

Renal and ureteric stones: assessment and management

Dietary interventions

NICE guideline

Intervention evidence review

July 2018

Consultation

*This evidence review was developed by
the National Guideline Centre*

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1 Dietary interventions

1.1 Review question: What is the clinical and cost-effectiveness of dietary interventions to reduce the risk of future stones in people who have had renal stones?

1.2 Introduction

Patients who have presented with renal colic due to stones have an increased lifetime risk of developing further stones. Though a stone metabolic workup may find a specific metabolic cause for their stone a significant number of patients do not have a specific correctable metabolic abnormality. These patients, as well as all those with a defined metabolic problem, often ask health professionals about specific dietary and lifestyle changes that can reduce the risk of further stone formation. There are no clear national guidelines on dietary interventions; and, as a result a wide variety of advice is given by all sectors in the health system, ranging from community to secondary care.

1.3 PICO table

For full details see the review protocol in appendix A.

Table 1: PICO characteristics of review question

Population	People (adults, children and young people) with symptomatic and asymptomatic renal or ureteric stones
Interventions	<ul style="list-style-type: none"> • Type of Fluid (soft drinks, fluid in general, water, lemonade, orange juice, cranberry juice, fizzy drinks, coffee, tea, alcohol) • Salt • Diet rich in Citrate (fruit and veg) • Protein /purines intake (animal protein intake) • Calcium • Magnesium • Fibre • Acid ash • Oxalate • Vitamin C
Comparisons	<ul style="list-style-type: none"> • To each other • No treatment • Placebo • To fluid (gold standard) • DASH (dietary approaches to stop hypertension) diet • Within intervention comparisons: fluid volume
Outcomes	<p>Critical outcomes:</p> <ul style="list-style-type: none"> • New stone formation/incidence of stones/recurrence rate • Change in metabolic test (urine calcium, urine pH, urine oxalate, urine sodium) • Change in stone risk score • Use of healthcare services/retreatment rate • Quality of life • Adverse events <p>Important outcomes:</p> <ul style="list-style-type: none"> • Compliance/adherence

	<ul style="list-style-type: none">• Kidney function
Study design	Randomised controlled trials (RCTs), systematic reviews of RCTs. If no RCT evidence is available, search for observational studies (for children)

1 **1.4 Clinical evidence**

2 **1.4.1 Included studies**

3 Nine RCTs from 10 papers were included in the review;^{3, 11, 12, 21, 42, 71, 73, 85, 88, 90} these are
4 summarised in Table 2 below. Evidence from these studies is summarised in the clinical
5 evidence summary below (Table 3).

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

8 **1.4.2 Excluded studies**

9 See the excluded studies list in appendix I.

10

1.4.3 Summary of clinical studies included in the evidence review

Table 2: Summary of studies included in the evidence review

Study	Intervention and comparison	Population	Outcomes	Comments
Aras 2008 ³	<p>Intervention (n=10): Fresh lemon juice (85 cc) per day (containing 60 mEq of citrate)</p> <p>Comparison (n=10): Diet group: water 3L/day, calcium 1200 mg/day, NaCl 5 g/day, protein intakes 1.0 g/kg/day</p> <p>Concurrent care: advised to increase water intake to 3L/day</p>	<p>n=20</p> <p>People with hypocitraturic urinary calcium stones</p> <p>Age (mean, SD): lemon juice group 36.8 (14.28); diet group 38.7 (12.01)</p> <p>Gender not reported</p> <p>Turkey</p>	<p>Urine calcium (3 months)</p> <p>Urine pH (3 months)</p> <p>Urine oxalate (3 months)</p>	Duration: 3 months
Borghi 1996 ¹¹	<p>Intervention (n=99): High water intake (to give a urine volume ≥ 2 l/day)</p> <p>Comparison (n=100): No intervention (not necessary to follow any special procedures)</p> <p>Concurrent care: not reported</p>	<p>n=199</p> <p>People with idiopathic calcium nephrolithiasis</p> <p>Age (mean, SD): water group 42.2 (11.6); no intervention 40.4 (13.2)</p> <p>Male to female ratio 134:65</p> <p>Italy</p>	<p>Recurrence (5 years): defined as stone expulsion during follow up or silent calculus on x-ray or echography</p>	Duration: 5 years
Borghi 2002 ¹²	<p>Intervention (n=60): Low calcium diet (approx. 10 mmol/day)</p> <p>Comparison (n=60): Normal-to-high calcium (30 mmol/day)</p>	<p>n=120</p> <p>People with idiopathic hypercalcuria</p>	<p>Recurrence (5 years): defined as presence of a radiographically identified stone</p>	Duration: 5 years

