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Water for preventing urinary stones (Review)

Bao Y, Tu X, Wei Q

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TABLE OF CONTENTS

[Intervention Review]

Water for preventing urinary stones

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ABSTRACT

Background

Urinary stone disease is a common condition characterised by increasing prevalence and high rates of recurrence. Observational studies have reported that increased water intake played a role in the prevention of urinary stone formation but with limited strength of evidence.

Objectives

To compare the effects of increased water intake with standard water intake for the prevention of urinary stone formation in participants with or without a history of urinary stones.

Search methods

We performed a systematic search of PubMed (MEDLINE), EMBASE (Ovid) and the Cochrane Library to 15 October 2019. We handsearched review articles, clinical trial registries, and reference lists of retrieved articles. We did not apply any restrictions to publication language or publication status.

Selection criteria

We included randomised controlled trials (RCTs) and quasi-RCTs looking at the benefits and harms of increased water intake versus standard water intake for the prevention of urinary stone formation in participants with or without a history of urinary stones.

Data collection and analysis

We used standard methodological procedures expected by Cochrane. Two review authors independently extracted data and assessed the risk of bias of included studies. We pooled dichotomous outcomes (e.g. incidence/recurrence rate of urinary stones; adverse events) using risk ratios (RRs) with 95% confidence intervals (CIs). We calculated hazard ratio (HRs) and corresponding 95% CIs to assess the intervention effect for time-to-event outcomes. We assessed the certainty of the evidence by using the GRADE criteria.

Main results

Our search identified no RCTs investigating the role of increased water intake for the prevention of urinary stone formation in participants with no history of urinary stones (primary prevention). We found one RCT assessing the effects of increased water intake versus standard water intake for the prevention of urinary stone formation in people with a history of urinary stones (secondary prevention). This trial randomised 220 participants (110 participants in the intervention group with increased water intake and 110 in the control group with standard water intake). Increased water intake was defined as achieving a urine volume of at least 2.0 L per day by drinking water.

Based on this study, increased water intake may decrease stone recurrences (RR 0.45, 95% CI 0.24 to 0.84; 199 participants; low-certainty evidence); this corresponds to 149 fewer (43 fewer to 205 fewer) stone recurrences per 1000 participants with 270 stone recurrence per 1000 participants over five years in the control group.

Increased water intake may also prolong the time to urinary stone recurrence compared to standard water intake (HR 0.40, 95% CI 0.20 to 0.79; 199 participants; low-certainty evidence); based on a stone recurrence rate of 270 per 1000 participants over five years, this corresponds to 152 fewer (209 fewer to 50 fewer) recurrences per 1000 participants.

For both outcomes we downgraded the certainty of evidence for study limitations and imprecision. We found no evidence for the outcome of adverse events

Authors' conclusions

We found no RCT evidence on the role of increased water intake for primary prevention of urinary stones. For secondary prevention, increased water intake achieving a urine volume of at least 2.0 L/day may reduce urinary stone recurrence and prolong time to recurrence for people with a history of urinary stone disease. However, our confidence in these findings is limited. We did not find evidence for adverse events.

PLAIN LANGUAGE SUMMARY

Increased water intake for preventing urinary stones

Review question

We performed this review to find out whether drinking more water prevents people from getting kidney stones.

Background

Kidney stones are common in people. Drinking more water may prevent people who have never had stones to get stones and/or help people who have had stones in the past to not get them again. We are uncertain how well this works and whether drinking more water has unwanted effects.

Study characteristics

We examined research published up to October 2019. We included studies which by chance decided whether people were asked to drink more water (to produce at least 2 litres of urine) or were given no special instructions. We found no studies of people who had never had kidney stones. We found one study, performed in 220 people who had calcium-containing stones in the past, but were stone-free when they started the study. The average age was approximately 41 years, and two-thirds of participants were men.

Key results

We found that drinking more water may reduce the risk of stones coming back. It may also prolong the time it takes for stones to come back. We found no evidence of unwanted effects.

Certainty of evidence

The certainty of evidence for both outcomes for which we found evidence was low. This means that the true results may be quite different.

Summary of findings for the main comparison. Increased water intake compared to standard water intake for secondary prevention of urinary stones

Increased water intake compared to standard water intake for secondary prevention of urinary stones

Patient or population: participants with a prior history of nephrolithiasis
Setting: community care, outpatient
Intervention: increased water intake (≥ 2 L/day)
Comparison: standard water intake

Outcomes	№ of participants (studies)	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)	
				Risk with standard water intake	Risk difference with increased water intake
Stone recurrence (assessed as symptomatic renal colic/stone expulsion episodes and imaging)	199 (1 RCT)	⊕⊕⊖⊖ Low[a,b]	RR 0.45 (0.24 to 0.84)	Study population	
				270 per 1000	149 fewer per 1000 (205 fewer to 43 fewer)
Time to recurrence (absolute event rate based on 5-year follow-up; assessed as symptomatic renal colic/stone expulsion episodes and imaging)	199 (1 RCT)	⊕⊕⊖⊖ Low[a,b]	HR 0.40 (0.20 to 0.79)	Study population	
				270 per 1000	152 fewer per 1000 (209 fewer to 50 fewer)
Adverse events	(0 studies)	N/A	not estimable	Study population	
				0 per 1000	0 fewer per 1000 (0 fewer to 0 fewer)

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the __relative effect__ of the intervention (and its 95% CI).

CI: confidence interval; **HR**: hazard ratio; **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.

[a]Downgraded for study limitations mainly for unclear risk of bias for selection bias and unclear or high risk of performance, detection bias, attrition and selective reporting bias.
[b]Downgraded for wide confidence interval that crossed threshold for a clinically relevant effect size (absolute risk reduction of 5%).

BACKGROUND

Description of the condition

Urinary stones are common in the general population and the prevalence varies regionally (Medina-Escobedo 2002; Pinduli 2006; Ramello 2000). A higher incidence rate is observed in certain parts of the world, like Southern England, Asia, the Middle East (Pak 1980), and South-East USA (Brikowski 2008). According to a more recent cross-sectional analysis of the National Health and Nutrition Examination Survey (NHANES), the overall prevalence of urinary stones in 2007 to 2010 was 8.8% in the USA, representing a 70% increase over the last 15 years (Scales 2012). Similar trends for increased stone prevalence were also observed in some other countries, like England and Japan (Rukin 2017; Yasui 2008).

Urinary stones can originate from the upper (kidney and ureter) and lower (bladder and urethra) urinary tract, with the majority occurring in the kidneys initially. Treatment options mainly include conservative treatment (observation), medical expulsive treatments and surgical procedures, based on stone size, location and with or without associated symptoms (Assimos 2016; Türk 2018). The application of minimal invasive technologies by using shock wave lithotripsy (SWL), as well as other endourologic procedures in recent years, has greatly improved efficiency in the managing process (Pradere 2018). However, the high probability of recurrence should not be ignored. The symptomatic recurrence rates at 10 and 15 years were reported to be 31% and 39%, respectively (Rule 2014). And a higher risk of recurrence was observed for those patients without sufficient preventive procedures (Kirkali 2015).

