.

Shock wave lithotripsy versus mini-percutaneous nephrolithotripsy for renal stones

SWL likely has a lower SFR. SWL appears to reduce serious adverse events but may require more secondary procedures.

Percutaneous nephrolithotripsy versus tubeless percutaneous nephrolithotripsy for renal stones

We are uncertain about the effects of PCNL on SFR, serious adverse events, and secondary procedures.

Percutaneous nephrolithotripsy versus tubeless mini-percutaneous nephrolithotripsy for renal stones

PCNL likely has similar effects on SFR. We did not find any data relating to serious adverse events. We are uncertain about secondary procedures.

Alpha-blockers versus placebo with/without analgesics for distal ureteric stones

Alpha-blockers may increase SFR. We are uncertain about serious adverse events or complications and secondary procedures.

Overall completeness and applicability of evidence

Studies included in this review examined an important and clinically relevant topic on the treatment of upper tract urinary stones in children. The population examined is very important as there is a lack of available research evidence compared to that available for the adult population.

- Although all interventions assessed in this review are used to treat stone disease, the patient populations they apply to vary greatly by stone size and age. This limits any assessments across randomised comparisons.

- The definition of the SFR varied across the studies. In some studies the SFR was accepted if the fragments post-treatment were less than or equal to 4 mm, whereas other studies classified SFR as no remaining fragments in the renal tract.

- The length of follow-up varied between the studies and was generally limited to short-term follow-up of three months or less. There is a need for long-term follow-up data.

- Regarding the predefined primary and secondary outcomes in this review, half of the studies reported on all primary outcomes (SFR, complications and rate of secondary procedures). Only three studies reported pain as an outcome and five studies reported on hospital stay.

- We were unable to conduct any of the predefined subgroup analyses except one comparison of SWL versus ureteroscopy. Questions around differential effectiveness and safety of these interventions therefore remain unanswered.

- A majority of the studies are recent. This is potentially due to the increasing incidence of the nephrolithiasis in children 18 years old and younger ([Sas 2010](#)) and increased recognition of the importance of trials in paediatric urology.

- The majority of comparisons assessed in this review relate to surgical innovation. In particular with regards to ureterorenoscopes and nephroscopes, there have been recent advancements in terms of miniaturisation, increased functionality (improved scope flexibility) and visualization (introduction of digital scopes; [Borofsky 2013](#)). These recent advances are not captured in this review, given the paucity of trials and limiting applicability.

- Factors which could have significant impact on the treatment outcomes - such as contributing metabolic abnormalities, stone composition and preoperative renal function - have not been considered in most of the studies. This could have an impact on the choice of treatment modality and treatment outcomes.

- The applicability of the findings to high-income countries needs consideration as the majority of the included studies were conducted in middle- and low-income countries with possible variation in risk factors for stone formation, availability of certain interventions and access to paediatric care.

- The focus of this systematic review was direct evidence from randomised trials in paediatric patient populations. Given that the QoE was very low, it is possible that indirect evidence from adult populations or observational studies may have yielded

higher quality evidence for at least some comparisons.

Quality of the evidence

We rated the QoE as very low for the majority of comparisons and outcomes. This means that our confidence in the effect estimate is very limited and that the true effect may be substantially different from the estimate of the effect or is likely to be substantially different from the estimate of effect. We found moderate-quality evidence for only three comparisons but not for all three of our primary outcomes. Therefore in each case, clinicians and guidelines developers would base their decision-making on lower quality evidence.

Consistent issues for downgrading our assessments of the quality of the evidence were: study limitations attributable to selection bias (unclear allocation concealment), performance bias (lack of blinding of patients and personnel) and detection bias (lack of blinding of outcome assessors). We also frequently downgraded our quality assessments by two levels for imprecision. There were few studies, with small samples sizes and low events rates resulting in wide CIs that crossed assumed thresholds of clinically important differences.

Potential biases in the review process

In this review we followed the rigorous methods outlined in the *Cochrane Handbook for Systematic Reviews of Interventions* to minimise biases (Higgins 2011) which includes publication of an a priori protocol. Potential residual biases are nevertheless possible and may relate to the following.

- Publication bias: although we attempted to conduct a comprehensive search irrespective of language and publication status, it is possible that we missed non-English studies in non-indexed journals.
- Selective reporting bias and missing data: the reporting quality of most included studies was poor, prompting us to contact the authors for further information. Due to the time-intensive nature of this effort, we limited this to one attempt only. Increased efforts may have yielded a better response rate.

Agreements and disagreements with other studies or reviews

To date, no Cochrane review has been published on this topic. In addition, we have not identified any non-Cochrane review that used similar rigorous methodology including a published protocol. One systematic review (Braga 2011) has previously described the limitations and challenges of systematic reviews in paediatric urology. We identified one study on medical expulsive therapy that used GRADE to assess methodological quality (Glina 2015; see below).

We identified two systematic reviews (Ishii 2014; Ishii 2015) assessing ureteroscopy and three systematic reviews assessing medical expulsive therapy (Glina 2015; Tian 2017; Velazquez 2015). Glina 2015 analysed alpha-1 adrenergic blockers as medical expulsive treatment in children with distal ureterolithiasis. They included three RCTs in the meta-analysis, looking at expulsion rates and pain episodes. They concluded that use of an alpha-1 adrenergic blocker is related to a greater incidence of expulsion of ureteral calculi and fewer episodes of pain when compared to ibuprofen. Ishii 2015 analysed 14 studies and included non-RCTs in the meta-analysis. They looked at ureteroscopic failure rates and complications. They concluded that the use of ureteroscopy as the first-line surgical management is a safe and highly effective intervention, with a small proportion of the study population having minor complications.

Ishii 2014 identified and analysed six studies looking at SFR and complication rates in flexible ureteroscopy and laser lithotripsy. All these studies were retrospective studies. They have concluded that flexible ureteroscopy and laser lithotripsy is an effective and safe procedure in high-volume centres.

Tian 2017 analysed effects of alpha-blockers (tamsulosin and doxazosin) on stone expulsion rate, stone expulsion time, and treatment-emergent adverse events. Four RCTs and one cohort study were included in the meta-analysis. The results of the review regarding the stone expulsion rate suggested that adrenergic alpha-antagonists significantly improved the stone expulsion rate compared to the placebo. There was no significant difference between the adrenergic alpha-antagonists and the placebo groups in terms of adverse events.

Velazquez 2015 analysed effects of alpha-blockers on stone expulsion rate and adverse events. They identified and included in the meta-analysis three RCTs and two retrospective cohort studies. The conclusion from the meta-analysis is that medical expulsion therapy results in increased ureteral stone passage and a low rate of adverse events.

Saad 2015 compared PCNL to ureterorenoscopy in 38 randomised patients. While they reported no difference in SFR, serious adverse events or complications of treatment and secondary procedures, they reported 43 renal units instead of randomised participants which causes unit of analysis error.

AUTHORS' CONCLUSIONS

Implications for practice

Based on the findings of this review, there is considerable uncertainty with regards to the effectiveness and adverse events associated with the various types of interventions used to treat paediatric upper renal tract stone disease. It is important for patients, clinicians, guideline developers and policy-makers to be aware of these limitations. Well-informed, shared decision-making is important

to achieve the right balance of SFRs and treatment related morbidity to match individual patients' personal circumstances, values and preferences. An important consideration is the surgeon's training and skills as well as the availability of various technologies in different geographical locations and healthcare systems.

Implications for research

Given the predominantly low- and very-low quality of the evidence we encountered to inform interventions for treating urinary stones in children, there is a critical need for higher quality trials which include adequate sample sizes, report findings transparently, and avoid study limitations. Additional things to consider are the explicit reporting of participants' baseline characteristics and the standardised reporting of patient-important outcomes. Prior studies have described the paucity of RCTs in paediatric urology and their poor quality of reporting (Welk 2006). These issues mirror the reporting of stone disease-related trials in the adult population (Zavitsanos 2014).

The challenges of trials related to surgical innovation have been well described (McCulloch 2009; McCulloch 2011). These include a reluctance to accept random allocation, challenges in blinding, and issues related to continued evolution of the intervention of interest and the surgical learning curves. Nevertheless, they are critically important to inform clinical decision-making. The

IDEAL Collaboration has provided recommendations for surgical innovation (McCulloch 2011) that have found recent adaptation to surgical devices (Sedraky 2016).

Short of surgical trials which are highly desirable, prospectively designed cohort studies that use statistical methods to adjust for baseline confounding and use standardised methods for outcome collection and assessment may also provide higher quality evidence in cases in which the QoE is only low or very low (Schunemann 2013). Although a search for such studies was outside of the scope of this review, we doubt whether they currently exist.

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies [ordered by study ID]

Aghamir 2012

Methods	<p>Study design: parallel-group randomised controlled trial.</p> <p>Setting: single centre/Iran.</p> <p>Dates when study was conducted: March 2010 to June 2011.</p>
Participants	<p>Inclusion criteria: age < 14, renal stone > 2.5 cm or renal stone with lesser diameter, and SWL failure</p> <p>Exclusion criteria: kidney anomalies, renal failure on admission, serious bleeding or perforation in the collecting system during the operation</p> <p>Diagnostic criteria: US or KUB and confirmed with IVU (spiral CT if sensitive to the dye - 5 patients)</p> <p>Total number of participants randomly assigned: 23.</p> <p>Group A (Standard PCNL)</p> <ul style="list-style-type: none"> • Number of participants randomly assigned: 10. • Age (mean): 11.10 ± 1.72. • Gender (M/F): 6/4. <p>Group B (Tubeless PCNL)</p> <ul style="list-style-type: none"> • Number of participants randomly assigned: 13. • Age (mean): 10.31 ± 2.68. • Gender (M/F): 10/3.
Interventions	<p>Group A (n = 10): standard PCNL - ureteral stent remained and a nephrostomy tube placed through the working sheath for 24-48 hours</p> <p>Group B (n = 10): tubeless PCNL - ureteral stent and sheath removed at end of procedure without placing a nephrostomy tube</p> <p>Co-interventions: standard bladder catheter.</p>
Outcomes	<p>Stone clearance</p> <ul style="list-style-type: none"> • How measured: considered as successful PCNL if there was no stone fragment remaining larger than 4 mm at sonography. • Time points measured: at 24-48 hours, at one week and one month after surgery. • Time points reported: not reported. • Subgroup: none. <p>Complications</p> <ul style="list-style-type: none"> • How measured: postoperative evaluations included physical examination, lab tests (hemoglobin concentration and renal function tests), and imaging (abdominal and pelvic ultrasound and plain abdominal X-ray). • Time points measured: at 24-48 hours after surgery. • Time points reported: not reported. • Subgroup: none
Notes	<p>Funding Sources: not stated.</p> <p>Declaration of interests: not stated.</p>
<i>Risk of bias</i>	

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomisation by envelopes. Randomisation sequence generation not clearly described
Allocation concealment (selection bias)	Unclear risk	Quote from publication: "At the end of procedure, the randomised envelope was opened by circulating nurse and the patients were assigned to tubeless or control group" Unclear whether envelopes were sequentially numbered, opaque and sealed
Blinding of participants and personnel (performance bias) All outcomes	High risk	No knowledge of which procedure prior to intervention as envelope opened 'at the end of the procedure'. However, blinding might be broken due to presence of nephrostomy tube and different follow-up schedule (additional visit for nephrostomy and ureteral stent removal)
Blinding of outcome assessment (detection bias) Subjective outcomes	Unclear risk	Not described.
Blinding of outcome assessment (detection bias) Objective outcomes	Low risk	Objective outcomes are not likely to be influenced by lack of blinding
Incomplete outcome data (attrition bias) Stone free rate	Low risk	All randomised participants were included in the analysis.
Incomplete outcome data (attrition bias) Serious adverse events or complications of treatment	Low risk	All randomised participants were included in the analysis.
Incomplete outcome data (attrition bias) Secondary procedures	Low risk	All randomised participants were included in the analysis.
Incomplete outcome data (attrition bias) Hospital stay	Low risk	All randomised participants were included in the analysis.
Incomplete outcome data (attrition bias) Pain	Low risk	All randomised participants were included in the analysis.
Selective reporting (reporting bias)	High risk	Quote from publication: "Two unsuccessful cases with perforation and bleeding were

		excluded from the study” No published protocol available. Only stone-free rate was prespecified, but all of the outcomes described in the result of article
Other bias	Unclear risk	Additional visit for nephrostomy and ureteral stent removal might be necessary, but no information was given