Study	Intervention and comparison	Population	Outcomes	Comments
	Concurrent care: 2-3L water/day	Age (mean, SD): low calcium group 45.4 (10.9); normal calcium group 44.8 (9.2) Male participants only Italy		
Dussol 2008 ²¹ Rotily 2000 ⁸⁵	Intervention (n=55): LAPD (low animal protein diet, limited to 3 servings of meat and fish per week, and no more than 100mg a day of milk products) Intervention (n=60): HFD (high fibre diet, increasing intake of fruit and vegetables and having whole grain dietary products to obtain a 25g/day increase in fibre) Comparison (n=60): Control/no intervention Concurrent care: advised to maintain high water intake and a calcium intake between 800-1000mg/day	n=175 People with idiopathic calcium stones (38% had hypercalciuria) Age (mean, SD): LAPD group 44 (12); HFD group 44 (12); no intervention group 45 (11) Male to female ratio 114:61 France	Recurrence (4 years): defined as renal colic, gross hematuria, expulsion or removal of stone, or appearance of a new asymptomatic stone of >50% increase in size of previously present stone on radiological or ultrasound exams Urine calcium (4 years) Urine oxalate (4 years) Urine sodium (4 years)	Duration: 4 years
Hiatt 1996 ⁴²	Intervention (n=50): LAPD (low animal protein diet. Participants instructed to decrease intake of animal flesh proteins and other purine containing foods. Total protein content was estimated at 56-64g) Comparison (n=49): No intervention Concurrent care: advice to drink 6-8 glasses of liquid daily, instructions to	n=99 People with calcium oxalate kidney stone (≥65%calcium oxalate) Age (mean, SE): LAPD group 43.1 (1.5); no intervention group 42.9 (1.4) Male to female ratio 78:21	Recurrence (4 years): defined as stones that were passed, removed or radiographically visible	Duration: 4 years

Study	Intervention and comparison	Population	Outcomes	Comments
	consume 2 daily servings of dairy products/500mg calcium carbonate	USA		
Noori 2014 ⁷¹	Intervention (n=21): DASH diet (high in fruits and vegetables, moderate in low-fat dairy, and low in animal protein) Comparison (n=20): Low oxalate diet Concurrent care: not reported	n=41 People with a history of at least 2 episodes of calcium oxalate kidney stones, with hyperoxaluria Age (mean, SD): 48 (13) Male to female ratio 28:13 Iran	Urine calcium (8 weeks) Urine pH (8 weeks) Urine oxalate (8 weeks) Urine sodium (8 weeks)	Duration: 8 weeks
Nouvenne 2010 ⁷³	Intervention (n=108): Low sodium diet (advice to eliminate kitchen salt and limit consumption of food with high salt content) Comparison (n=102): No intervention (no dietary changes) Concurrent care: advice to drink 2-3 L/d	n=210 People with idiopathic calcium stone and hypercalcinuria Age (mean, SD): low sodium group 39 (9); no intervention group 40 (10) Male to female ratio 150:60 Italy	Urine calcium (3 months) Urine pH (3 months) Urine oxalate (3 months) Urine sodium (3 months)	Duration: 3 months
Shuster 1992 ⁸⁸	Intervention (n=504): No soft (carbonated) drinks Comparison (n=505): Soft (carbonated) drinks (soda, ≥160 ml/day)	n=1009 People who had completed an episode of urinary stone disease who consumed at least 160ml/day soft drinks. All stone subtypes were included.	Recurrence (3 years): not defined	Duration: 3 years

Study	Intervention and comparison	Population	Outcomes	Comments
		Age >18 years Male participants only USA		
Silverio 2000 ⁹⁰	Intervention (n=192): Mineral water (calcium content 15 mg/l) Comparison (n=192): Tap water (calcium content ranged 55-130 mg/l) Concurrent care: a varied diet with a mean calcium content of 600mg/day	n=384 People with idiopathic calcium urolithiasis Age (range): 24-65 Male to female ratio 231:153 Italy	Recurrence (19 months): not defined	Duration: 19 months

See appendix D for full evidence tables.