The increasing prevalence and high recurrence rate of urinary stone disease pose a significant healthcare burden. In the USA, emergency department visit rates for urinary stones has nearly doubled from 1992 to 2009, with recurrent episodes accounting for about 10% of emergency care visits (Fwu 2013). Furthermore, the annual direct medical cost of urinary stone disease was estimated to be USD 10 billion, making it one of the most expensive urologic conditions (Litwin 2012). Therefore, there is an urgency to improve prevention strategies for urinary stones.

Description of the intervention

The prevention of urinary stones aims at modifying concentrations of lithogenic factors in the urine. A variety of pharmacologic interventions and dietary changes may help (Qaseem 2014). For example, preventive medications might work for specific patients under risk. However, the financial burden, potential side effects as well as poor patient compliance limits their routine use in clinical practice (Escribano 2009). Dietary changes mainly refer to reducing intake of oxalate, animal protein and other purines (Taylor 2006). However, these modifications were usually combined as a multi-component diet. Their independent role remained unclear and could not be easily assessed separately (Dussol 2008; Muldowney 2002).

Increasing water intake is an effective and economical way to increase urine volume and decrease concentration of calcium, oxalate and other salts in the urine, which may help slow down the stone formation process. The potential role of water intake in preventing urinary stones was firstly introduced by Frank et al in the 1960s. They reported that people living in a tropical climate without adequate fluid intake harboured higher incidence of urinary stones (Frank 1966). More direct evidence of its prevention effect came from two large observational studies. The National Health Professionals cohort recruited 51,529 participants without a history of nephrolithiasis. During a follow-up of 14 years, they found that participants drinking more than 2.5 L water/day had decreased stone formation risk compared with those drinking less than 1.2 L/day (Curhan 1997a; Taylor 2004). Another study covered more than 90,000 women (Nurses' Health Study I) with no history of kidney stones. The study reported that the daily water intake of more than 2.5 L resulted in a lower incidence of urinary stones compared with that of less than 1.4 L (116 cases/100,000 person-years versus 232 cases/100,000 person-years) (Curhan 1997b). The association was strengthened by revealing an inverse relationship between the volume of water intake and the risk of stone formation in the Nurses' Health Study II in 2004 (Curhan 2004).

On the other hand, researchers have also reported the role of water intake in the secondary prevention of urinary stones in their studies with sample size ranging from 108 to 256 participants and follow-up time ranging from 3.0 to 5.2 years (Daudon 2005; Embon 1990; Hosking 1983; Strauss 1982). Participants with a history of urinary stones in these studies were encouraged to increase daily water intake (ranging from 1.9 L/day to 3.0 L/day). Their results indicated that participants who suffered from stone recurrence tended to have less daily urine volume compared with those who remained stone-free.

Taking into account all the evidence reported, increased water intake may potentially play a role for the prevention of stone formation in people with or without a history of urinary stones.

How the intervention might work

One prevailing hypothesis is that increasing water intake leads to an increased urine volume and helps increase the threshold level at which calcium oxalate crystallises. Eventually, the formation potential of urinary stones decreases. The rationale is that the prerequisite of stone formation is considered to be the result of supersaturation of stone-forming compounds including calcium, oxalate, phosphorus and uric acid. Increasing urine volume may help reduce the saturation of calcium oxalate, calcium phosphate and monosodium urate, and theoretically benefit all people predisposed to the disease.

Why it is important to do this review

Urinary stone disease is common, affecting almost one out of every 11 people, and poses a significant healthcare burden worldwide. Given the increasing prevalence and high recurrence rate of urinary stone disease, there is an urgency to improve prevention strategies. Increasing water intake is an effective and economical way to increase urine volume and reduce saturation of stone-forming compounds, which may help slow down the stone formation process. Observational studies have reported that increasing water intake played a role in the prevention of urinary stone formation. And our previous work revealed potential effects of increased water intake in preventing recurrence of urinary stones on the basis of prospective intervention trials (Bao 2012). We have updated our previous work based on the latest evidence and rated the certainty of evidence using GRADE.

OBJECTIVES

To compare the effects of increased water intake with standard water intake for the prevention of urinary stone formation in participants with or without a history of urinary stones.

METHODS

Criteria for considering studies for this review

Types of studies

All randomised controlled studies (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) looking at the benefits and harms of increased water intake for the prevention of urinary stone disease. We included the first period of randomised cross-over studies.

Types of participants

Inclusion criteria

- Participants without a history of urinary stones (primary prevention)
  - aged more than 18 years old
  - with no history of urinary stones
- Participants with a history of urinary stones (secondary prevention)
  - aged more than 18 years old
  - with a history of urinary stones, as documented on imaging by ultrasound; kidney, ureter and bladder (KUB) radiography; or computer tomography (CT) scan
  - the primary stone episode was resolved by spontaneous expulsion of the calculus, medical expulsive treatment, shock wave lithotripsy (SWL), percutaneous nephrolithotomy or other procedures (primary procedures)

Exclusion criteria

- Studies recruiting participants with genetically defined metabolic stone diseases (e.g. cystinuria, primary hyperoxaluria etc.)
- Studies recruiting participants on medications predisposing to urinary stones, or participants taking urinary stone preventive medications (e.g. thiazide diuretics, potassium salts, allopurinol, phosphate etc.)

Types of interventions

We investigated the following comparisons of experimental versus comparator interventions.

Experimental interventions

- Increased water intake

Participants were put into an enforced fluid intake programme (e.g. plain drinking water, beverages, mineral water, and carbonated water etc.) to achieve a daily urine volume of at least 2 litres and with a minimum duration of intervention for 12 months.

Comparator interventions

- Standard water intake

No specific diet changes apart from close follow-up.

Comparisons

- Increased water intake versus standard water intake for the primary/secondary prevention of urinary stones

If we included a study with more than two intervention arms, we only included experimental and comparator intervention groups that met the eligibility criteria of the review.

Types of outcome measures

- Proportion of participants with new urinary stones
- Time to urinary stone formation, as measured from the date of randomisation to the date of new urinary stone formation (symptomatic stones in case of colic or expulsion of calculi during follow-up, or asymptomatic stones detected by imaging studies)
- Proportion of participants with adverse events

Main outcomes for 'Summary of findings' table

We presented all outcomes of this updated review in a GRADE 'Summary of findings' table.

Search methods for identification of studies

This is an updated review originally published in 2004 and updated in 2011. We performed a systematic and updated search (from January 2011 to October 2019) with no restriction on publication status or languages.

Electronic searches

We searched the following databases using search terms relevant to this review (See Appendix 1).

- The Cochrane Library
  - *Cochrane Database of Systematic Reviews* (CDSR)
  - Cochrane Central Register of Controlled Trials (CENTRAL)
  - Database of Abstracts of Reviews of Effects (DARE)
  - Health Technology Assessment Database (HTA)
- PubMed (MEDLINE)
- EMBASE (Journals@Ovid, EMBASE)

We also searched the following trial registries.