Aldaquadossi 2015

Methods	Study design: parallel-group randomised controlled trial. Setting: single centre/Egypt. Dates when study was conducted: February 2010 to July 2013.
Participants	Inclusion criteria: distal ureteric stone of < 1 cm. Exclusion criteria: bilateral ureteric stones, multiple stones, marked hydronephrosis, urinary tract infection, urinary tract anomalies, voiding dysfunction, previous open or endoscopic ureteric surgery Diagnostic criteria: plain abdominal film, urinary tract US, and unenhanced CT of the abdomen and pelvis Total number of participants randomly assigned: 67. Group A (Tamsulosin) <ul style="list-style-type: none"> Number of participants randomly assigned: 33. Age (mean): 7.7. Gender (M/F): 17/14. Group B (Ibuprofen only) <ul style="list-style-type: none"> Number of participants randomly assigned: 34. Age (mean): 7.25. Gender (M/F): 19/13.
Interventions	Group A (n = 33): tamsulosin 0.4 mg for patients aged > 5 years and 0.2 mg for younger children and Ibuprofen 4-10 mg/kg orally every 6-8 h as needed Group B (n = 34): ibuprofen 4-10 mg/kg orally every 6-8 h as needed. Co-interventions: Ketorolac 0.5-1 mg/kg intramuscularly.
Outcomes	Stone clearance <ul style="list-style-type: none"> How measured: spontaneous stone expulsion rate confirmed by plain film and USS. Time points measured: weekly for 4 weeks. Time points reported: not reported. Subgroup: none. Analgesic requirement <ul style="list-style-type: none"> How measured: patient-reported painful episodes. Time points measured: not reported. Time points reported: not reported. Subgroup: none.

Notes	Funding Sources: none. Declaration of interests: none.	
<i>Risk of bias</i>		
Bias	Authors’ judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote from publication: “The method of randomisation was simple random allocation of the children into the study groups.” No other description of randomisation.
Allocation concealment (selection bias)	Unclear risk	Not described.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote from publication: “We discussed with families the off-label use of tamsulosin” The outcomes might be affected by lack of blinding.
Blinding of outcome assessment (detection bias) Subjective outcomes	Unclear risk	Not described.
Blinding of outcome assessment (detection bias) Objective outcomes	Low risk	Not described, but objective outcomes are not likely to be influenced by lack of blinding
Incomplete outcome data (attrition bias) Stone free rate	Low risk	4 children were lost to follow-up, 63 participants out of 67 (94.0%) were included in the evaluation
Incomplete outcome data (attrition bias) Serious adverse events or complications of treatment	Low risk	4 children were lost to follow-up, 63 participants out of 67 (94.0%) were included in the evaluation
Incomplete outcome data (attrition bias) Secondary procedures	Unclear risk	No information given.
Incomplete outcome data (attrition bias) Hospital stay	Unclear risk	No information given.
Incomplete outcome data (attrition bias) Pain	Low risk	4 children were lost to follow-up, 63 participants out of 67 (94.0%) were included in the evaluation

Selective reporting (reporting bias)	Unclear risk	No published protocol available. No events of serious adverse event without any pre-specified description
Other bias	Low risk	Not detected.

Aydogdu 2009

Methods	Study design: parallel-group randomised controlled trial. Setting: single centre/Turkey. Dates when study was conducted: May 2005 to February 2008.
Participants	Inclusion criteria: radiopaque lower ureteral stones 2 to 10 mm in diameter (mean +/- SD 6.2 +/- 1.1 mm) Exclusion criteria: anatomical abnormalities, previously diagnosed reflux, voiding dysfunction, history of ureteral surgery, calcium channel blockers Diagnostic criteria: US/XR or CT and renal function tests. Total number of participants randomly assigned: 39. Group A (ibuprofen and doxazosin) <ul style="list-style-type: none"> Number of participants randomly assigned: 19. Age: 6.2 +/- 2.4. Gender (M/F): 10/3. Group B (Ibuprofen) <ul style="list-style-type: none"> Number of participants randomly assigned: 20. Age (mean): 5.1 +/- 2.2. Gender (M/F): 10/9.
Interventions	Group A (n = 19): ibuprofen 20 mg/kg daily 2 equal doses + doxazosin 0.03 mg/kg daily at night orally, until expulsion or 3 week review Group B (n = 20): ibuprofen 20 mg/kg daily 2 equal doses orally, duration until expulsion or 3 week review Co-interventions: none.
Outcomes	Stone clearance <ul style="list-style-type: none"> How measured: parents of all children were asked to filter the urine. Time points measured: time points not reported. Time points reported: not reported. Subgroup: stones 0-5 mm and stones 5-10 mm. Secondary procedures <ul style="list-style-type: none"> How measured: not reported. Time points measured: at 3 weeks since the start of medical management. Time points reported: not reported. Subgroup: none.
Notes	Funding Sources: not stated. Declaration of interests: not stated.
<i>Risk of bias</i>	

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote from publication: 'We randomly divided patients into 2 groups' Process of randomisation not described.
Allocation concealment (selection bias)	Unclear risk	Not described.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not described.
Blinding of outcome assessment (detection bias) Subjective outcomes	Unclear risk	Not described.
Blinding of outcome assessment (detection bias) Objective outcomes	Low risk	Objective outcomes are not likely to be influenced by lack of blinding
Incomplete outcome data (attrition bias) Stone free rate	Low risk	Quote from publication: "All patients completed the study and outcome data available"
Incomplete outcome data (attrition bias) Serious adverse events or complications of treatment	Unclear risk	No information given.
Incomplete outcome data (attrition bias) Secondary procedures	Low risk	Quote from publication: "All patients completed the study and outcome data available"
Incomplete outcome data (attrition bias) Hospital stay	Unclear risk	No information given.
Incomplete outcome data (attrition bias) Pain	Unclear risk	No information given.
Selective reporting (reporting bias)	High risk	No published protocol available. All of the outcomes were not prespecified. Study author describe that secondary procedures (SWL or ureteroscopic procedures) were applied in participants who could not pass the stone after 3 weeks, but the result was omitted
Other bias	Low risk	Not detected.

Methods	<p>Study design: parallel-group randomised controlled trial.</p> <p>Setting: multi-centred (6 centres)/Iran.</p> <p>Dates when study was conducted: February 2007 to October 2009.</p>
Participants	<p>Inclusion criteria: distal ureteral calculi.</p> <p>Exclusion criteria: poorly controlled coagulation disorders, active urinary tract infection, urinary tract anomalies, non-functioning kidney and hypertension</p> <p>Diagnostic criteria: not reported.</p> <p>Total number of participants randomly assigned: 100.</p> <p>Group A (SWL)</p> <ul style="list-style-type: none"> • Number of participants randomly assigned: 50. • Age (mean): 5.5 +/-4.7. • Gender (M/F): 29/21. <p>Group B (TUL)</p> <ul style="list-style-type: none"> • Number of participants randomly assigned: 50. • Age (mean): 6.5+/-3.9. • Gender (M/F): 27/23.
Interventions	<p>Group A (n = 50): SWL using an under table Compact Delta II lithotripter (Dornier MedTech, Kennesaw, Georgia) under ultrasound (66%) or fluoroscopic (34%) guidance, impulse rate 1,250-2,400 (mean 1,530) and power 11-13 kV</p> <p>Group B (n = 50): transureteral lithotripsy (TUL) with holmium laser (5) or pneumatic lithotripter (45). 6 Fr (48 patients) or 8.5 Fr (2 patients) semirigid ureteroscope passed to facilitate this</p> <p>Co-interventions: none.</p>
Outcomes	<p>Stone clearance</p> <ul style="list-style-type: none"> • How measured: US KUB. (If stone free excretory urography at 3 months). • Time points measured: 2 weeks and 3 months. • Time points reported: at discharge, at 2 weeks and 3 months. • Subgroup: none. <p>Complications</p> <ul style="list-style-type: none"> • How measured: during the surgical procedure direct visualisation, USS KUB. • Time points measured: at the time of surgery, at 2 weeks and 3 months. • Time points reported: not reported. • Subgroup: none. <p>Secondary procedures</p> <ul style="list-style-type: none"> • How measured: US KUB. (If stone free excretory urography at 3 months). • Time points measured: 2 weeks and 3 months. • Time points reported: not reported. • Subgroup: none. <p>Hospital stay</p> <ul style="list-style-type: none"> • How measured: measured the time of anaesthesia and post operative hospital stay. • Time points measured: during the surgery and from surgery to discharge. • Time points reported: not reported. • Subgroup: none.
Notes	<p>Funding Sources: not stated.</p> <p>Declaration of interests: not stated.</p>

<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote from publication: 'Patients were included in the study based on the randomised numerical schedule'
Allocation concealment (selection bias)	Unclear risk	Quote from publication: 'A total of 100 children with distal ureteral calculi were consecutively assigned by Peto randomisation' Not enough information on whether this was an open schedule.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not described.
Blinding of outcome assessment (detection bias) Subjective outcomes	Unclear risk	Not described.
Blinding of outcome assessment (detection bias) Objective outcomes	Low risk	Objective outcomes are not likely to be influenced by lack of blinding
Incomplete outcome data (attrition bias) Stone free rate	Low risk	Quote from publication: "Follow up was completed in all patients"
Incomplete outcome data (attrition bias) Serious adverse events or complications of treatment	Low risk	Quote from publication: "Follow up was completed in all patients"
Incomplete outcome data (attrition bias) Secondary procedures	Low risk	Quote from publication: "Follow up was completed in all patients"
Incomplete outcome data (attrition bias) Hospital stay	Low risk	Quote from publication: "Follow up was completed in all patients"
Incomplete outcome data (attrition bias) Pain	Unclear risk	No information given.
Selective reporting (reporting bias)	High risk	No published protocol available. All of the outcomes were not prespecified but described in the result of article
Other bias	Low risk	Not detected.

Methods	<p>Study design: parallel-group randomised controlled trial.</p> <p>Setting: single centre/Italy.</p> <p>Dates when study was conducted: July 2002 to July 2003.</p>
Participants	<p>Inclusion criteria: radio-opaque calculi in the distal ureter treated with SWL or ULT as primary therapy</p> <p>Exclusion criteria: not reported.</p> <p>Diagnostic criteria: US and IVU.</p> <p>Total number of participants randomly assigned: 31.</p> <p>Group A (SWL)</p> <ul style="list-style-type: none"> • Number of participants randomly assigned: 13. • Age (mean): 7.2. • Gender (M/F): 14/9. <p>Group B (ULT)</p> <ul style="list-style-type: none"> • Number of participants randomly assigned: 17. • Age (mean): 7.2. • Gender (M/F): 5/12.
Interventions	<p>Group A (n = 14): SWL was administered using a second-generation lithotripter. EDAP sonolith 4000+ lithotripter while prone, ~2500 shock waves (1900-3500) were delivered, usually at 450 kJ (330-694)</p> <p>Group B (n = 17): A 7.5 F ureteroscope with a 5 F operative channel; Storz, Germany) combined with a ballistic lithotripter (Lithoclast^R) (1.9 F tapered semi-flexible probe) or holmium-YAG laser (400 um fibres) was used for ULT. Retrograde endoscopy with or without basket extraction of the fragments</p> <p>Co-interventions: ureteric open-ended catheter left in place for 24-72 hours. Double-pigtail ureteric stent for 1 week if ureteric dilatation was used</p>
Outcomes	<p>Stone clearance</p> <ul style="list-style-type: none"> • How measured: US KUB and X-ray. • Time points measured: 3-4 weeks after treatment. • Time points reported: not reported. • Subgroup: none. <p>Complications</p> <ul style="list-style-type: none"> • How measured: not reported. • Time points measured: not reported. • Time points reported: not reported. • Subgroup: none. <p>Secondary procedures</p> <ul style="list-style-type: none"> • How measured: US KUB and X-ray. • Time points measured: 3-4 weeks after treatment. • Time points reported: not reported. • Subgroup: none.
Notes	<p>Funding Sources: not stated.</p> <p>Declaration of interests: not stated.</p>
<i>Risk of bias</i>	

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote from publication: 'The patients were assigned to SWL or ULT using a randomised computer system...'
Allocation concealment (selection bias)	Low risk	Quote from publication: '...patients were given a number and sealed treatment envelopes with printed numbers used for the allocation...'
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not described.
Blinding of outcome assessment (detection bias) Subjective outcomes	Unclear risk	Not described.
Blinding of outcome assessment (detection bias) Objective outcomes	Low risk	Objective outcomes are not likely to be influenced by lack of blinding
Incomplete outcome data (attrition bias) Stone free rate	Low risk	All randomised participants were included in the analysis.
Incomplete outcome data (attrition bias) Serious adverse events or complications of treatment	Low risk	All randomised participants were included in the analysis.
Incomplete outcome data (attrition bias) Secondary procedures	Low risk	All randomised participants were included in the analysis.
Incomplete outcome data (attrition bias) Hospital stay	Low risk	All randomised participants were included in the analysis.
Incomplete outcome data (attrition bias) Pain	Unclear risk	No information given.
Selective reporting (reporting bias)	High risk	No published protocol available. Complication rate not specified as set in the objectives but authors quote 'no major complications in any procedure'. Operation time and length of hospital stay were not pre-specified
Other bias	Low risk	Not detected.