1.4.4 Quality assessment of clinical studies included in the evidence review

Table 3: Clinical evidence summary: High water intake versus normal water intake

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with normal water intake	Risk difference with High water intake (95% CI)
Number of stone recurrences	199 (1 study) 5 years	⊕⊕⊖⊖ LOW ^{1,2} due to risk of bias, imprecision	RR 0.45 (0.24 to 0.84)	270 per 1000	149 fewer per 1000 (from 43 fewer to 205 fewer)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with normal water intake	Risk difference with High water intake (95% CI)
1 Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias 2 Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs.					

Table 4: Clinical evidence summary: Lemonade (fresh lemon juice in water) versus diet

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with water	Risk difference with Lemonade (95% CI)
Calcium level	20 (1 study)	⊕⊕⊖⊖ LOW ^{1,2} due to risk of bias, imprecision		The mean calcium level in the control group was 185.6 mg/day	The mean calcium level in the intervention groups was 67.3 lower (132.96 to 1.64 lower)
pH	20 (1 study) 3 months	⊕⊕⊖⊖ LOW ^{1,2} due to risk of bias, imprecision		The mean pH in the control group was 5.8	The mean pH in the intervention groups was 0.2 higher (0.06 lower to 0.46 higher)
Oxalate level	20 (1 study) 3 months	⊕⊖⊖⊖ VERY LOW ^{1,2} due to risk of bias, imprecision		The mean oxalate level in the control group was 22.6 mg/day	The mean oxalate level in the intervention groups was 3.85 higher (10.73 lower to 18.43 higher)
1 Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias 2 Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs					

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Table 5: Clinical evidence summary: Mineral water (low calcium content) versus tap water

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Tap water	Risk difference with Mineral water (95% CI)
Recurrence	384 (1 study) 19 months	⊕⊕⊖⊖ LOW1,2 due to risk of bias, imprecision	RR 0.73 (0.48 to 1.09)	229 per 1000	62 fewer per 1000 (from 119 fewer to 21 more)
1 Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias 2 Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs					

Table 6: Clinical evidence summary: Non-carbonated drinks versus carbonated drinks ((soda, >160 ml/day)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Soft drinks (>160 ml/day)	Risk difference with No soft drinks (95% CI)
Recurrence	1009 (1 study) 3 years	⊕⊕⊖⊖ LOW1,2 due to risk of bias, imprecision	RR 0.83 (0.71 to 0.98)	406 per 1000	69 fewer per 1000 (from 8 fewer to 118 fewer)
1 Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias 2 4 Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs					

Table 7: Clinical evidence summary: Low calcium diet versus normal calcium diet

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with normal calcium diet	Risk difference with Low calcium diet (95% CI)
Number of stone recurrences	120 (1 study) 5 years	⊕⊕⊖⊖ LOW1,2	RR 1.92 (1.05 to 3.49)	200 per 1000	184 more per 1000 (from 10 more to 498 more)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with normal calcium diet	Risk difference with Low calcium diet (95% CI)
		due to risk of bias, imprecision			
1 Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias 2 Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs					

Table 8: Clinical evidence summary: DASH (dietary approaches to stop hypertension) diet versus low oxalate diet

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Low oxalate diet	Risk difference with DASH diet (95% CI)
Urine calcium	41 (1 study) 8 weeks	⊕⊕⊕⊖ VERY LOW ^{1,2} due to risk of bias, imprecision		The mean calcium level in the control group was 175.2 (mg/d)	The mean urine calcium in the intervention groups was 3.6 lower (50.86 lower to 43.66 higher)
pH	41 (1 study) 8 weeks	⊕⊕⊕⊖ LOW ^{1,2} due to risk of bias, imprecision		The mean pH in the control group was 6	The mean pH in the intervention groups was 0.1 lower (0.45 lower to 0.25 higher)
Urine oxalate	41 (1 study) 8 weeks	⊕⊕⊕⊖ LOW ^{1,2} due to risk of bias, imprecision		The mean oxalate level in the control group was 47 (mg/d)	The mean urine oxalate in the intervention groups was 6.9 higher (1.49 lower to 15.29 higher)
Urine sodium	41 (1 study) 8 weeks	⊕⊕⊕⊖ LOW ^{1,2} due to risk of bias, imprecision		The mean sodium level in the control group was 159.3 (mEq/d)	The mean urine sodium in the intervention groups was 12.1 lower (63.75 lower to 39.55 higher)
1 Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias 2 Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs					