- ClinicalTrials.gov (www.clinicaltrials.gov/).
- World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP) search portal (apps.who.int/trialsearch/).

Searching other resources

We identified other potentially eligible trials or ancillary publications by screening reference lists of retrieved included trials, reviews, meta-analyses and health technology assessment reports (from January 2011 to October 2019). We contacted study authors of included trials to identify any further studies that we might have missed.

We also searched abstract proceedings of major relevant meetings (American Urological Association and European Association of

Urology) for the last three years (2017 to 2019) to identify unpublished studies.

Data collection and analysis

Selection of studies

After removing duplicate records, two review authors (Bao Y, Tu X) independently screened abstracts and titles of the remaining records to determine which studies should be assessed further. We then investigated all potentially relevant records as full-text and classified studies as included studies, excluded studies, studies awaiting classification, or ongoing studies (Higgins 2011a). We documented reasons for exclusion of studies. We resolved discrepancies through consensus or recourse to a third review author (Wei Q). We presented the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram showing the process of study selection (Liberati 2009).

Data extraction and management

We developed a dedicated data extraction form. For studies that fulfilled inclusion criteria, two review authors (Bao Y, Tu X) independently extracted the following information.

- Study design
- Study dates
- 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 fluid type and volume
- Definitions of relevant outcomes, and method and timing of outcome measurement as well as any relevant subgroups
- Study funding sources
- Declarations of interest by primary investigators

We extracted outcome data relevant to this Cochrane Review as needed for calculation of summary statistics and measures of variance. For dichotomous outcomes, we obtained numbers of events and totals for population of a 2 x 2 table, as well as summary statistics with corresponding measures of variance. For continuous outcomes, we obtained means and standard deviations (SDs) or data necessary to calculate this information. We resolved any disagreements by discussion, or, if required, by consultation with a third review author (Wei Q). We provided information, including trial identifier, about potentially relevant ongoing studies in the table 'Characteristics of ongoing studies'. We attempted to contact authors of included studies to obtain key 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 sought to maximise the yield of information by mapping all publications to unique studies and collating all available data. We used the most complete data set aggregated across all known publications. In case of doubt, we had planned to give priority to the publication reporting the longest follow-up associated with our primary outcomes.

Assessment of risk of bias in included studies

Two review authors (Bao Y, Tu X) assessed the risk of bias for each included study independently. We resolved disagreements by consensus, or by consultation with a third review author (Wei Q). We assessed the risk of bias using Cochrane's 'Risk of bias' assessment tool which included the following domains (Higgins 2011b).

- Random sequence generation (selection bias)
- Allocation concealment (selection bias)
- Blinding of participants and personnel (performance bias)
- Blinding of outcome assessment (detection bias)
- Incomplete outcome data (attrition bias)
- Selective reporting (reporting bias)
- Other sources of bias

We judged the domains as 'low risk', 'high risk' or 'unclear risk' as well as evaluated individual bias items as described in the *Cochrane Handbook for Systematic Reviews of Interventions*(Higgins 2011b, see Appendix 2). We presented a 'Risk of bias' summary figure to illustrate these findings.

We assessed 'Risk of bias' on a per outcome basis. Since the two outcomes for which we found data had identical risk of bias ratings, we collapsed their risk of bias presentation.

Measures of treatment effect

We pooled dichotomous outcomes (e.g. incidence/recurrence rate of urinary stones; adverse events) using risk ratio (RRs) with 95% confidence intervals (CIs). We calculated hazard ratio (HRs) and corresponding 95% CIs to assess the intervention effect for time-to-event outcomes. Estimated HRs were to be calculated on the basis of Tierney's relevant equations in case of the absence of individual participant data (Tierney 2007). When data aggregation was not feasible, results were presented in a descriptive analysis.

Unit of analysis issues

The unit of analysis was the individual participant. We handled trials with more than two intervention groups for inclusion in the review in accordance with guidance provided in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011c).

Dealing with missing data

Any further information required from the original trial author was requested by contacting the authors (email to corresponding author) and any relevant information obtained was included in the review. We performed intention-to-treat (ITT) analyses if data were available. Otherwise we performed available case analyses.

Assessment of heterogeneity

We planned to identify heterogeneity (inconsistency) through visual inspection of the forest plots to assess the amount of overlap of CIs, and the I^2 statistic, which quantified inconsistency across studies to assess the impact of heterogeneity in the meta-analysis (Higgins 2002; Higgins 2003); We interpreted the I^2 statistic as follows (Deeks 2011):

- 0% to 40%: may not be important;
- 30% to 60%: may indicate moderate heterogeneity;
- 50% to 90%: may indicate substantial heterogeneity;

- 75% to 100%: considerable heterogeneity.

Since we only found a single study, we did not assess inconsistency.

Assessment of reporting biases

We planned to assess publication bias using funnel plot analysis if we had included 10 studies or more investigating a particular outcome (Higgins 2011a).

Data synthesis

We performed statistical analyses according to the statistical guidelines contained in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011a). For dichotomous outcomes, we used the Mantel-Haenszel method; for continuous outcomes and time-to-event outcomes, we used the inverse variance method. The summary estimates were generated using a fixed-effect model considering that only one RCT was included. A random-effect model was to be performed in case of the presence of heterogeneity when we included more than one study. We used Review Manager 5 to perform analysis (Review Manager 2014).

Subgroup analysis and investigation of heterogeneity

The increased water intake may help prevent stone formation by increasing urine volume and reducing the concentration of calcium, oxalate and other salts in the urine. Different volumes of water intake may have different impacts on the concentration of urinary stones; this may produce heterogeneity. And the adverse events (e.g. water intoxication) may be related to water volume. Besides, different types of water may be used to increase urine volume which may also have different effects on the outcomes. And participants with different types of primary stones may have different reactions to the water therapy. With sufficient studies, we planned to perform the following subgroup analyses to determine whether the effects of the intervention vary and whether these subgroups introduce heterogeneity.

- Different volumes of water intake (to determine the threshold level for water intake).
- Different types of water (e.g. plain drinking water, beverages, mineral water, and carbonated water etc.)
- Different types of urinary stones (e.g. calcium, uric acid).

We were unable to conduct any of the preplanned subgroup analyses.

Sensitivity analysis

We planned to perform sensitivity analyses by excluding studies judged to be at 'high risk' or 'unclear risk' of bias for the particular outcome but were unable to do so.

'Summary of findings' table

We presented the overall certainty of the evidence for each outcome according to the GRADE approach, which considers five criteria related to internal validity (risk of bias, inconsistency, imprecision, publication bias) and external validity (directness of results) (Guyatt 2008). For each comparison, two review authors (Bao Y and Tu X) independently rated the certainty of evidence for each outcome as 'high,' 'moderate,' 'low' or 'very low' using GRADEpro GDT (GRADEpro GDT 2015). We resolved any discrepancies by consensus, or, if needed, by arbitration with a third review author (Wei Q). For each comparison, we presented a summary of the evidence for the main outcomes in a 'Summary of findings' table, which provided 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 2011; Schünemann 2011).