Methods	<p>Study design: parallel-group quasi-randomised controlled trial.</p> <p>Setting: single centre/Egypt.</p> <p>Dates when study was conducted: September 2010 to September 2012.</p>
Participants	<p>Inclusion criteria: uncomplicated radiolucent stone, mean stone density < 500 HU on NCCT, total stone length < 25 mm and a normal upper urinary tract or grade 1 hydronephrosis</p> <p>Exclusion criteria: not stated however 239 assessed for eligibility and 96 included</p> <p>Diagnostic criteria: KUB, US, abdominopelvic NCCT, urinalysis and urine culture, complete blood count, serum uric acid, serum calcium and phosphorus, and a coagulation profile</p> <p>Total number of participants randomly assigned: 96.</p> <p>Group A (SWL)</p> <ul style="list-style-type: none"> • Number of participants randomly assigned: 39. • Age (median): 2.5. • Gender (M/F): not reported. <p>Group B (potassium sodium hydrogen citrate)</p> <ul style="list-style-type: none"> • Number of participants randomly assigned: 48. • Age (median): 2.5. • Gender (M/F): not reported.
Interventions	<p>Group A (n = 39): SWL group. Lithotripter S under general anaesthesia. Single dose of intravenous first-generation cephalosporin before induction. US monitoring used and a total count of 2000 per session at 12 to 14 kV power and a frequency of 60 to 70 per minute</p> <p>Group B (n = 48): oral potassium sodium hydrogen citrate at a dose of 1 mEq/kg per day in 2-3 divided doses after meals for 1-3 months</p> <p>Co-interventions: 15 mg/kg dose of oral paracetamol every 8 hours for 3-5 days and to maintain a high fluid intake</p>
Outcomes	<p>Stone clearance</p> <ul style="list-style-type: none"> • How measured: stone-free when US within 3 months showed no evidence of stones. • Time points measured: every 3-4 weeks, by Urinalysis and US, and every 3-4 months thereafter. • Time points reported: 1 month, 2 month and 3 month for medical therapy. Not reported for SWL. • Subgroup: none. <p>Complications</p> <ul style="list-style-type: none"> • How measured: US. • Time points measured: as 'at end of study'. • Time points reported: as 'at end of study'. • Subgroup: none. <p>Secondary procedures</p> <ul style="list-style-type: none"> • How measured: not reported. • Time points measured: not reported. • Time points reported: not reported. • Subgroup: none.

Notes	Funding Sources: not stated. Declaration of interests: not stated.	
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Patients were quasi-randomised into 2 treatment groups by month of presentation. Those who presented in odd months received oral dissolution therapy and those who presented in even months were treated with SWL
Allocation concealment (selection bias)	Unclear risk	Not described.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not described.
Blinding of outcome assessment (detection bias) Subjective outcomes	Low risk	Quote from publication: "Radiologist were blinded to the procedures"
Blinding of outcome assessment (detection bias) Objective outcomes	Low risk	Objective outcomes are not likely to be influenced by lack of blinding
Incomplete outcome data (attrition bias) Stone free rate	Unclear risk	3/51 (5.8%) and 6/45 (13.3%) participants in medical and SWL group were not included in the analysis, respectively. Adherence of participants may not be balanced across intervention groups
Incomplete outcome data (attrition bias) Serious adverse events or complications of treatment	Unclear risk	3/51 (5.8%) and 6/45 (13.3%) participants in medical and SWL group were not included in the analysis, respectively. Adherence of participants may not be balanced across intervention groups
Incomplete outcome data (attrition bias) Secondary procedures	Unclear risk	3/51 (5.8%) and 6/45 (13.3%) participants in medical and SWL group were not included in the analysis, respectively. Adherence of participants may not be balanced across intervention groups
Incomplete outcome data (attrition bias) Hospital stay	Unclear risk	No information given.

Elderwy 2014 (Continued)

Incomplete outcome data (attrition bias) Pain	Unclear risk	No information given.
Selective reporting (reporting bias)	Unclear risk	Prespecified outcomes were fully described, but no published protocol available
Other bias	Low risk	Not detected.

Elgalaly 2017

Methods	<p>Study design: parallel-group randomised controlled trial.</p> <p>Setting: single centre/Egypt.</p> <p>Dates when study was conducted: September 2014 to October 2015.</p>
Participants	<p>Inclusion criteria: age < 18 years, single unilateral radiopaque DUS, and largest stone diameter of 10 mm</p> <p>Exclusion criteria: multiple, bilateral or recurrent stones, radiolucent stone, largest stone diameter > 10 mm, UTI or urosepsis, anomalies of the ureter or the kidney, previous urinary tract endoscopy or surgery, marked hydronephrosis, and abnormal renal function</p> <p>Diagnostic criteria: history, physical examination, laboratory investigations including urine analysis and serum creatinine, radiological assessment with plain abdominal KUB radiograph and abdomino-pelvic ultrasonography</p> <p>Total number of participants randomly assigned: 40.</p> <p>Group A (silodosin)</p> <ul style="list-style-type: none"> • Number of participants randomly assigned: 20. • Age (mean): 8.4 (3.1). • Gender (M/F): 12/8. <p>Group B (placebo)</p> <ul style="list-style-type: none"> • Number of participants randomly assigned: 20. • Age (mean): 7.7 (2.3). • Gender (M/F): 15/5.
Interventions	<p>Group A (n = 20): silodosin 4 mg at bedtime.</p> <p>Group B (n = 20): placebo.</p> <p>Co-interventions: none.</p>
Outcomes	<p>Stone clearance</p> <ul style="list-style-type: none"> • How measured: children were advised to urinate in a potty under parent or guardian observation to ensure the exact time of stone passage by visual confirmation of the stone and subsequently confirmed radiologically. • Time points measured: 2- or 4-weeks. • Time points reported: not reported. • Subgroup: none.
Notes	<p>Funding Sources: none.</p> <p>Declaration of interests: none.</p>

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote from publication: "Treatment was assigned on a randomised basis using the closed envelope randomisation method into two equal groups..."
Allocation concealment (selection bias)	Unclear risk	Not described.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote from publication: "This single-blinded study". It is unclear who was blinded.
Blinding of outcome assessment (detection bias) Subjective outcomes	Unclear risk	Quote from publication: "This single-blinded study". It is unclear who was blinded.
Blinding of outcome assessment (detection bias) Objective outcomes	Low risk	Objective outcomes are not likely to be influenced by lack of blinding
Incomplete outcome data (attrition bias) Stone free rate	Low risk	2/20 (10.0%) and 1/20 (5.0%) participants in silodosin and placebo group were not included in the analysis, respectively
Incomplete outcome data (attrition bias) Serious adverse events or complications of treatment	Low risk	2/20 (10.0%) and 1/20 (5.0%) participants in silodosin and placebo group were not included in the analysis, respectively
Incomplete outcome data (attrition bias) Secondary procedures	Unclear risk	No information given.
Incomplete outcome data (attrition bias) Hospital stay	Unclear risk	No information given.
Incomplete outcome data (attrition bias) Pain	Low risk	2/20 (10.0%) and 1/20 (5.0%) participants in silodosin and placebo group were not included in the analysis, respectively
Selective reporting (reporting bias)	Unclear risk	Prespecified outcomes were fully described, but no published protocol available
Other bias	Low risk	Not detected.

Methods	Study design: parallel-group randomised controlled trial. Setting: multicentre (number not stated)/Turkey. Dates when study was conducted: not specified.
Participants	Inclusion criteria: single radio-opaque lower ureteral stone. Exclusion criteria: ureteral and/or bladder surgery, anatomic urinary system abnormality, vesicouretral reflux, neurogenic/non-urogenic voiding dysfunction, bilateral or non-opaque renal stones, severe hydronephrosis, colic pain attacks, and the use of diuretic and/or calcium channel blockers Diagnostic criteria: KUB and US or NCCT. Total number of participants randomly assigned: 50 (45 completed the study). Group A (doxazosin) <ul style="list-style-type: none"> • Number of participants randomly assigned: 24. • Age (mean): 7.2 +/- 3.5. • Gender (M/F): 14/10. Group B (ibuprofen only) <ul style="list-style-type: none"> • Number of participants randomly assigned: 21. • Age (mean): 7.2 +/- 3.5. • Gender (M/F): 10/11.
Interventions	Group A (n = 24): 0.03 mg/kg/d doxazosin once daily before bed plus the above dose of ibuprofen Group B (n = 21): ibuprofen 20 mg/kg/d divided into 2 equal doses. No placebo Co-interventions: none.
Outcomes	Stone clearance <ul style="list-style-type: none"> • How measured: stone passage was assessed using KUB radiography and ultrasonography and non contrast-enhanced spiral computed tomography. • Time points measured: weekly for 3 weeks. • Time points reported: as 'during the 3 week follow up period'. • Subgroup: none.
Notes	Funding Sources: authors declare no relevant financial interests. Declaration of interests: not stated.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomisation was performed using the permuted block method in MedCalc, version 11.5.1, program for the 50 participants
Allocation concealment (selection bias)	Unclear risk	Concealment not detailed.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote from publication: 'absence of placebo and therefore absence of blinding were additional limitations'

Erturhan 2013 (Continued)

		Described as a limitation by authors.
Blinding of outcome assessment (detection bias) Subjective outcomes	High risk	Quote from publication: 'absence of placebo and therefore absence of blinding were additional limitations' Described as a limitation by authors.
Blinding of outcome assessment (detection bias) Objective outcomes	Low risk	Objective outcomes are not likely to be influenced by lack of blinding
Incomplete outcome data (attrition bias) Stone free rate	High risk	1/25 (4.0%) and 4/25 (16.0%) participants in doxazosin and ibuprofen group were not included in the analysis, respectively. Adherence of participants are not balanced across intervention groups
Incomplete outcome data (attrition bias) Serious adverse events or complications of treatment	Unclear risk	Participants with adverse events were excluded in analysis.
Incomplete outcome data (attrition bias) Secondary procedures	Unclear risk	No information given.
Incomplete outcome data (attrition bias) Hospital stay	Unclear risk	No information given.
Incomplete outcome data (attrition bias) Pain	High risk	1/25 (4.0%) and 4/25 (16.0%) participants in doxazosin and ibuprofen group were not included in the analysis, respectively. Adherence of participants are not balanced across intervention groups
Selective reporting (reporting bias)	High risk	Patients with adverse events were excluded in analysis and no published protocol available
Other bias	Low risk	Not detected.

Fahmy 2017

Methods	Study design: parallel-group randomised controlled trial. Setting: not specified/Egypt. Dates: not specified.
Participants	Inclusion criteria: unilateral, single, radio-opaque distal ureteral stones < 10 mm in size Exclusion criteria: not available. Diagnostic criteria: not available.