Table 9: Clinical evidence summary: Low animal protein diet versus high fibre diet

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with high fibre diet	Risk difference with Low animal protein diet (95% CI)
Recurrence	50 (1 study) 4 years	⊕⊕⊖⊖ LOW1 due to imprecision	RR 0.76 (0.45 to 1.27)	630 per 1000	151 fewer per 1000 (from 347 fewer to 170 more)
Urine calcium	50 (1 study) 4 years	⊕⊕⊕⊖ MODERATE1 due to imprecision		The mean calcium level in the control group was 5.3 (mmol/d)	The mean urine calcium in the intervention groups was 2.4 higher (0.14 to 4.66 higher)
Urine oxalate	50 (1 study) 4 years	⊕⊕⊖⊖ LOW1 due to imprecision		The mean oxalate level in the control group was 0.31 (mmol/d)	The mean urine oxalate in the intervention groups was 0 higher (0.09 lower to 0.09 higher)
Urine sodium	50 (1 study) 4 years	⊕⊕⊕⊖ MODERATE1 due to imprecision		The mean sodium level in the control group was 133 (mmol/d)	The mean urine sodium in the intervention groups was 40 higher (1.55 to 78.45 higher)

1 Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

Table 10: Clinical evidence summary: Low animal protein diet versus no intervention

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with no intervention	Risk difference with Low animal protein diet (95% CI)
Recurrence	145 (2 studies) 4 years	⊕⊖⊖⊖ VERY LOW1,2 due to inconsistency, imprecision	RR 2.19 (0.32 to 14.77)	181 per 1000	309 more per 1000 (from 177 fewer to 1000 more)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with no intervention	Risk difference with Low animal protein diet (95% CI)
Urine calcium	46 (1 study) 4 years	⊕⊕⊕⊖ MODERATE ² due to imprecision		The mean calcium level in the control group was 6.1 (mmol/d)	The mean urine calcium in the intervention groups was 1.6 higher (0.52 lower to 3.72 higher)
Urine oxalate	46 (1 study) 4 years	⊕⊕⊕⊖ MODERATE ² due to imprecision		The mean oxalate level in the control group was 0.28 (mmol/d)	The mean urine oxalate in the intervention groups was 0.03 higher (0.09 lower to 0.15 higher)
Urine sodium	46 (1 study) 4 years	⊕⊕⊖⊖ LOW ² due to imprecision		The mean sodium level in the control group was 163 (mmol/d)	The mean urine sodium in the intervention groups was 10 higher (31.76 lower to 51.76 higher)

1 Downgraded by 1 or 2 increments because heterogeneity, I²= 83%, p= > 0.1, unexplained by subgroup analysis
2 Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

Table 11: Clinical evidence summary: High fibre diet versus no intervention

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with no intervention	Risk difference with High fibre diet (95% CI)
Recurrence	50 (1 study) 4 years	⊕⊕⊕⊖ MODERATE ¹ due to imprecision	RR 1.32 (0.79 to 2.2)	478 per 1000	153 more per 1000 (from 100 fewer to 574 more)
Urine calcium	50 (1 study) 4 years	⊕⊕⊕⊖ MODERATE ¹ due to imprecision		The mean calcium level in the control group was 6.1 (mmol/d)	The mean urine calcium in the intervention groups was 0.8 lower (2.42 lower to 0.82 higher)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with no intervention	Risk difference with High fibre diet (95% CI)
Urine oxalate	50 (1 study) 4 years	⊕⊕⊕⊖ MODERATE1 due to imprecision		The mean oxalate level in the control group was 0.28 (mmol/d)	The mean urine oxalate in the intervention groups was 0.03 higher (0.06 lower to 0.12 higher)
Urine sodium	50 (1 study) 4 years	⊕⊕⊕⊖ MODERATE1 due to imprecision		The mean sodium level in the control group was 163 (mmol/d)	The mean urine sodium in the intervention groups was 30 lower (64.49 lower to 4.49 higher)