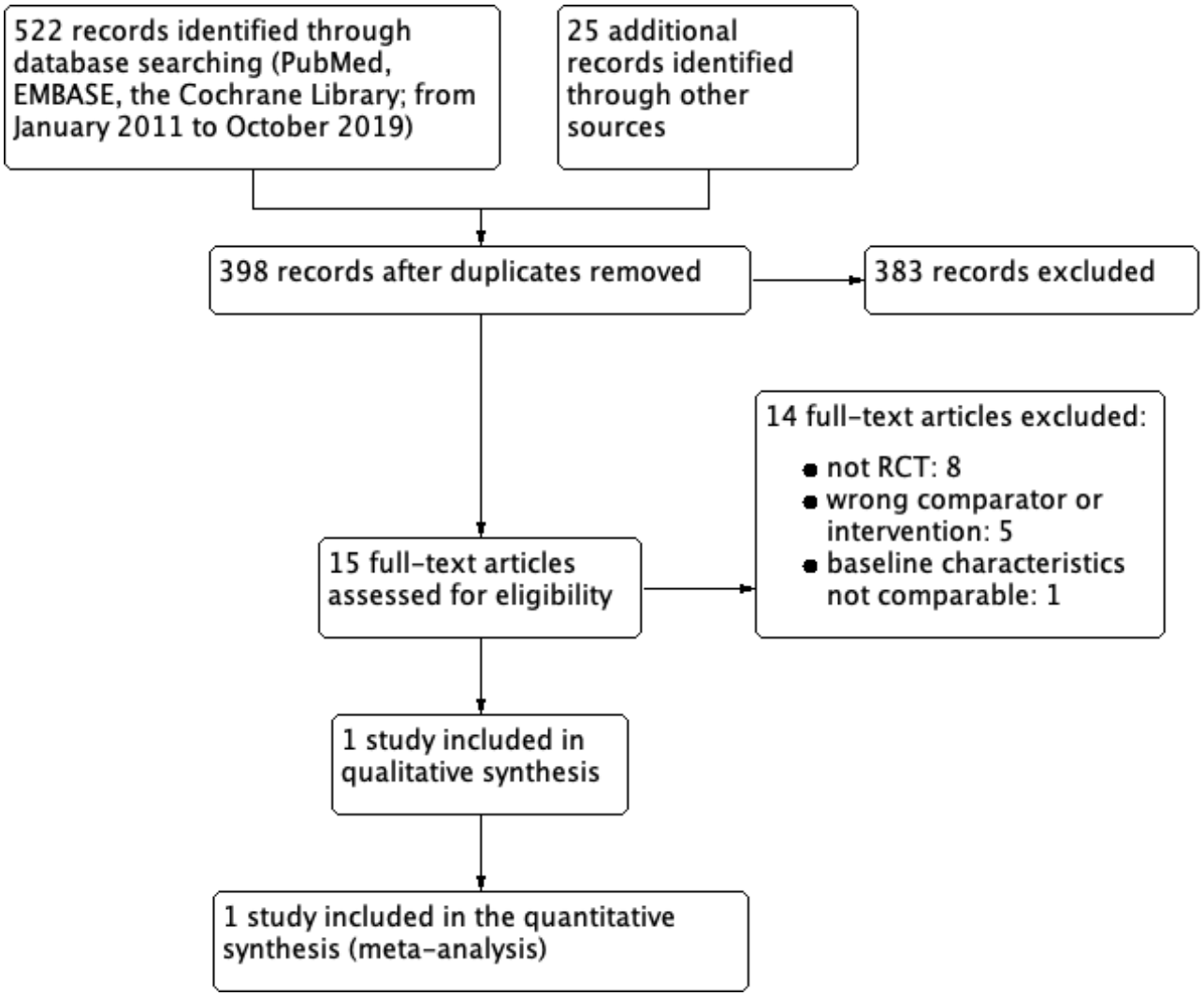
RESULTS

Description of studies

Results of the search

Through an updated search of PubMed (MEDLINE), EMBASE (Ovid) and the Cochrane Library, we identified 522 records from January 2011 to October 2019 (See Figure 1). We identified 25 additional records by searching trial registries and manually searching citing and reference lists. We screened 15 full-text studies and excluded studies that were reviews, wrong comparator or non-randomised controlled trial (RCTs) (Characteristics of excluded studies). We also excluded one RCT (Sarica 2006; see below) which randomised participants with renal stone disease prior to shock wave lithotripsy (SWL). Ultimately, only one RCT was eligible for quantitative analysis (Borghi 1996).

Figure 1. Study flow diagram.



Included studies

We found no studies that investigated the role of increased water intake for the primary prevention of urinary stone formation.

For patients with a history of urinary stones, we included one study with 220 participants which evaluated the preventive effects of increased water intake for stone recurrence (Characteristics of included studies; Table 1; Table 2). The study was conducted in Parma, Italy and enrolled patients with one prior episode of idiopathic calcium nephrolithiasis (with chemical analysis showing a calcium oxalate stone with or without traces of calcium phosphate) that had resolved by spontaneous stone passage or had been treated with SWL, percutaneous technique or other procedures (Borghi 1996). It randomised 220 participants to either increase water intake reaching a urine volume ≥ 2 L/day (intervention group) or to drink water as usual (control group). With a follow-up of five years, 199 participants completed the study (intervention group: 99; control group: 100).

Excluded studies

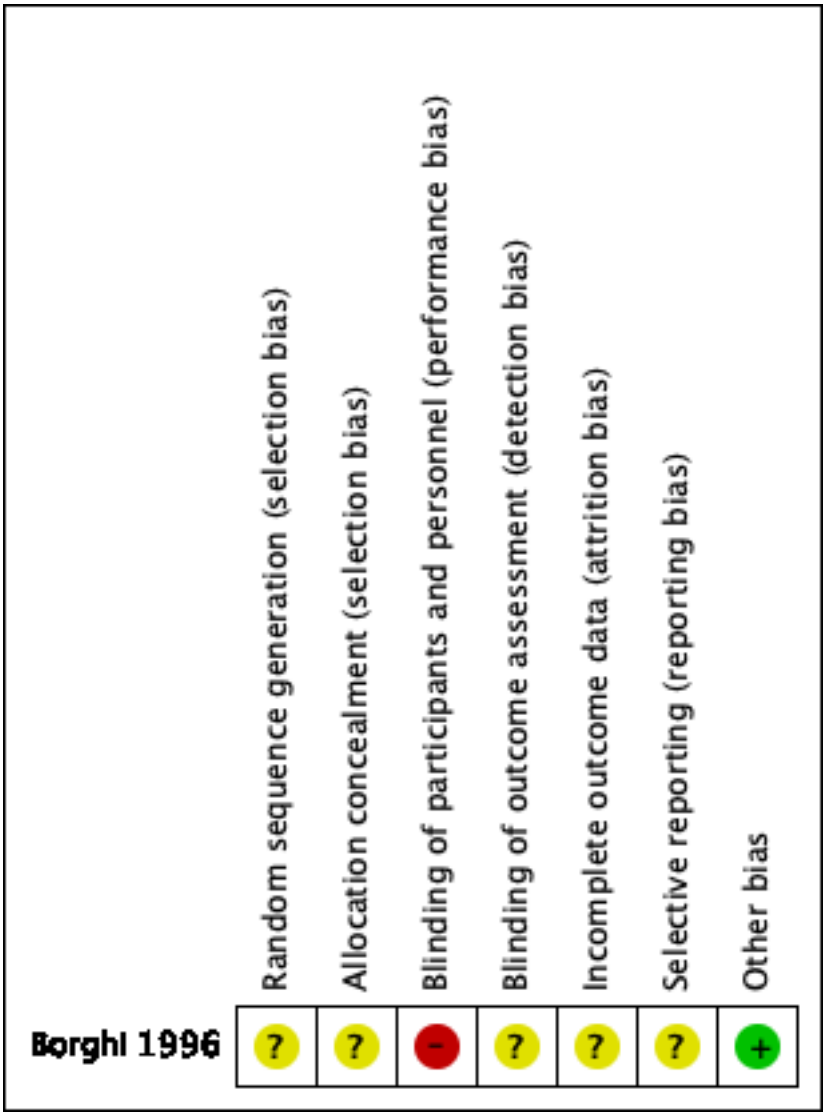
We identified 14 studies which we fully screened and subsequently excluded (see Characteristics of excluded studies). One ongoing study previously identified was not yet recruiting participants (NCT01100580; Characteristics of ongoing studies).