	Total number of participants randomly assigned: 90. Group A (silodosin) <ul style="list-style-type: none">• Number of participants randomly assigned: 30.• Age (median): not specified.• Gender (M/F): not specified. Group B (tamsulosin) <ul style="list-style-type: none">• Number of participants randomly assigned: 30.• Age (median): not specified.• Gender (M/F): not specified. Group C (placebo) <ul style="list-style-type: none">• Number of participants randomly assigned: 30• Age (median): not specified• Gender (M/F): not specified	
Interventions	Group A (n = 30): 8 mg silodosin daily. Group B (n = 30): 0.4 mg tamsulosin daily. Group C (n = 30): not given any of the above medications. Co-interventions: not specified.	
Outcomes	Stone clearance <ul style="list-style-type: none">• How measured: not specified.• Time points measured: not reported.• Time points reported: not reported.• Subgroup: none. Complications <ul style="list-style-type: none">• How measured: during the surgical procedure direct visualisation.• Time points measured: at the time of surgery.• Time points reported: not reported.• Subgroup: none.	
Notes	Funding Sources: none. Declaration of interests: none declared.	
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote from publication: "Patients were randomised into three groups..." Not described.
Allocation concealment (selection bias)	Unclear risk	Not described.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote from publication: "placebo-controlled study".

Fahmy 2017 (Continued)

Blinding of outcome assessment (detection bias) Subjective outcomes	Low risk	Quote from publication: “placebo-controlled study”.
Blinding of outcome assessment (detection bias) Objective outcomes	Low risk	Objective outcomes are not likely to be influenced by lack of blinding
Incomplete outcome data (attrition bias) Stone free rate	High risk	The number of participants in the analysis were not reported
Incomplete outcome data (attrition bias) Serious adverse events or complications of treatment	High risk	The number of participants in the analysis were not reported
Incomplete outcome data (attrition bias) Secondary procedures	Unclear risk	No information given.
Incomplete outcome data (attrition bias) Hospital stay	Unclear risk	No information given.
Incomplete outcome data (attrition bias) Pain	Unclear risk	No information given.
Selective reporting (reporting bias)	Unclear risk	Study outcomes were not specified.
Other bias	Unclear risk	Abstract only.

Gamal 2017

Methods	Study design: parallel-group randomised controlled trial. Setting: number of centres not specified/Egypt. Dates when study was conducted: April 2011 to April 2016.
Participants	Inclusion criteria: children < 15 years old with a renal stones (1-2) cm in a solitary kidney Exclusion criteria: not available. Diagnostic criteria: not available. Total number of participants randomly assigned: 22. Group A (SWL) <ul style="list-style-type: none"> • Number of participants randomly assigned: 11. • Age (median): 9.6. • Gender (M/F): not available. Group B (Flexible URS) <ul style="list-style-type: none"> • Number of participants randomly assigned: 11. • Age (median): 9.3. • Gender (M/F): not available.

Interventions	Group A (n = 11): not available. Group B (n = 11): a 7.5 Fr flexible ureteroscope (FURS) was introduced into the ureter over a hydrophilic guidewire under visual and fluoroscopic guidance without access sheath. Complete stone dusting using 200 mm laser fibre (0.2 - 1.0 joules power and 15 - 30 Hz frequency) was done in all cases ended with a 5 Fr JJ stent insertion Co-interventions: JJ stent.	
Outcomes	Stone clearance <ul style="list-style-type: none">• How measured: not specified.• Time points measured: not reported.• Time points reported: not reported.• Subgroup: none. Complications <ul style="list-style-type: none">• How measured: during the surgical procedure direct visualisation.• Time points measured: at the time of surgery.• Time points reported: not reported.• Subgroup: none. Secondary procedures <ul style="list-style-type: none">• How measured: not specified.• Time points measured: not specified.• Time points reported: not reported.• Subgroup: none.	
Notes	Funding sources: none. Declaration of interests: none declared.	
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not described.
Allocation concealment (selection bias)	Unclear risk	Not described.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not described.
Blinding of outcome assessment (detection bias) Subjective outcomes	Unclear risk	Not described.
Blinding of outcome assessment (detection bias) Objective outcomes	Low risk	Objective outcomes are not likely to be influenced by lack of blinding

Incomplete outcome data (attrition bias) Stone free rate	Unclear risk	The number of randomised participant was not reported.
Incomplete outcome data (attrition bias) Serious adverse events or complications of treatment	Unclear risk	The number of randomised participant was not reported.
Incomplete outcome data (attrition bias) Secondary procedures	Unclear risk	The number of randomised participant was not reported.
Incomplete outcome data (attrition bias) Hospital stay	Unclear risk	The number of randomised participant was not reported.
Incomplete outcome data (attrition bias) Pain	Unclear risk	No information given.
Selective reporting (reporting bias)	Unclear risk	Study outcomes were not specified.
Other bias	Unclear risk	Abstract only.

Kumar 2015

Methods	<p>Study design: parallel-group randomised controlled trial.</p> <p>Setting: single centre/India.</p> <p>Dates when study was conducted: March 2012 to September 2013.</p>
Participants	<p>Inclusion criteria: age < 15 years and single radio-opaque lower calyceal calculus 1-2 cm</p> <p>Exclusion criteria: bleeding disorders, radiolucent stones, active urinary tract infection, severe hydronephrosis, unfit for anaesthesia, serum creatinine > 1.5 mg/dL, anatomically abnormal kidney and co-existing ureteral pathology including tumour/stricture</p> <p>Diagnostic criteria: USS KUB, radiography of the KUB to assess radiopacity of the calculus, IVU. CT in some cases to assess the pelvicaliceal anatomy including lower caliceal infundibulopelvic angle, degree of hydronephrosis, and urinary drainage pattern</p> <p>Total number of participants randomly assigned: 221.</p> <p>Group A (SWL)</p> <ul style="list-style-type: none"> • Number of participants randomly assigned: 111. • Age (mean): 10.7. • Gender (M/F): 52/54 finished trial. <p>Group B (Mini PCNL)</p> <ul style="list-style-type: none"> • Number of participants randomly assigned: 110. • Age (mean): 10.3. • Gender (M/F): 51/55 finished trial.
Interventions	<p>Group A (n = 111): SWL (5 patients lost to follow-up (106 included in analysis). Outpatient procedure using the electromagnetic lithotripter (Dornier Alpha Compact system, Wessling, Germany). Shockwave delivery rate 90 pulses per minute</p> <p>Group B (n =110): Miniperc (4 patients lost to follow-up (106 included in analysis).</p>

	One experienced consultant and under general anaesthesia Co-interventions: double J stent and nephrostomy in PCNL.	
Outcomes	Stone clearance <ul style="list-style-type: none">• How measured: KUB radiography.• Time points measured: 3 weeks after surgery.• Time points reported: not reported.• Subgroup: none. Complications <ul style="list-style-type: none">• How measured: perioperative evaluations, some not reported.• Time points measured: some during surgery, some not reported.• Time points reported: not reported.• Subgroup: none. Secondary procedures <ul style="list-style-type: none">• How measured: KUB radiography.• Time points measured: 3 weeks after surgery.• Time points reported: not reported.• Subgroup: none.	
Notes	Funding Sources: not stated Declaration of interests: no competing financial interests exist.	
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote from publication: 'Using a computer generated randomisation table, the eligible patients were randomised into two groups: Groups A, patients who underwent mini-perc, and group B, patients who underwent SWL.'
Allocation concealment (selection bias)	Unclear risk	Not described by the authors. No clarification regarding open or concealed randomisation schedule
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not described.
Blinding of outcome assessment (detection bias) Subjective outcomes	Unclear risk	Not described.
Blinding of outcome assessment (detection bias) Objective outcomes	Low risk	Objective outcomes are not likely to be influenced by lack of blinding

Kumar 2015 (Continued)

Incomplete outcome data (attrition bias) Stone free rate	Low risk	5/111 (4.5%) and 4/110 (3.6%) participants in SWL and mini-PCNL group were not included in the analysis, respectively
Incomplete outcome data (attrition bias) Serious adverse events or complications of treatment	Low risk	5/111 (4.5%) and 4/110 (3.6%) participants in SWL and mini-PCNL group were not included in the analysis, respectively
Incomplete outcome data (attrition bias) Secondary procedures	Low risk	5/111 (4.5%) and 4/110 (3.6%) participants in SWL and mini-PCNL group were not included in the analysis, respectively
Incomplete outcome data (attrition bias) Hospital stay	Low risk	5/111 (4.5%) and 4/110 (3.6%) participants in SWL and mini-PCNL group were not included in the analysis, respectively
Incomplete outcome data (attrition bias) Pain	Unclear risk	No information given.
Selective reporting (reporting bias)	Unclear risk	The outcomes were not prespecified and no published protocol available
Other bias	Low risk	Not detected

Mokhless 2012

Methods	<p>Study design: parallel-group randomised controlled trial.</p> <p>Setting: single centre/Egypt.</p> <p>Dates when study was conducted: April 2007 to July 2010.</p>
Participants	<p>Inclusion criteria: radiopaque distal ureteric calculi < 12 mm.</p> <p>Exclusion criteria: anatomical abnormalities, non-radio-opaque stones, voiding dysfunction, urinary tract infection, severe hydronephrosis, or history of endoscopic or open ureteral surgery were excluded</p> <p>Diagnostic criteria: US urinary tract, KUB and renal function. NCCT in selected cases</p> <p>Total number of participants randomly assigned: 61.</p> <p>Group A (tamsulosin)</p> <ul style="list-style-type: none"> • Number of participants randomly assigned: 32. • Age (mean): 7.3 ± 4.2. • Gender (M/F): 18/15. <p>Group B (placebo)</p> <ul style="list-style-type: none"> • Number of participants randomly assigned: 28. • Age (mean): 7.1 ± 3.2. • Gender (M/F): 18/10.
Interventions	<p>Group A (n = 33): tamsulosin 0.4 mg for children > 4 years and 0.2 mg for younger children at bedtime</p> <p>Group B (n = 28): placebo.</p>

	Co-interventions: standard analgesia ibuprofen.	
Outcomes	Stone clearance <ul style="list-style-type: none">• How measured: parents were asked to filter the urine to detect fragments of stone expulsion, KUB or NCCT to confirm passage of stone.• Time points measured: 4 weeks.• Time points reported: not reported.• Subgroup: none.	
Notes	Funding Sources: none. Declaration of interests: no conflict of interest.	
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote from publication: "Children were randomly divided into two groups" Not specified.
Allocation concealment (selection bias)	Unclear risk	Not described.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not described.
Blinding of outcome assessment (detection bias) Subjective outcomes	Unclear risk	Not described.
Blinding of outcome assessment (detection bias) Objective outcomes	Low risk	Objective outcomes are not likely to be influenced by lack of blinding
Incomplete outcome data (attrition bias) Stone free rate	Low risk	Quote from publication: "All patients completed the study".
Incomplete outcome data (attrition bias) Serious adverse events or complications of treatment	Low risk	Quote from publication: "All patients completed the study".
Incomplete outcome data (attrition bias) Secondary procedures	Low risk	Quote from publication: "All patients completed the study".
Incomplete outcome data (attrition bias) Hospital stay	Low risk	Quote from publication: "All patients completed the study".
Incomplete outcome data (attrition bias) Pain	Unclear risk	No information given.

Selective reporting (reporting bias)	Unclear risk	Secondary procedures was not specified and no published protocol available
Other bias	Low risk	Not detected.

Salem 2014

Methods	<p>Study design: parallel-group randomised controlled trial.</p> <p>Setting: single centre/Egypt.</p> <p>Dates when study was conducted: August 2011 to July 2012.</p>
Participants	<p>Inclusion criteria: solitary radiopaque renal stones (10 to 20 mm).</p> <p>Exclusion criteria: multiple stones, moderate or severe hydronephrosis, active infection, coagulopathy, stone size < 10 mm or > 20 mm, bilateral renal stones, radiolucent stones, anatomical abnormality in the ureter or ureteropelvic junction, cardiac pacemaker and uremia</p> <p>Diagnostic criteria: US, KUB and/or excretory urography.</p> <p>Total number of participants randomly assigned: 60.</p> <p>Group A (Slow SWL)</p> <ul style="list-style-type: none"> • Number of participants randomly assigned: 30. • Age (mean): 5.35 ± 3.67. • Gender (M/F): 20/10. <p>Group B (Fast SWL)</p> <ul style="list-style-type: none"> • Number of participants randomly assigned: 30. • Age (mean): 6.67 ± 2.94. • Gender (M/F): 18/12.
Interventions	<p>Group A (n = 30): SWL at 80 shock waves per minute.</p> <p>Group B (n = 30): SWL at 120 shock waves per minute.</p> <p>Co-interventions: diclofenac paediatric suppository was prescribed as analgesia on discharge home</p>
Outcomes	<p>Stone clearance</p> <ul style="list-style-type: none"> • How measured: measured as no residual fragment or only one clinically insignificant fragment <3mm (which was non-symptomatic, non-infectious and non-obstructive) on KUB and US. • Time points measured: at 2 and 4 weeks after surgery. • Time points reported: at 2 and 4 weeks after surgery. • Subgroup: none. <p>Secondary procedures</p> <ul style="list-style-type: none"> • How measured: not reported. • Time points measured: not reported. • Time points reported: not reported. • Subgroup: none.
Notes	<p>Funding Sources: not stated</p> <p>Declaration of interests: not stated</p>

<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote from publication: 'Patients were recruited from the outpatient clinic and were prospectively randomised (envelope method) into 2 groups.' Randomisation sequence generation not described.
Allocation concealment (selection bias)	Unclear risk	Envelope method used. Unclear whether envelopes were sequentially numbered and opaque
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not described.
Blinding of outcome assessment (detection bias) Subjective outcomes	Unclear risk	Not described.
Blinding of outcome assessment (detection bias) Objective outcomes	Low risk	Objective outcomes are not likely to be influenced by lack of blinding
Incomplete outcome data (attrition bias) Stone free rate	Low risk	All randomised participants were included in the analysis.
Incomplete outcome data (attrition bias) Serious adverse events or complications of treatment	Low risk	All randomised participants were included in the analysis.
Incomplete outcome data (attrition bias) Secondary procedures	Low risk	All randomised participants were included in the analysis.
Incomplete outcome data (attrition bias) Hospital stay	Unclear risk	No information given.
Incomplete outcome data (attrition bias) Pain	Unclear risk	No information given.
Selective reporting (reporting bias)	Unclear risk	Prespecified outcomes were fully described, but no published protocol available

Other bias	High risk	Stone component and stone size were different between the groups
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Song 2015

Methods	<p>Study design: parallel-group randomised controlled trial.</p> <p>Setting: single centre/China.</p> <p>Dates when study was conducted: September 2009 to September 2012.</p>
Participants	<p>Inclusion criteria: renal calculi confirmed by spiral CT, 7-36 months old, stone diameter < 4.5 cm, no previous SWL</p> <p>Exclusion criteria: renal anatomical abnormalities, ureteropelvic junction stenosis, pyelonephrosis combined with stones, or isolated kidney</p> <p>Diagnostic criteria: US, spiral CT, IVU.</p> <p>Total number of participants randomly assigned: 78.</p> <p>Group A (Standard PCNL)</p> <ul style="list-style-type: none"> • Number of participants randomly assigned: 38. • Age (mean): 20.10 ± 7.22 months. • Gender (M/F): not reported. <p>Group B (Tubeless Mini PCNL)</p> <ul style="list-style-type: none"> • Number of participants randomly assigned: 40. • Age: 20.30 ± 6.35 months. • Gender (M/F): not reported.
Interventions	<p>Group A (n = 38): in PCNL, the method of surgery was the same, except post procedure the nephrostomy tube was inserted</p> <p>Group B (n = 40): in MPCNL 18 G (gauge) biopsy needle was inserted at the posterior axillary line, the ureteral catheter was expanded by a fascia dilator to F14 or F16 while the sheath was left in place. The paediatric nephroscope or ureteroscope was then inserted, and the stones were smashed by holmium laser and picked out by clamps or washed out by lavage fluid</p> <p>Co-interventions: ureteral and Foley catheters.</p>
Outcomes	<p>Stone clearance</p> <ul style="list-style-type: none"> • How measured: CT or B-mode US. Residual stones of ≤ 4 mm were considered negligible. • Time points measured: at 1,3,6 and 12 months postoperatively. • Time points reported: reported in counts and percentages but no time points. • Subgroup: none. <p>Complications</p> <ul style="list-style-type: none"> • How measured: perioperative evaluation. • Time points measured: some during surgery, some not reported. • Time points reported: not reported. • Subgroup: none. <p>Secondary procedures</p> <ul style="list-style-type: none"> • How measured: not reported. • Time points measured: not reported. • Time points reported: not reported.

	● Subgroup: none.	
Notes	Funding Sources: not stated Declaration of interests: not stated	
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote from publication: "Preschool children were randomised into MPCNL and standard PCNL groups by generation of a random number table"
Allocation concealment (selection bias)	Unclear risk	Quote from publication: "Surgical nurses randomly selected an envelope containing each patient's group" Unclear whether envelopes were sequentially numbered, opaque and sealed
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not described.
Blinding of outcome assessment (detection bias) Subjective outcomes	Unclear risk	Not described.
Blinding of outcome assessment (detection bias) Objective outcomes	Low risk	Objective outcomes are not likely to be influenced by lack of blinding
Incomplete outcome data (attrition bias) Stone free rate	Unclear risk	3/38 (7.8%) and 5/40 (12.5%) participants in PCNL and mini-PCNL group were not included in the analysis, respectively
Incomplete outcome data (attrition bias) Serious adverse events or complications of treatment	Unclear risk	3/38 (7.8%) and 5/40 (12.5%) participants in PCNL and mini-PCNL group were not included in the analysis, respectively
Incomplete outcome data (attrition bias) Secondary procedures	Unclear risk	3/38 (7.8%) and 5/40 (12.5%) participants in PCNL and mini-PCNL group were not included in the analysis, respectively
Incomplete outcome data (attrition bias) Hospital stay	Unclear risk	No information given.
Incomplete outcome data (attrition bias) Pain	Unclear risk	No information given.

Song 2015 (Continued)

Selective reporting (reporting bias)	Unclear risk	The outcomes were not prespecified and no published protocol available
Other bias	Low risk	Not detected.

Abbreviations

CT: computerised tomography; **DUS:** distal ureteric stone; **IVU:** intravenous urethrogram; **KUB:** kidney ureter bladder; **MPCNL:** mini percutaneous nephro lithotomy; **NCCT:** non-contrast computerised tomography; **RIRS:** retrograde intrarenal surgery; **SWL:** shock wave lithotripsy; **TUL:** trans-urethral lithotripsy; **ULT:** ureteroscopic lithotripsy; **URS:** ureteroscopy; **US/USS:** ultrasound; **XR:** x-ray.

Characteristics of excluded studies [ordered by study ID]

Study	Reason for exclusion
Basiri 2009	Conference abstract, 27 th WCE & SWL only. Full study not available. Author contacted without a response. Relates to the Basiri 2010 included study
Burgu 2009	Conference abstract ESPU 2009. Same data as the included Aydogdu study
Saad 2015	Used renal units
Samad 2012	Used renal units
Zaidi 2009	Conference abstract ESPU 2009. Same data as the Samad 2012 paper

DATA AND ANALYSES

Comparison 1. Shock wave lithotripsy versus dissolution therapy for renal stones

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Stone-free rate	1	87	Risk Ratio (M-H, Random, 95% CI)	1.13 [0.90, 1.41]
2 Serious adverse events or complications	1	87	Risk Ratio (M-H, Random, 95% CI)	1.23 [0.08, 19.05]
3 Secondary procedures	1	87	Risk Ratio (M-H, Random, 95% CI)	0.66 [0.29, 1.50]

Comparison 2. Slow shock wave lithotripsy versus rapid shock wave lithotripsy for renal stones

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Stone-free rate	1	60	Risk Ratio (M-H, Random, 95% CI)	2.25 [1.16, 4.36]
2 Serious adverse events or complications	1	60	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
3 Secondary procedures	1	60	Risk Ratio (M-H, Random, 95% CI)	0.38 [0.11, 1.28]

Comparison 3. Shock wave lithotripsy versus ureteroscopy with holmium laser or pneumatic lithotripsy for renal and ureteric stones

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Stone-free rate	3	153	Risk Ratio (M-H, Random, 95% CI)	0.62 [0.43, 0.88]
1.1 Renal stone	1	22	Risk Ratio (M-H, Random, 95% CI)	0.5 [0.25, 0.98]
1.2 Distal ureteral stone	2	131	Risk Ratio (M-H, Random, 95% CI)	0.63 [0.39, 1.03]
2 Serious adverse events or complications of treatment	3	153	Risk Ratio (M-H, Random, 95% CI)	0.56 [0.12, 2.58]
2.1 Renal stone	1	22	Risk Ratio (M-H, Random, 95% CI)	0.33 [0.02, 7.39]
2.2 Distal ureteral stone	2	131	Risk Ratio (M-H, Random, 95% CI)	0.67 [0.12, 3.82]
3 Second procedures	3	153	Risk Ratio (M-H, Random, 95% CI)	3.47 [1.32, 9.15]
3.1 Renal stone	1	22	Risk Ratio (M-H, Random, 95% CI)	6.0 [0.86, 41.96]
3.2 Distal ureteral stone	2	131	Risk Ratio (M-H, Random, 95% CI)	3.46 [0.82, 14.58]
4 Hospital stay (hours)	2	122	Mean Difference (IV, Random, 95% CI)	-10.71 [-34.09, 12.67]
4.1 Renal stone	1	22	Mean Difference (IV, Random, 95% CI)	0.0 [-1.07, 1.07]
4.2 Distal ureteral stone	1	100	Mean Difference (IV, Random, 95% CI)	-24.0 [-39.45, -8.55]

Comparison 4. Shock wave lithotripsy versus mini-percutaneous nephrolithotripsy for renal stones

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Stone-free rate	1	212	Risk Ratio (M-H, Random, 95% CI)	0.88 [0.80, 0.97]
2 Serious adverse events or complications of treatment	1	212	Risk Ratio (M-H, Random, 95% CI)	0.13 [0.02, 0.98]
3 Secondary procedures	1	212	Risk Ratio (M-H, Random, 95% CI)	2.5 [1.01, 6.20]
4 Hospital stay (days)	1	212	Mean Difference (IV, Random, 95% CI)	-3.40 [-5.43, -1.37]

Comparison 5. Percutaneous nephrolithotripsy versus tubeless percutaneous nephrolithotripsy for renal stones

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Stone-free rate	1	23	Risk Ratio (M-H, Random, 95% CI)	1.16 [0.88, 1.53]
2 Serious adverse events or complications of treatments	1	23	Risk Ratio (M-H, Random, 95% CI)	0.42 [0.02, 9.43]
3 Secondary procedures	1	23	Risk Ratio (M-H, Random, 95% CI)	0.42 [0.02, 9.43]
4 Hospital stay (hours)	1	23	Mean Difference (IV, Random, 95% CI)	19.16 [10.24, 28.08]
5 Pain (dose of morphine)	1	23	Mean Difference (IV, Random, 95% CI)	0.08 [0.05, 0.11]

Comparison 6. Percutaneous nephrolithotripsy versus tubeless mini-percutaneous nephrolithotripsy for renal stones

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Stone-free rate	1	70	Risk Ratio (M-H, Random, 95% CI)	1.03 [0.93, 1.14]
2 Secondary procedures	1	70	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
3 Hospital stay (days)	1	70	Mean Difference (IV, Random, 95% CI)	3.14 [2.78, 3.50]

Comparison 7. Alpha-blockers versus placebo with/without analgesics for distal ureteric stones

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Stone-free rate	6	335	Risk Ratio (M-H, Random, 95% CI)	1.34 [1.16, 1.54]
2 Serious adverse events or complications of treatments	1	63	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
3 Secondary procedures	1	39	Risk Ratio (M-H, Random, 95% CI)	0.53 [0.15, 1.81]
4 Pain (episode)	2	98	Mean Difference (IV, Random, 95% CI)	-1.49 [-3.04, 0.06]

Analysis 1.1. Comparison 1 Shock wave lithotripsy versus dissolution therapy for renal stones, Outcome 1 Stone-free rate.