Of note, we identified one RCT which recruited 70 consecutive patients with urinary stones in the renal pelvis (Sarica 2006). Participants were randomised prior to SWL into three different groups (medication group: 25; increased water intake group: 25; control group: 20). Participants in the increased water intake group (intervention group) were put into an enforced fluid intake programme (to achieve urine volume of more than 2.5 L/day) and those in the control group received no intervention. Only a subset of 21 participants who achieved stone freedom after SWL (intervention group: 12; control group: 9) were then followed up for stone recurrence for three years. Given that these participants were randomised prior to SWL, we cannot assume that the subset of participants that become stone-free and were then followed represented two groups that were comparable at baseline; thus, we excluded this study.

Risk of bias in included studies

We assessed risk of bias according to the Cochrane 'Risk of bias' tool (Higgins 2011b; Figure 2; Characteristics of included studies).

Figure 2. Risk of bias summary: review authors' judgements about each risk of bias item for each included study.



Allocation

The included study provided no sufficient information for random sequence generation or allocation concealment. The risk of bias was unclear.

Blinding

Performance bias

Blinding was not performed for participants (not feasible). We assessed the risk of performance bias as high.

Detection bias

No sufficient available data reported blinding outcome assessment in the included study. We rated the risk of bias as unclear.

Incomplete outcome data

The missing outcome data balanced in numbers across intervention (11 out of 110 participants) and control group (10 out of 110 participants) in the included study (Borghi 1996). Given the attrition rate of 10% we judged the risk of bias as unclear.

Selective reporting

There was no protocol available for the included study; therefore we rated the risk of bias as unclear.

Other potential sources of bias

We detected no other potential threats to validity; therefore we rated the risk of bias as low.

Effects of interventions

See: **Summary of findings for the main comparison** Increased water intake compared to standard water intake for secondary prevention of urinary stones

Increased water intake versus standard water intake for primary prevention

No available studies investigated the effects of increased water intake for the prevention of urinary stone formation in participants with no history of urinary stones.

Increased water intake versus standard water intake for secondary prevention

One study with 220 participants evaluated the preventive effects of increased water intake for participants with a history of urinary stones and reported the time to recurrence for both groups (Borghi 1996). See Summary of findings for the main comparison.

Primary outcomes

Stone recurrence

Increased water intake may reduce the recurrence rate of urinary stones (risk ratio (RR) 0.45, 95% confidence interval (CI) 0.24 to 0.84; 1 study, 199 participants; Analysis 1.1). This would correspond to 149 fewer (43 fewer to 205 fewer) stone recurrences per 1000 patients. We rated the certainty of evidence to low due to study limitations and imprecision.

Time to recurrence

Increased water intake prolonged the time to urinary stone recurrence compared with standard water intake (hazard ratio (HR) 0.40, 95% CI 0.20 to 0.79; 1 study, 199 participants; Analysis 1.2). The duration of follow-up was five years. This would correspond to 152 fewer (50 fewer to 209 fewer) stone recurrences per 1000 patients. We downgraded the certainty of evidence to low due to study limitations and imprecision.

Secondary outcomes

Adverse events

The included study reported similar withdrawal rates (9.5%) in participants in the increased water intake group versus standard water intake group, but without explicitly reporting details on adverse events (Borghi 1996). Therefore, no data were available for this outcome.

Subgroup and sensitivity analysis

We were unable to perform any of the planned subgroup/sensitivity analyses due to paucity of included studies or lack of relevant data in the included studies.

DISCUSSION

Summary of main results

We found no randomised controlled trials (RCTs) investigating the role of increased water intake for the prevention of urinary stone formation in participants without a history of urinary stones.

For secondary prevention, we identified one study suggesting that increased water intake may reduce the risk of recurrent urinary stones and prolong the time to stone recurrence. However, our confidence in both findings is limited. We did not find evidence for adverse events.

Overall completeness and applicability of evidence

- The only study included in this review focused on the role of secondary stone prevention for calcium oxalate and phosphate stone formers with a single prior stone episode (Borghi 1996); it does not address primary prevention or the impact of increased fluid intake in individuals who have had multiple stones or other types of stones.
- The study predated modern imaging technology for stone disease using computer tomography (CT) and relied entirely on ultrasound and plain x-rays in identifying recurrent stone formers.
- It is unclear from the reported study what percentage of patients presented with symptoms of renal colic versus asymptomatic stone disease and in what location of the kidney.
- The study also does not provide information about participants' consumption of other non-water beverages; this matters as certain types of beverages, such as coffee, teas, juices and soda may have potentially different effects on urinary stone risk (Ticinesi 2017).
- Our review did not find evidence on adverse events related to increased water intake. However, we expect the risk to be low in healthy individuals without cardiovascular disease. Pollakisuria and nocturia have been reported to be the most common complications for patients with increased water intake (Wang 2013).

Quality of the evidence

We downgraded the certainty of evidence due to study limitations and imprecision (risk of bias and small sample size). For study limitations, the included study did not provide sufficient information about random sequence generation, allocation concealment as well as blinding process, rasing concerns about selection bias and detection bias. We further downgraded one level further for imprecision given the small sample size, low event rate and resulting wide confidence intervals. As a result, we judged the certainty of evidence for recurrence rate and time to recurrence to be low. Our confidence in these effect size estimates is therefore limited.