Review: Medical and surgical interventions for the treatment of urinary stones in children

Comparison: 1 Shock wave lithotripsy versus dissolution therapy for renal stones

Outcome: 1 Stone-free rate

Analysis 1.2. Comparison 1 Shock wave lithotripsy versus dissolution therapy for renal stones, Outcome 2 Serious adverse events or complications.

Review: Medical and surgical interventions for the treatment of urinary stones in children

Comparison: 1 Shock wave lithotripsy versus dissolution therapy for renal stones

Outcome: 2 Serious adverse events or complications

Analysis 1.3. Comparison 1 Shock wave lithotripsy versus dissolution therapy for renal stones, Outcome 3 Secondary procedures.

Review: Medical and surgical interventions for the treatment of urinary stones in children

Comparison: 1 Shock wave lithotripsy versus dissolution therapy for renal stones

Outcome: 3 Secondary procedures

Analysis 2.1. Comparison 2 Slow shock wave lithotripsy versus rapid shock wave lithotripsy for renal stones, Outcome 1 Stone-free rate.

Review: Medical and surgical interventions for the treatment of urinary stones in children

Comparison: 2 Slow shock wave lithotripsy versus rapid shock wave lithotripsy for renal stones

Outcome: 1 Stone-free rate

Analysis 2.2. Comparison 2 Slow shock wave lithotripsy versus rapid shock wave lithotripsy for renal stones, Outcome 2 Serious adverse events or complications.

Review: Medical and surgical interventions for the treatment of urinary stones in children

Comparison: 2 Slow shock wave lithotripsy versus rapid shock wave lithotripsy for renal stones

Outcome: 2 Serious adverse events or complications

Analysis 2.3. Comparison 2 Slow shock wave lithotripsy versus rapid shock wave lithotripsy for renal stones, Outcome 3 Secondary procedures.

Review: Medical and surgical interventions for the treatment of urinary stones in children

Comparison: 2 Slow shock wave lithotripsy versus rapid shock wave lithotripsy for renal stones

Outcome: 3 Secondary procedures

Analysis 3.1. Comparison 3 Shock wave lithotripsy versus ureteroscopy with holmium laser or pneumatic lithotripsy for renal and ureteric stones, Outcome 1 Stone-free rate.

Review: Medical and surgical interventions for the treatment of urinary stones in children

Comparison: 3 Shock wave lithotripsy versus ureteroscopy with holmium laser or pneumatic lithotripsy for renal and ureteric stones

Outcome: 1 Stone-free rate

Analysis 3.2. Comparison 3 Shock wave lithotripsy versus ureteroscopy with holmium laser or pneumatic lithotripsy for renal and ureteric stones, Outcome 2 Serious adverse events or complications of treatment.

Review: Medical and surgical interventions for the treatment of urinary stones in children

Comparison: 3 Shock wave lithotripsy versus ureteroscopy with holmium laser or pneumatic lithotripsy for renal and ureteric stones

Outcome: 2 Serious adverse events or complications of treatment

Analysis 3.3. Comparison 3 Shock wave lithotripsy versus ureteroscopy with holmium laser or pneumatic lithotripsy for renal and ureteric stones, Outcome 3 Second procedures.

Review: Medical and surgical interventions for the treatment of urinary stones in children

Comparison: 3 Shock wave lithotripsy versus ureteroscopy with holmium laser or pneumatic lithotripsy for renal and ureteric stones

Outcome: 3 Second procedures

Analysis 3.4. Comparison 3 Shock wave lithotripsy versus ureteroscopy with holmium laser or pneumatic lithotripsy for renal and ureteric stones, Outcome 4 Hospital stay (hours).

Review: Medical and surgical interventions for the treatment of urinary stones in children

Comparison: 3 Shock wave lithotripsy versus ureteroscopy with holmium laser or pneumatic lithotripsy for renal and ureteric stones

Outcome: 4 Hospital stay (hours)

Analysis 4.1. Comparison 4 Shock wave lithotripsy versus mini-percutaneous nephrolithotripsy for renal stones, Outcome 1 Stone-free rate.

Review: Medical and surgical interventions for the treatment of urinary stones in children

Comparison: 4 Shock wave lithotripsy versus mini-percutaneous nephrolithotripsy for renal stones

Outcome: 1 Stone-free rate

Analysis 4.2. Comparison 4 Shock wave lithotripsy versus mini-percutaneous nephrolithotripsy for renal stones, Outcome 2 Serious adverse events or complications of treatment.

Review: Medical and surgical interventions for the treatment of urinary stones in children

Comparison: 4 Shock wave lithotripsy versus mini-percutaneous nephrolithotripsy for renal stones

Outcome: 2 Serious adverse events or complications of treatment

Analysis 4.3. Comparison 4 Shock wave lithotripsy versus mini-percutaneous nephrolithotripsy for renal stones, Outcome 3 Secondary procedures.

Review: Medical and surgical interventions for the treatment of urinary stones in children

Comparison: 4 Shock wave lithotripsy versus mini-percutaneous nephrolithotripsy for renal stones

Outcome: 3 Secondary procedures

Analysis 4.4. Comparison 4 Shock wave lithotripsy versus mini-percutaneous nephrolithotripsy for renal stones, Outcome 4 Hospital stay (days).

Review: Medical and surgical interventions for the treatment of urinary stones in children

Comparison: 4 Shock wave lithotripsy versus mini-percutaneous nephrolithotripsy for renal stones

Outcome: 4 Hospital stay (days)

Analysis 5.1. Comparison 5 Percutaneous nephrolithotripsy versus tubeless percutaneous nephrolithotripsy for renal stones, Outcome 1 Stone-free rate.

Review: Medical and surgical interventions for the treatment of urinary stones in children

Comparison: 5 Percutaneous nephrolithotripsy versus tubeless percutaneous nephrolithotripsy for renal stones

Outcome: 1 Stone-free rate

Analysis 5.2. Comparison 5 Percutaneous nephrolithotripsy versus tubeless percutaneous nephrolithotripsy for renal stones, Outcome 2 Serious adverse events or complications of treatments.

Review: Medical and surgical interventions for the treatment of urinary stones in children

Comparison: 5 Percutaneous nephrolithotripsy versus tubeless percutaneous nephrolithotripsy for renal stones

Outcome: 2 Serious adverse events or complications of treatments

Analysis 5.3. Comparison 5 Percutaneous nephrolithotripsy versus tubeless percutaneous nephrolithotripsy for renal stones, Outcome 3 Secondary procedures.

Review: Medical and surgical interventions for the treatment of urinary stones in children

Comparison: 5 Percutaneous nephrolithotripsy versus tubeless percutaneous nephrolithotripsy for renal stones

Outcome: 3 Secondary procedures

Analysis 5.4. Comparison 5 Percutaneous nephrolithotripsy versus tubeless percutaneous nephrolithotripsy for renal stones, Outcome 4 Hospital stay (hours).

Review: Medical and surgical interventions for the treatment of urinary stones in children

Comparison: 5 Percutaneous nephrolithotripsy versus tubeless percutaneous nephrolithotripsy for renal stones

Outcome: 4 Hospital stay (hours)

Analysis 5.5. Comparison 5 Percutaneous nephrolithotripsy versus tubeless percutaneous nephrolithotripsy for renal stones, Outcome 5 Pain (dose of morphine).

Review: Medical and surgical interventions for the treatment of urinary stones in children

Comparison: 5 Percutaneous nephrolithotripsy versus tubeless percutaneous nephrolithotripsy for renal stones

Outcome: 5 Pain (dose of morphine)

Analysis 6.1. Comparison 6 Percutaneous nephrolithotripsy versus tubeless mini-percutaneous nephrolithotripsy for renal stones, Outcome 1 Stone-free rate.

Review: Medical and surgical interventions for the treatment of urinary stones in children

Comparison: 6 Percutaneous nephrolithotripsy versus tubeless mini-percutaneous nephrolithotripsy for renal stones

Outcome: 1 Stone-free rate

Analysis 6.2. Comparison 6 Percutaneous nephrolithotripsy versus tubeless mini-percutaneous nephrolithotripsy for renal stones, Outcome 2 Secondary procedures.

Review: Medical and surgical interventions for the treatment of urinary stones in children

Comparison: 6 Percutaneous nephrolithotripsy versus tubeless mini-percutaneous nephrolithotripsy for renal stones

Outcome: 2 Secondary procedures

Analysis 6.3. Comparison 6 Percutaneous nephrolithotripsy versus tubeless mini-percutaneous nephrolithotripsy for renal stones, Outcome 3 Hospital stay (days).

Review: Medical and surgical interventions for the treatment of urinary stones in children

Comparison: 6 Percutaneous nephrolithotripsy versus tubeless mini-percutaneous nephrolithotripsy for renal stones

Outcome: 3 Hospital stay (days)

Analysis 7.1. Comparison 7 Alpha-blockers versus placebo with/without analgesics for distal ureteric stones, Outcome 1 Stone-free rate.

Review: Medical and surgical interventions for the treatment of urinary stones in children

Comparison: 7 Alpha-blockers versus placebo with/without analgesics for distal ureteric stones

Outcome: 1 Stone-free rate

Analysis 7.2. Comparison 7 Alpha-blockers versus placebo with/without analgesics for distal ureteric stones, Outcome 2 Serious adverse events or complications of treatments.

Review: Medical and surgical interventions for the treatment of urinary stones in children

Comparison: 7 Alpha-blockers versus placebo with/without analgesics for distal ureteric stones

Outcome: 2 Serious adverse events or complications of treatments

Analysis 7.3. Comparison 7 Alpha-blockers versus placebo with/without analgesics for distal ureteric stones, Outcome 3 Secondary procedures.

Review: Medical and surgical interventions for the treatment of urinary stones in children

Comparison: 7 Alpha-blockers versus placebo with/without analgesics for distal ureteric stones

Outcome: 3 Secondary procedures

Analysis 7.4. Comparison 7 Alpha-blockers versus placebo with/without analgesics for distal ureteric stones, Outcome 4 Pain (episode).

Review: Medical and surgical interventions for the treatment of urinary stones in children

Comparison: 7 Alpha-blockers versus placebo with/without analgesics for distal ureteric stones

Outcome: 4 Pain (episode)

ADDITIONAL TABLES

Table 1. Description of the interventions

	Intervention(s)	Intervention(s) appropriate as applied in a clinical practice setting ^a	Comparator(s)	Comparator(s) appropriate as applied in a clinical practice setting ^a
Aghamir 2012	I: Tubeless percutaneous nephrolithotomy	Puncture was performed in the prone position by 18-gauge nephrostomy needle, under fluoroscopic guidance the tract was dilated by coaxial serial metallic dilators, an Amplatz sheath	C: Standard percutaneous nephrolithotomy	Puncture was performed in the prone position by 18-gauge nephrostomy needle, under fluoroscopic guidance the tract was dilated by coaxial serial metallic dilators, an Amplatz sheath

Table 1. Description of the interventions (Continued)

		up to 28 F, and up to 26 F Storz nephroscope was used, the stone fragmentation was performed with a pneumatic lithotripter (EMS Swiss lithoclast) and residual stones were extracted with a grasper, both ureteral stent and the working sheath were removed at the end of procedure without placing any nephrostomy tube		up to 28 F, and up to 26 F Storz nephroscope was used, the stone fragmentation was performed with a pneumatic lithotripter (EMS Swiss lithoclast) and residual stones were extracted with a grasper, ureteral stent was remained and a nephrostomy tube was placed through the working sheath for 24-48 hours
Aldaquadosi 2015	I: alpha-1 blocker (tamsulosin) therapy in addition to ibuprofen	Tamsulosin 0.4 mg for patients aged > 5 years and 0.2 mg for younger children and Ibuprofen 4-10 mg/kg orally every 6-8 h as needed	C: Ibuprofen only	Ibuprofen 4-10 mg/kg orally every 6-8 h as needed.
Aydogdu 2009	I: Ibuprofen	Ibuprofen (20 mg/kg daily divided into 2 equal doses).	C: Doxazosin and ibuprofen	Ibuprofen (20 mg/kg daily divided into 2 equal doses) and doxazosin dose was approximately 0.03 mg/kg once daily
Basiri 2010	I: Transureteral lithotripsy	Patients were placed in the lithotomy position and a 6 Fr or 8.5 Fr semi-rigid ureteroscope was passed into the ureter using a safety guidewire, the ureteral calculus fragmentation was performed with holmium laser or pneumatic lithotripsy	C: Shock wave lithotripsy	Shock wave was delivered by under-table Compact Delta II electromagnetic sources, with patients in the prone position under ultrasound or fluoroscopic guidance, impulse rate per treatment varied from 1,250 to 2,400 (mean 1,530) and power ranged from 11 to 13 kV
De Domenicis 2005	I: Ureterscopy plus intracorporeal lithotripsy	For ureteroscopy the 7.5 F ureteroscope with a 5 F operative channel was used (Storz, Germany) and the Lithoclast® ballistic lithotripter (1.9 F tapered semiflexible probe) or holmium-YAG	C: Extracorporeal shock wave lithotripsy	EDAP-Sonolith 4000 + lithotripter was used in prone prone position, 2500 shock waves (1900-3500) were delivered, usually at 450 KJ (330-694), ureteric open-ended catheter was left in