Potential biases in the review process

To reduce publication bias in our review, we followed the Cochrane guidelines and conducted an extensive literature search without restriction of publication language or publication status. In addition, we searched trial registries for unpublished or ongoing studies and identified other potentially eligible trials by screening reference lists of retrieved studies. It is possible that additional studies have been published but not yet identified, or conducted but not published. Should any such studies be identified, we would include them in the updates of this review. Moreover, two review authors performed study selection, assessment of the risk of bias, and data extraction which may help reduce the risk of error and bias.

We considered only RCTs or quasi-RCTs for inclusion in our review. Evidence suggested that there may not be significant differences in the risk estimates of events between RCTs and observational

studies (Golder 2011). Of note, for the comprehensive assessment of some rare or serious adverse events, studies of other designs (such as cohort studies, case-control studies, case series and other observational studies) may offer information, nevertheless, which was beyond the scope of this review.

Agreements and disagreements with other studies or reviews

The Health Professionals Follow-Up Study (Curhan 1997a; Taylor 2004), and the Nurses' Health Study I (Curhan 1997b) and II (Curhan 2004) were large observational studies that supported an important role for increased fluid intake to reduce the risk of stone recurrence (see Background).

We identified several reviews which assessed the effects of increased water intake for the prevention of urinary stones. However, no review has applied the same rigorous Cochrane methodology to this topic that includes rating the certainty of evidence using GRADE. Prasetyo 2013 included five studies: the RCT which we included in our review (Borghi 1996), three prospective cohort studies, as well as one case-control study. Results of the three cohorts separately demonstrated increased water intake of more than 2.5 L/day for participants with no history of urinary stones had a positive effect to decrease the risk of stone formation (Curhan 1996; Curhan 1998; Taylor 2004). The result of the case-control study confirmed its protective role (fluid intake volume of more than 2.0 L/day versus fluid intake volume of less than 500 mLs/day) (odds ratio (OR) 0.57, 95% CI 0.36 to 0.88; Dai 2013). Two other reviews reported that increased water intake may help lower the risk of recurrence for participants with a history of urinary stones (Cheungpasitporn 2016a; Fink 2013). Cheungpasitporn 2016a did not perform a pooled analysis. Fink 2013 differs in that it included Sarica 2006 which addressed a different question (effect of increased water intake in patients undergoing shock wave lithotripsy (SWL)), which is different than the question addressed by this review.

AUTHORS' CONCLUSIONS

Implications for practice

Based on this review, there is evidence of low certainty that increasing water intake to achieve a urine volume of at least 2.0 L reduces stone recurrence and extends time to recurrence for secondary prevention. Given these findings and indirect evidence (although not formally assessed in this review) that there are no associated serious adverse effects of this intervention, increasing water intake to achieve at least 2.0 L urine daily is also the basis of current evidence-based practice guidelines of the American Urological Association (Pearle 2014), the American College of Physicians (Qaseem 2015), and the European Association of Urology (Skolarikos 2015).

Implications for research

- There are no prospective randomised controlled trials (RCTs) available to assess the effects of increased water intake for the primary prevention of urinary stones. Given the increasing incidence of urinary stone disease and its economic burden on society, such trials appear important, especially in geographic areas with a high incidence of urinary stone disease.
- We identified only one study which defined increased water intake as achieving a daily urine volume of more than 2.0 L. Further studies should further assess the association of fluid volume and stone risk to confirm these findings.
- Further studies should further study the effects of increased water intake for prevention of different types of stone formers including non-calcium stones.
- Future studies should provide more detailed information on potential adverse events of increased water intake, especially for those patients with a high probability of urinary stone recurrence and volume-sensitive diseases (cirrhosis, heart failure and moderate to severe chronic kidney disease).

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CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Borghi 1996

Methods	• Study design: prospective randomised controlled trial • Study duration: started in 1996, with five years follow-up • Setting: single-centre • Country: Italy
Participants	• Inclusion criteria: participants with first episode of idiopathic calcium nephrolithiasis (calculus found at the chemical examination to be composed of pure calcium oxalate or mixed with traces of calcium phosphate) • Exclusion criteria: participants with other retained calculi found by renal echography/infusion excretory urography or with arterial hypertension or other metabolic pathology that required regular dietary measures and drug therapy • Number: 220 enrolled (199 analysed)

Borghi 1996 *(Continued)*

	○ Group 1: 110 (99) ○ Group 2: 110 (100) • Mean age ± SD years: group 1 (42.2 ± 11.6); group 2 (40.4 ± 13.2) • Sex (M/F): group 1 (70/29); group 2 (64/36)
Interventions	Group 1 (n = 99) (intervention group) • Once the lithiasic episode had been resolved (through spontaneous expulsion of the calculus, shock wave lithotripsy, percutaneous techniques or other procedures), each patient was then thoroughly encouraged to drink a high water intake which would give a urine volume ≥ 2 L/day. • Each year for the 5-year follow-up period, a 24-hour urine collection was brought to the stone centre to determine the urine stone risk profile, and participants received a complete physical examination, a flat plain abdominal x-ray and renal echography. Group 2 (n = 100) (control group) • Doctors did not provide for any high water treatment and patients were told that, since it was an isolated stone episode, it was not necessary at least at that time to follow any special procedures.
Outcomes	• Recurrence: symptomatic stones in case of colic or expulsion of calculi during follow-up; and asymptomatic stones from imaging studies (renal echography/x-ray each year during follow-up) • Time to recurrence: intervals between initiation of intervention and recurrence event • Adverse events: not reported
Funding Sources	Not reported
Declarations of interest	Not reported
Notes	Baseline of the intervention group, including urine volume, creatine, urea etc. was equal to that of the control group. During the study period, urine volume of the intervention group was significantly greater than that of the control group (2621 ± 443 mL/24h versus 1014 ± 195 mL/24 h, P < 0.0001).

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote from publication: "... patients were randomly placed in 2 different follow-up programs..." Comment: the study did not provide information about the sequence generation process. We judged the risk of bias as unclear.
Allocation concealment (selection bias)	Unclear risk	Quote from publication: N/A Comment: method of concealment was not described. We judged the risk of bias as unclear.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote from publication: N/A Comment: participants in group 1 were instructed to tailor their fluid intake to a urinary output of ≥ 2 L/day; participants in group 2 were given no such instructions. We therefore judged participants and personnel to have been unblinded.
Blinding of outcome assessment (detection bias)	Unclear risk	Quote from publication: N/A

Borghi 1996 *(Continued)*

		Comment: no information was provided as to whether outcome assessors were masked to the group assignment; we judged the risk of bias as unclear.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Quote from publication: "... 11 dropouts during follow-up in group 1 and 10 in group 2 ..." Comment: 99/110 participants in the intervention group and 100/110 in the control group were included in the analyses of outcomes. Given the attrition rate of 10% we judged the risk of bias as unclear.
Selective reporting (reporting bias)	Unclear risk	No protocol was available to assess the risk of bias from selective reporting.
Other bias	Low risk	We detected no other potential threats to validity.