Table 1. Description of the interventions (Continued)

		laser (400 mm fibres) was used for disintegrating the stones in the distal ureter, patient in the dorsal lithotomy position, paediatric cystoscope was used to place a 4.8 F open-ended catheter to the level of the intramural ureter, and a low-pressure retrograde ureteropyelogram was done, a 0.9 mm PTFE guidewire was used as a safety wire, the second/ working guidewire was used for insertion of the ureterscope, ureteric dilators (6-9 F) were used in two cases, the semiflexible probe of the Lithoclast or laser fibre was used for the lithotripsy		place and removed in the next 24-72 h
Elderwy 2014	I: Dissolution therapy	Oral potassium sodium hydrogen citrate was administered at a dose of 1 mEq/kg per day in 2 or 3 divided doses after meals for 1 to 3 months	C: Standard shock wave lithotripsy	Lithotripter S was used, a total count of 2,000 shock waves per session at 12 to 14 kV power and a frequency of 60 to 70 per minute
Elgalaly 2017	I: Silodosin	Silodosin 4 mg at bedtime. Ibuprofen (20 mg/kg/day) was divided into two doses for pain episodes.	C: Placebo	Placebo at bedtime. Ibuprofen (20 mg/kg/day) was divided into two doses for pain episodes
Erturhan 2013	I: Ibuprofen only	Ibuprofen 20 mg/kg/d divided into 2 equal doses.	C: alpha-1 blocker (doxazosin) therapy in addition to ibuprofen	Ibuprofen 20 mg/kg/d divided into 2 equal doses and 0.03 mg/kg/d doxazosin once daily, before bed
Fahmy 2017	I: Silodosin	8 mg silodosin daily	C: Tamsulosin or placebo	Tamsulosin group 0.4 mg tamsulosin daily, placebo group were not given any medications
Gamal 2017	I: Flexible ureteroscopy plus lasertripsy	A 7.5 Fr flexible ureterscope (FURS) was intro-	C: Shockwave lithotripsy	Not specified.

Table 1. Description of the interventions (Continued)

		duced into the ureter over a hydrophilic guidewire under visual and fluoroscopic guidance without access sheath. Complete stone dusting using 200 mm laser fiber (0.2-1.0 joules power and 15-30 Hz frequency) was done in all cases ending with a 5 Fr JJ stent insertion		
Kumar 2015	I: Mini percutaneous nephrolithotomy	5F open-ended ureteral catheter was placed in the renal pelvis cystoscopically, anatomy of the pelvicaliceal system was assessed by infusing contrast media via the ureteral catheter, selected calix was punctured under fluoroscopy guidance by an 18-gauge needle using the "bull's eye technique," the tract was dilated to 18F, 15F miniature nephroscope (Richard Wolf, Vernon Hills, IL) was used with pneumatic intracorporeal lithotripsy, stone fragmentation and clearance were confirmed by direct vision and under fluoroscopy, 12F nephrostomy tube, kept in situ for drainage, was removed once urine was clear	C: Shockwave lithotripsy	60 minutes before the procedure 5 gm of a eutectic mixture of lidocaine and prilocaine was applied on approximately 30 cm ² area of skin corresponding to the site of entry of shockwaves electromagnetic lithotripter (Dornier Alpha Compact system, Wessling, Germany), the shockwave delivery rate was 90 pulses per minute, the maximum number of shockwaves was 2500 per session
Mokhless 2012	I: Tamsulosin and standard analgesia	Tamsulosin 0.4 mg for children older than 4 years and 0.2 mg for younger children at bed time in addition to standard analgesia (ibuprofen)	C: Placebo and standard analgesia	Standard analgesia (ibuprofen) and placebo.

Table 1. Description of the interventions (Continued)

Salem 2014	I: Slow delivery rate shock wave lithotripsy	Using the Dornier Lithotripter S (Dornier Medical Systems, Kennesaw, Georgia) with the 220 electromagnetic shock wave emitter, fluoroscopy was used for stone localisation, energy was increased gradually from 14 to 20 kV, in children younger than 4 years the energy was increased to 18 kV, 80 shock waves per minute were used, maximum number of shock waves delivered was 2,500	C: Rapid delivery rate shock wave lithotripsy	Using the Dornier Lithotripter S (Dornier Medical Systems, Kennesaw, Georgia) with the 220 electromagnetic shock wave emitter, fluoroscopy was used for stone localisation, energy was increased gradually from 14 to 20 kV, in children younger than 4 years the energy was increased to 18 kV, 120 shock waves per minute were used, maximum number of shock waves delivered was 2,500
Song 2015	I: Tubeless mini-percutaneous nephrolithotomy	F4 ureteral catheter inserted into the affected renal pelvis through the paediatric cystoscope, Foley catheter was placed and fixed to the ureteral catheter with surgical threads, sterile saline was flushed into the kidney through the ureteral catheter to create an artificial hydronephrosis, 18G biopsy needle was inserted to the targeted renal pelvis, ureteral catheter was expanded by fascia dilator to F14 or F16 while the sheath was left in place, paediatric nephroscope or ureteroscopy was inserted and stones fragmented by holmium laser, fragments were picked or washed out by lavage fluid, residual stones were removed completely or the second nephrostomy access tract for lithotripsy was	C: Standard percutaneous nephrolithotomy	F4 ureteral catheter inserted into the affected renal pelvis through the paediatric cystoscope, Foley catheter was placed and fixed to the ureteral catheter with surgical threads, sterile saline was flushed into the kidney through the ureteral catheter to create an artificial hydronephrosis, 18G biopsy needle was inserted to the targeted renal pelvis, ureteral catheter was expanded by fascia dilator to F14 or F16 while the sheath was left in place, paediatric nephroscope or ureteroscopy was inserted and stones fragmented by holmium laser, fragments were picked or washed out by lavage fluid, residual stones were removed completely or the second nephrostomy access tract

Table 1. Description of the interventions (Continued)

		selected for complete clearance.		for lithotripsy was selected for complete clearance, the nephrostomy tube was removed 24 hours later
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- denotes not reported

^aThe term 'clinical practice setting' refers to the specification of the intervention/comparator as used in the course of a standard medical treatment (such as dose, dose escalation, dosing scheme, provision for contraindications and other important features)

C: comparator; **I:** intervention; **IL:** Illinois; **h:** hours **PTFE:** polytetrafluoroethylen; **YAG:** yattrium aluminium garnet.

Table 2. Baseline characteristics

	Intervention(s) and comparator (s)	Duration of intervention (duration of follow-up)	Description of participants	Trial period	Country	Setting
Aghamir 2012	I: Tubeless percutaneous nephrolithotomy C: Standard percutaneous nephrolithotomy	Follow-up: 24-48 hours after surgery, one week and one month after surgery	< 14 years old, renal stone > 2.5 cm or renal stone with lesser diameter, and extracorporeal shock-wave lithotripsy failure	2010-2011	Iran	Hospital
Aldaquadossi 2015	I: alpha-1 blocker (tamsulosin) therapy in addition to ibuprofen C: Ibuprofen only	Follow-up: weekly for 4 weeks	Group 1: 33 children - mean age 7.7 years; group 2: 34 children - mean age 7.25 years, distal ureteric stone of < 1 cm, and below the common iliac vessels	2010-2013	Egypt	Hospital
Aydogdu 2009	I: Ibuprofen C: Doxazosin and ibuprofen	Follow-up: 19 days (mean)	2-14 years old, radio-opaque lower ureteral stone 2-10 mm	2005-2008	Turkey	Hospital
Basiri 2010	I: Transureteral lithotripsy	Follow-up: 2 weeks postopera-	1-13 years old, dis-	2007-2009	Iran	Hospital

Table 2. Baseline characteristics (Continued)

		tively with ultrasound, another at 3 months with excretory urography (more frequent if persistent stone present)	tal ureteral calculi 15-56 mm ²			
	C: Shock wave lithotripsy					
De Domenicis 2005	I: Ureterscopy plus intracorporeal lithotripsy	Follow-up: 6-8 months	2-17 years old, radio-opaque calculi in distal ureter	1 year (time range not specified)	Italy	Hospital
	C: Extracorporeal shock wave lithotripsy					
Elderwy 2014	I: Dissolution therapy	Follow-up: every 3-4 weeks and every 3-4 months thereafter length of treatment: 3 months	0.5-13 years old, renal calculi 7-24 mm < 500 HU	2010-2012	Egypt	Hospital
	C: Standard shock wave lithotripsy					
Elgalaly 2017	I: Silodosin	Follow-up: history, physical examination, urine analysis, KUB, ultrasonography at 2 and 4 weeks	< 18 years old, single unilateral radiopaque DUS, and largest stone diameter of ≤ 10 mm	2014-2015	Egypt	Hospital
	C: Placebo					
Erturhan 2013	I: Ibuprofen only	Follow-up: for 3 weeks with weekly examinations length of treatment: 3 weeks	3-15 years old, lower ureteral stones (group 1: 4.45 ± 1.5 mm, group 2: 4.58 ± 1.7 mm)	not disclosed in the study	Turkey	Hospital
	C: alpha-1 blocker (doxazosin) therapy in addition to ibuprofen					
Fahmy 2017	I: Silodosin	Follow-up: stone free rate assessed after 4 weeks. Further details of follow up not supplied	< 18 years old, unilateral, single, radio-opaque distal ureteral stones < 10 mm in size	Not specified	Egypt	Hospital

Table 2. Baseline characteristics (Continued)

	C: Tamsulosin or placebo					
Gamal 2017	I: Flexible ureteroscopy plus lasertripsy	Follow-up: stone free rate assessed after 1 month. Further details of follow up not supplied	< 15 years old, with a renal stones (1-2) cm in a solitary kidney	2011-2016	Egypt	Hospital
	C: Shockwave lithotripsy					
Kumar 2015	I: Mini percutaneous nephrolithotomy	Follow-up: 3 weeks	< 15 years old, single lower caliceal stone 1-2 cm	2012-2013	India	Hospital
	C: Shockwave lithotripsy					
Mokhless 2012	I: Tamsulosin and standard analgesia	Follow-up: close for 4 weeks Length of treatment: 4 weeks	2-15 years old, distal ureteric calculi < 12 mm	2007-2010	Egypt	Hospital
	C: Placebo and standard analgesia					
Salem 2014	I: Slow delivery rate shock wave lithotripsy	Follow-up: 2 and 4 weeks	3-14 years old, renal calculi 10-20 mm	2011-2012	Egypt	Hospital
	C: Rapid delivery rate shock wave lithotripsy					
Song 2015	I: Tubeless mini-percutaneous nephrolithotomy	Follow-up: 1, 3, 6, 12 months postoperatively	7-36 months old, renal stones with cumulative diameter < 4.5 cm	2009-2012	China	Hospital
	C: Standard percutaneous nephrolithotomy					

If a field is left empty, the study did not contain the required information

KUB: kidney, ureter, and bladder.