SD: standard deviation

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Cheungpasitporn 2016a	Not RCT
Cheungpasitporn 2016b	Wrong comparator
de La Guéronnière 2011	Intervention given for only 6 days
Ferraro 2017	Not RCT
Fink 2013	Not RCT
Khan 2015	Wrong comparator
Lotan 2013	Not RCT
Lotan 2016	Not RCT
Maughan 2016	Wrong comparator
Prasetyo 2013	Not RCT
Sarica 2006	Participants were randomised prior to SWL; only a subset of participants who were determined stone-free were then followed, thereby addressing a different question. Participants followed may not have been comparable at baseline.
Ticinesi 2015	Not RCT
Tsang 2012	Wrong comparator
Wang 2013	Not RCT

RCT: randomised controlled trial
SWL: shock wave lithotripsy

Characteristics of ongoing studies *[ordered by study ID]*

NCT01100580

Trial name or title	The links between water and salt intake, body weight, hypertension and kidney stones: a difficult puzzle
Methods	Prospective, randomised, open-label, interventional study
Participants	For stone formers main inclusion criteria • age between 20 and 70 years • Caucasian race • idiopathic calcium stone disease • normal renal function (creatininemia < 1.2 mg/dL)
Interventions	Dietary supplement: low salt diet + water therapy
Outcomes	Primary outcome • Normalisation of urinary stone risk factors Secondary outcomes • Urinary sodium/calcium relationship • Blood pressure reduction • Relationship between 24-h calciuria and blood pressure • Stone rate reduction • Correlation BMI-urinary stone risk factors • Compliance
Starting date	May 2010
Contact information	Prof Loris Borghi +390521703375 loris.borghi@unipr.it
Notes	Latest information: Study not yet recruiting (1 December 2018)

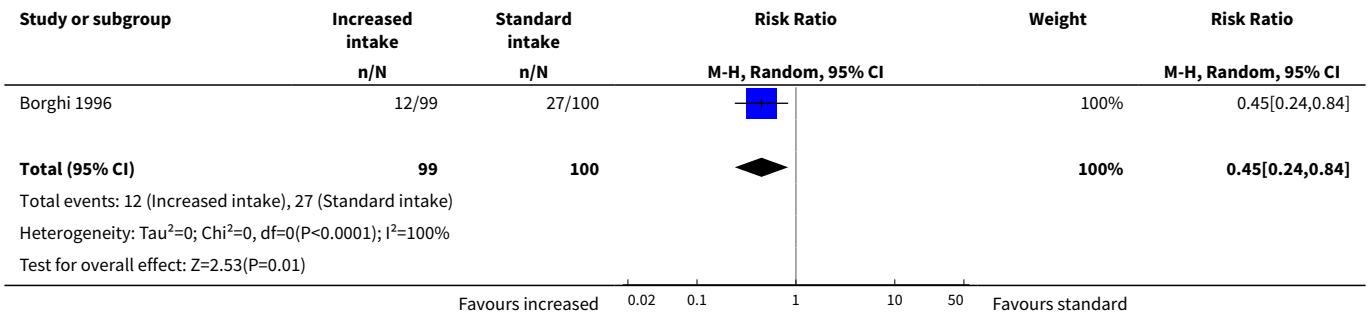
BMI: body mass index

DATA AND ANALYSES

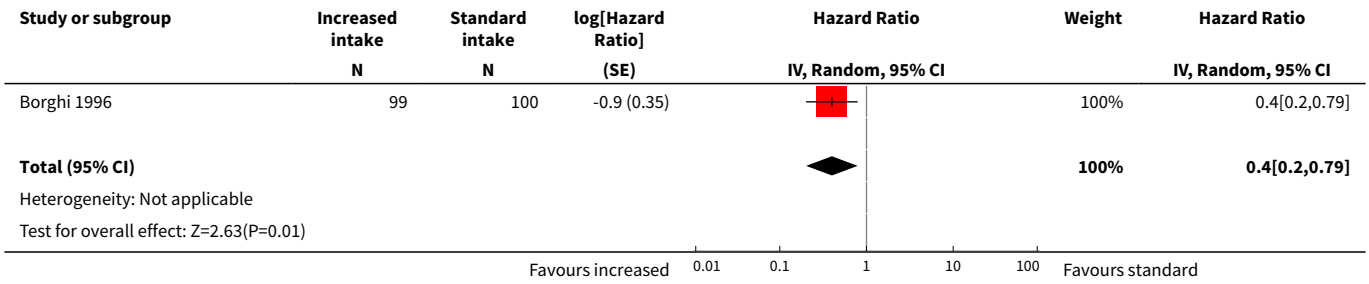
Comparison 1. Increased water intake versus standard water intake for secondary prevention

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Stone recurrence	1	199	Risk Ratio (M-H, Random, 95% CI)	0.45 [0.24, 0.84]
2 Time-to-recurrence	1	199	Hazard Ratio (Random, 95% CI)	0.40 [0.20, 0.79]

Analysis 1.1. Comparison 1 Increased water intake versus standard water intake for secondary prevention, Outcome 1 Stone recurrence.



Analysis 1.2. Comparison 1 Increased water intake versus standard water intake for secondary prevention, Outcome 2 Time-to-recurrence.



ADDITIONAL TABLES

Table 1. Description of the interventions

	Intervention(s) (route, frequency, total dose/day)	Intervention(s) appropriate as applied in a clinical practice setting[a] (description)	Comparator(s) (route, frequency, total dose/day)	Comparator(s) appropriate as applied in a clinical practice setting[a] (description)
Borghi 1996	High water intake (give a urine volume ≥ 2 L/day)	N/CPS	No high water treatment or any special procedures	N/CPS

[a]The 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).

N/CPS: no specification of clinical practice setting possible

Table 2. Baseline characteristics

	Intervention(s) and comparator(s)	Duration of intervention (duration of follow-up) (days, months, years)	Description of participants	Trial period (year to year)	Country	Setting	Ethnic groups (%)	Duration of disease (mean/ range years (SD), or as reported)
Borghi 1996	I1: high water intake (≥ 2 L/ day for urine volume)	5 years	Participants had first episode of idiopathic calcium nephrolithiasis (calculus found at the chemical examination to be composed of pure calcium oxalate or mixed with traces of calcium phosphate) without other retained calculi (renal echography and intravenous pyelography) or arterial hypertension or other metabolic pathology that required regular dietary measures or drug therapy	1986 to 1991	Italy	Group 1 (I1, n =110) A high water intake which would give a urine volume ≥ 2 L/day Group 2 (C1, n = 110) No treatment	-	-
	C1: no treatment						-	-

- denotes not reported

C: comparator; I: intervention.

APPENDICES

Appendix 1. Electronic search strategies

DATABASE	Search terms
PubMed (MEDLINE)	1. water[mh] OR water[tiab]
	2. drinking water[mh] OR drinking water[tiab]
	3. fluid therapy[mh] OR fluid therapy[tiab]
	4. beverages[mh] OR beverages[tiab]
	5. mineral water[mh] OR mineral water[tiab]
	6. carbonated water[mh] OR carbonated water[tiab]
	7. water* OR fluid* OR drink*
	8. 1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7
	9. urinary calculi[mh] OR urinary calculi[tiab]
	10. urolithiasis[mh] OR urolithiasis[tiab]
	11. urin*stone* OR uin* calcul*
	12. 9 OR 10 OR 11
	13. 8 AND 12
	14. randomized controlled trial[pt]
	15. controlled clinical trial[pt]
	16. randomized[tiab]
	17. placebo[tiab]
	18. clinical trials as topic[mesh:noexp]
	19. randomly[tiab]
	20. trial[ti]
	21. animals[mh] NOT human[mh]
	22. 14 OR 15 OR 16 OR 17 OR 18 OR 19 OR 20
	23. 22 NOT 21
	24. 13 AND 23
EMBASE & Ovid	#1 exp Urinary Calculi/ or exp Urolithiasis/
	#2 urolithiasis or urin* ston* or urin* calcul* .af.
	#3 (#1 or #2)
	#4 exp Water/ OR exp Drinking water/ OR exp Fluid Therapy/ OR exp Body Water/ OR exp Beverages/ OR exp Mineral Water/ OR exp Carbonated Water/
	#5 water* or fluid* or drink* .af.

(Continued)

	#7 (#4 or #5) #8 (#3 and #7) #9 exp crossover-procedure/ or exp double-blind procedure/ or exp randomized controlled trial/ or exp single-blind procedure/ #10 (random* or factorial* or crossover* or placebo*) .af. #11 (#9 or #10) #12 (#8 and #11)
Cochrane Library	#1 MeSH descriptor: [Urinary Calculi] explode all trees #2 MeSH descriptor: [Urolithiasis] explode all trees #3 urolithiasis or urin* ston* or urin* calcul* #4 (#1 or #2 or #3) #5 MeSH descriptor: [Water] explode all trees #6 MeSH descriptor: [Drinking Water] explode all trees #7 MeSH descriptor: [Fluid Therapy] explode all trees #8 MeSH descriptor: [Body Water] explode all trees #9 MeSH descriptor: [Beverages] explode all trees #10 MeSH descriptor: [Mineral Water] explode all trees #11 MeSH descriptor: [Carbonated Water] explode all trees #12 water* or fluid* or drink* #13 (#5 or #6 or #7 or #8 or #9 or #10 or #11 or #12) #14 (#4 and #13)

Appendix 2. '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	**Low risk of bias**: random number table; computer random number generator; coin tossing; shuffling cards or envelopes; throwing dice; drawing of lots; minimization (minimisation may be implemented without a random element, and this is considered to be equivalent to being random).
	High risk of bias: 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.
	Unclear: insufficient information about the sequence generation process to permit judgement.
Allocation concealment Selection bias (biased allocation to interventions) due to	**Low risk of bias**: 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; sequen-

(Continued)

inadequate concealment of allocations prior to assignment	tially numbered drug containers of identical appearance; sequentially numbered, opaque, sealed envelopes).
	High risk of bias: 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.
	Unclear: 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	**Low risk of bias**: 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.
	High risk of bias: 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.
	Unclear: insufficient information to permit judgement.
Blinding of outcome assessment Detection bias due to knowledge of the allocated interventions by outcome assessors	**Low risk of bias**: 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.
	High risk of bias: 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.
	Unclear: insufficient information to permit judgement.
Incomplete outcome data Attrition bias due to amount, nature or handling of incomplete outcome data	**Low risk of bias**: 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 standardised 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.
	High risk of bias: 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 standardised 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.
	Unclear: insufficient information to permit judgement.
Selective reporting Reporting bias due to selective outcome reporting	**Low risk of bias**: the study protocol is available and all of the study's prespecified (primary and secondary) outcomes that are of interest in the review have been reported in the prespecified way; the study protocol is not available but it is clear that the published reports include all expected outcomes, including those that were prespecified (convincing text of this nature may be uncommon).
	High risk of bias: not all of the study's prespecified 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 prespecified; one or more reported primary outcomes were not pre-

(Continued)

	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.
	Unclear: insufficient information to permit judgement.
Other bias Bias due to problems not covered elsewhere in the table	**Low risk of bias**: the study appears to be free of other sources of bias.
	High risk of bias: 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.
	Unclear: insufficient information to assess whether an important risk of bias exists; insufficient rationale or evidence that an identified problem will introduce bias.

WHAT'S NEW

Date	Event	Description
25 March 2020	Amended	Added "not" to second sentence of Background section. No other changes.

HISTORY

Protocol first published: Issue 3, 2003
Review first published: Issue 3, 2004

Date	Event	Description
20 November 2019	New search has been performed	Updated electronic search strategies (up to October 2019); GRADE assessment and 'Summary of findings' tables using GRADEpro GDT software were reported; 'time to recurrence' analysed as 'time-to-event' outcome; review updated in accordance with current guidance provided in the MECIR standards and the MECIR standards for Plain Language Summaries (PLEACS standards).
20 November 2019	New citation required but conclusions have not changed	Conclusions not changed.
18 April 2012	New citation required but conclusions have not changed	One ongoing study identified
18 April 2012	New search has been performed	Updated electronic search strategies; 'Risk of bias' assessment tool used; PRISMA flowchart included.
15 October 2008	Amended	Converted to new review format

CONTRIBUTIONS OF AUTHORS

- BY: updating the review, selection of studies, 'Risk of bias' assessment, data extraction, data analysis
- TX: updating the review, selection of studies, 'Risk of bias' assessment, data extraction, data analysis
- WQ: conception and study design, provision of clinical and methodological advice on the updated review, drafting of the review, and final approval

DECLARATIONS OF INTEREST

BY: none known
TX: none known
WQ: none known

SOURCES OF SUPPORT

Internal sources

- Chinese Cochrane Centre, Chinese Centre of Evidence-based Medicine, West China Hospital of Sichuan University, China.
- Department of Urology, Institute of Urology, West China Hospital of Sichuan University, China.

External sources

- National Natural Science Foundation of China, China.

  Grant number: 81500522

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

The review is based on a published protocol (Wei 2003), with any differences described below.

- The review was updated in accordance with current guidance provided in the MECIR standards, the MECIR standards for Plain Language Summaries (PLEACS standards), and the latest online version of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011a). We reported GRADE assessments in 'Summary of findings' tables using GRADEpro GDT software in the updated review (GRADEpro GDT 2015).
- We found no studies that reported incidence rate/patient/year and recurrence rate/patient/year. We therefore chose to report proportion of participants (no history of urinary stones/stone-free after primary procedures) who developed a new urinary stone after initiation of intervention as primary outcomes instead. We calculated hazard ratios (HRs) and corresponding 95% confidence intervals (CIs) to assess the intervention effect for time-to-event outcomes. Estimated HRs were to be calculated on the basis of Tierney's relevant equations in the case of the absence of individual participant data (Tierney 2007).

INDEX TERMS

Medical Subject Headings (MeSH)

*Drinking Water; Randomized Controlled Trials as Topic; Recurrence; Secondary Prevention; Urinary Calculi [*prevention & control]

MeSH check words

Humans