APPENDICES

Appendix I. Electronic search strategies

Database	Search terms
CENTRAL	<ol style="list-style-type: none"> 1. MeSH descriptor Urolithiasis explode all trees 2. (urolithiasis):ti,ab,kw in Trials 3. (nephrolithiasis):ti,ab,kw in Trials 4. (renal NEXT stone*):ti,ab,kw or (renal NEXT calcul*):ti,ab,kw or "renal colic":ti,ab,kw in Trials 5. (kidney NEXT stone*):ti,ab,kw or (kidney NEXT calcul*):ti,ab,kw or "kidney colic":ti,ab,kw in Trials 6. "ureteral NEXT stone*":ti,ab,kw or (ureteral NEXT calcul*):ti,ab,kw or "ureteral colic" or "ureteric colic":ti,ab,kw or (ureteric NEXT stone*):ti,ab,kw or (ureteric NEXT calcul*):ti,ab,kw in Trials 7. (urinary NEXT stone*):ti,ab,kw or (urinary NEXT calcul*):ti,ab,kw in Trials 8. (#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7) 9. MeSH descriptor Child explode all trees 10. MeSH descriptor Infant explode all trees 11. MeSH descriptor Adolescent, this term only 12. (#9 OR #10 OR #11) 13. (#8 AND #12)
MEDLINE	<ol style="list-style-type: none"> 1. urolithiasis.mp. or exp Urolithiasis/ 2. (renal stone\$ or renal calcul\$ or renal colic).mp. 3. (kidney stone\$ or kidney calcul\$ or kidney colic).mp. 4. (ureter\$ stone\$ or ureter\$ calcul\$ or ureter\$ colic).mp 5. (urinary stone\$ or urinary calcul\$ or urinary colic).mp. 6. (urethra\$ stone\$ or urethra\$ calcul\$ or urethra\$ colic).mp. 7. nephrolithiasis.mp. 8. or/1-7 9. adult/ or exp aged/ or exp middle aged/ 10. exp adolescent/ or exp young adult/ or exp child/ or exp infant/ 11. 10 not 9 12. and/8,11 13. randomized controlled trial.pt. 14. controlled clinical trial.pt. 15. randomized.ab. 16. placebo.ab. 17. clinical trials as topic/ 18. randomly.ab. 19. (crossover or cross-over).tw. 20. Cross-over Studies/ 21. trial.ti. 22. or/13-21 23. animals/not (humans/ and animals/ 24. 22 not 23 25. and/12,24 26. and/8,10, 24 27. 26 not 25

(Continued)

EMBASE	<ol style="list-style-type: none"> 1. exp urolithiasis/ 2. (renal stone\$ or renal calcul\$ or renal colic).tw. 3. (kidney stone\$ or kidney calcul\$ or kidney colic).tw. 4. (ureter\$ stone\$ or ureter\$ calcul\$ or ureter\$ colic).tw. 5. (urinary stone\$ or urinary calcul\$).tw. 6. urolithiasis.tw. 7. nephrolithiasis.tw. 8. or/1-7 9. newborn/ 10. child/ 11. adolescent/ 12. or/9-11 13. and/8,12
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Appendix 2. Conference abstracts search

Congress of British Association of Paediatric Urologists	Cambridge, 2012-2016
Annual Congress of European Society for Paediatric Urology	27th: Harrogate 2016 26th: Prague 2015 25th: Innsbruck 2014 24th: Genoa 2013 23th: Zurich 2012
American Association of Paediatric Urologists annual meetings	2012: Herradura, Costa Rica 2013: Jackson Hole, Wyoming 2014: La Romana, Dominican Republic 2015: Lake Louise, Alberta, Canada 2016: Guanacaste, Costa Rica
Asia Pacific Association of Paeds Urologists congress	2016: Zhengzhou, China 2015: Kuala Lumpur 2014: Tochigi, Japan 2013: Hualien, Taiwan 2012: Busan, Korea

Appendix 3. Risk of bias assessment tool

Potential source of bias	Assessment criteria
Random sequence generation Selection bias (biased allocation to interventions) due to inadequate generation of a randomised sequence	<i>Low risk of bias:</i> Random number table; computer random number generator; coin tossing; shuffling cards or envelopes; throwing dice; drawing of lots; minimization (minimization may be implemented without a random element, and this is considered to be equivalent to being random)
	<i>High risk of bias:</i> Sequence generated by odd or even date of birth; date (or day) of admission; sequence generated by hospital or clinic record number; allocation by judgement of the clinician; by preference of the participant; based on the results of a laboratory test or a series of tests; by availability of the intervention
	<i>Unclear:</i> Insufficient information about the sequence generation process to permit judgement
Allocation concealment Selection bias (biased allocation to interventions) due to inadequate concealment of allocations prior to assignment	<i>Low risk of bias:</i> Randomisation method described that would not allow investigator/participant to know or influence intervention group before eligible participant entered in the study (e.g. central allocation, including telephone, web-based, and pharmacy-controlled, randomisation; sequentially numbered drug containers of identical appearance; sequentially numbered, opaque, sealed envelopes)
	<i>High risk of bias:</i> Using an open random allocation schedule (e.g. a list of random numbers); assignment envelopes were used without appropriate safeguards (e.g. if envelopes were unsealed or non-opaque or not sequentially numbered); alternation or rotation; date of birth; case record number; any other explicitly unconcealed procedure
	<i>Unclear:</i> Randomisation stated but no information on method used is available
Blinding of participants and personnel Performance bias due to knowledge of the allocated interventions by participants and personnel during the study	<i>Low risk of bias:</i> No blinding or incomplete blinding, but the review authors judge that the outcome is not likely to be influenced by lack of blinding; blinding of participants and key study personnel ensured, and unlikely that the blinding could have been broken
	<i>High risk of bias:</i> No blinding or incomplete blinding, and the outcome is likely to be influenced by lack of blinding; blinding of key study participants and personnel attempted, but likely that the blinding could have been broken, and the outcome is likely to be influenced by lack of blinding
	<i>Unclear:</i> Insufficient information to permit judgement

(Continued)

<p>Blinding of outcome assessment Detection bias due to knowledge of the allocated interventions by outcome assessors</p>	<p><i>Low risk of bias:</i> No blinding of outcome assessment, but the review authors judge that the outcome measurement is not likely to be influenced by lack of blinding; blinding of outcome assessment ensured, and unlikely that the blinding could have been broken</p> <p><i>High risk of bias:</i> No blinding of outcome assessment, and the outcome measurement is likely to be influenced by lack of blinding; blinding of outcome assessment, but likely that the blinding could have been broken, and the outcome measurement is likely to be influenced by lack of blinding</p> <p><i>Unclear:</i> Insufficient information to permit judgement</p>
<p>Incomplete outcome data Attrition bias due to amount, nature or handling of incomplete outcome data</p>	<p><i>Low risk of bias:</i> No missing outcome data; reasons for missing outcome data unlikely to be related to true outcome (for survival data, censoring unlikely to be introducing bias); missing outcome data balanced in numbers across intervention groups, with similar reasons for missing data across groups; for dichotomous outcome data, the proportion of missing outcomes compared with observed event risk not enough to have a clinically relevant impact on the intervention effect estimate; for continuous outcome data, plausible effect size (difference in means or standardized difference in means) among missing outcomes not enough to have a clinically relevant impact on observed effect size; missing data have been imputed using appropriate methods</p> <p><i>High risk of bias:</i> Reason for missing outcome data likely to be related to true outcome, with either imbalance in numbers or reasons for missing data across intervention groups; for dichotomous outcome data, the proportion of missing outcomes compared with observed event risk enough to induce clinically relevant bias in intervention effect estimate; for continuous outcome data, plausible effect size (difference in means or standardized difference in means) among missing outcomes enough to induce clinically relevant bias in observed effect size; 'as-treated' analysis done with substantial departure of the intervention received from that assigned at randomisation; potentially inappropriate application of simple imputation</p> <p><i>Unclear:</i> Insufficient information to permit judgement</p>
<p>Selective reporting Reporting bias due to selective outcome reporting</p>	<p><i>Low risk of bias:</i> The study protocol is available and all of the study's pre-specified (primary and secondary) outcomes that are of interest in the review have been reported in the pre-specified way; the study protocol is not available but it is clear that the published reports include all expected outcomes, including those that were pre-specified (convincing text of this nature may be uncommon)</p>

(Continued)

	<p><i>High risk of bias:</i> Not all of the study's pre-specified primary outcomes have been reported; one or more primary outcomes is reported using measurements, analysis methods or subsets of the data (e.g. subscales) that were not pre-specified; one or more reported primary outcomes were not pre-specified (unless clear justification for their reporting is provided, such as an unexpected adverse effect); one or more outcomes of interest in the review are reported incompletely so that they cannot be entered in a meta-analysis; the study report fails to include results for a key outcome that would be expected to have been reported for such a study</p> <p><i>Unclear:</i> Insufficient information to permit judgement</p>
<p>Other bias Bias due to problems not covered elsewhere in the table</p>	<p><i>Low risk of bias:</i> The study appears to be free of other sources of bias.</p> <p><i>High risk of bias:</i> Had a potential source of bias related to the specific study design used; stopped early due to some data-dependent process (including a formal-stopping rule); had extreme baseline imbalance; has been claimed to have been fraudulent; had some other problem</p> <p><i>Unclear:</i> Insufficient information to assess whether an important risk of bias exists; insufficient rationale or evidence that an identified problem will introduce bias</p>

CONTRIBUTIONS OF AUTHORS

- Drafting the protocol: LB
- Study selection: LB, AA
- Extracting data from studies: LB, MK
- Entering data into Review Manager: LB, AA, JHJ
- Carrying out the analysis: LB, JHJ
- Interpreting the analysis: JHJ, LB, GPCD
- Drafting the final review: LB, JHJ, AA, MA
- Disagreement resolution: MK
- Updating the review: LB, AA

All review authors read and approved the final review draft.

DECLARATIONS OF INTEREST

LB: none known.

AA: none known.

JHJ: none known.

MA: none known.

GPCD: none known.

MK: none known.

SOURCES OF SUPPORT

Internal sources

- Departmental, UK.

External sources

- None to declare, UK.

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

We provided more detail of the type of participants by clarification of the exclusion criteria.

We excluded trials of children with lower urinary tract stones such as urinary bladder or urethral stones.

We added methodological explanations in the [Search methods for identification of studies](#) and [Data collection and analysis](#) sections, in accordance with suggestions from Cochrane Urology.

We revised the primary outcomes ([Types of outcome measures](#)).

- From: SFR defined as complete stone clearance or clinically insignificant residual fragments ≤ 3 mm, to: SFR defined as complete stone clearance or clinically insignificant residual fragments measuring less than 4 mm. This change was made because fragments 4 mm and less are generally accepted as not clinically significant.

- From: adverse events and complications after treatment, to: serious adverse events or complications of treatment defined as Clavien-Dindo classification 3 or over. This change was made because the Clavien-Dindo classification is widely used for grading adverse events and is now used in most urology units.

- From: number of second procedures for residual fragments ≥ 4 mm, to: secondary procedures for residual fragments measuring 4 mm or more. This change was made because fragments of smaller size don't usually require surgical intervention.

We revised the secondary outcomes ([Types of outcome measures](#)).

- We removed rate of second procedures for clinically insignificant residual fragments ≤ 3 mm. This change was made because fragments 3 mm and less in size are not clinically significant and under normal circumstances do not require surgical intervention.

- We changed mean hospital stay to hospital stay measured in days.

We addressed definition of clinically meaningful threshold for continuous outcomes to assess imprecision in GRADE.

We added main outcomes for 'Summary of findings' table.

We revised subgroup analysis and added the reason to perform the analysis.

- From: size of the kidney stone (≥ 4 mm and < 5 mm; 5 mm to 10 mm; > 10 mm), to: size of the kidney stone (less than 10 mm versus 10 mm or more).

NOTES

We have based parts of the background and methods sections, the 'Characteristics of studies' tables and 'Summary of findings' tables and Figures 1 to 3 of this review on a standard template established by the Cochrane Renal Group. The additional tables are based on the template established by the Cochrane Metabolic and Endocrine Disorders Group.

INDEX TERMS

Medical Subject Headings (MeSH)

Adrenergic alpha-Antagonists [*therapeutic use]; Lasers, Solid-State [therapeutic use]; Length of Stay; Lithotripsy [adverse effects; *methods]; Nephrolithiasis [*therapy]; Randomized Controlled Trials as Topic; Ureterolithiasis [*therapy]; Ureteroscopy [adverse effects; *methods]

MeSH check words

Adolescent; Child; Child, Preschool; Humans; Infant; Infant, Newborn