1 Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

Table 12: Clinical evidence summary: Low salt diet versus no intervention

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with no intervention	Risk difference with Low salt diet (95% CI)
Urine calcium	197 (1 study) 3 months	⊕⊕⊕⊖ MODERATE1 due to imprecision		The mean calcium level in the control group was 361 (mg/d)	The mean urine calcium in the intervention groups was 90 lower (120.53 to 59.47 lower)
Urine pH	197 (1 study) 3 months	⊕⊕⊕⊕ HIGH		The mean pH in the control group was 6.01	The mean urine pH in the intervention groups was 0 higher (0.12 lower to 0.12 higher)
Urine oxalate	197 (1 study) 3 months	⊕⊕⊕⊖ MODERATE1 due to imprecision		The mean oxalate level in the control group was 32 (mg/d)	The mean urine oxalate in the intervention groups was 4 lower (6.53 to 1.47 lower)
Urine sodium	197 (1 study) 3 months	⊕⊕⊕⊕ HIGH		The mean sodium level in the control group was 200 (mmol/d)	The mean urine sodium in the intervention groups was 132 lower (146.7 to 117.3 lower)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with no intervention	Risk difference with Low salt diet (95% CI)
1 Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs					

See Appendix F: for full GRADE tables.

1 1.5 Economic evidence

2 1.5.1 Included studies

3 No relevant health economic studies were identified.

4 1.5.2 Excluded studies

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

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

8 1.6 Resource costs

9 The recommendations made in this review are not expected to have a substantial impact on
10 resources.

11 1.7 Evidence statements

12 1.7.1 Clinical evidence statements

13 Fluid

14 One study compared high water intake to normal water intake. There was a clinical benefit of
15 high water intake in terms of number of stone recurrence (n=199). The quality of the
16 evidence was Low due to risk of bias and imprecision.

17 One study compared fresh lemon juice in water to a moderate protein, low salt, normal
18 calcium diet. There was a clinical benefit of lemon juice in terms of calcium level and pH, but
19 no clinical difference between the two groups in terms of oxalate level (n=20). The quality of
20 the evidence ranged from Low to Very Low due to risk of bias and imprecision.

21 One study compared mineral water to tap water. There was a clinical benefit of mineral water
22 in terms of recurrence (n=384). The quality of the evidence was Low due to risk of bias and
23 imprecision.

24 One study compared non-carbonated drinks to carbonated drinks (>160ml/day). There was a
25 clinical benefit of no carbonation drinks in terms of recurrence (n=1009). The quality of the
26 evidence was Low due to risk of bias and imprecision.

27 Calcium

28 One study compared a low calcium diet to a normal calcium diet. There was a clinical benefit
29 of normal calcium in terms of the number of stone recurrences (n=120). The quality of the
30 evidence was Low due to risk of bias and imprecision.

31 DASH/oxalate

32 One study compared the DASH diet to a low oxalate diet. There was no difference between
33 the two interventions in terms of urine calcium, urine sodium, and pH. There was a clinical
34 benefit of low oxalate diet in terms of urine oxalate (n=41). The quality of the evidence was
35 Low due to risk of bias and imprecision.

36 Protein/fibre

1 One study compared a low animal protein diet to a high fibre diet. There was a clinical
2 benefit of low animal protein in terms of recurrence, and no difference between the groups in
3 terms of urine sodium, calcium, and oxalate. The quality of the evidence ranged from
4 Moderate to Low due to imprecision.

5 Two studies compared a low animal protein diet to no intervention. Evidence from the two
6 studies suggested a clinical benefit of no intervention in terms of recurrence (n=145). One
7 study reported the outcomes urine sodium, calcium and oxalate. There was no clinical
8 difference between the two groups in terms of urine sodium and oxalate, and a clinical
9 benefit of no intervention in terms of urine calcium. The quality of the evidence ranged from
10 Moderate to Very Low due to inconsistency and imprecision.

11 One study compared a high fibre diet to no intervention. There was a clinical benefit of no
12 intervention in terms of recurrence. There was no clinical difference between the two groups
13 in terms of urine sodium, calcium or oxalate (n=50). The quality of the evidence was
14 Moderate due to imprecision.

15 **Salt**

16 One study compared a low salt diet to no intervention. There was a clinical benefit of low
17 sodium in terms of urine sodium and urine calcium, and no clinical difference between
18 groups in terms of urine oxalate and urine pH. The quality of the evidence ranged from High
19 to Moderate due to imprecision.

20 **1.7.2 Health economic evidence statements**

- 21 • No relevant economic evaluations were identified.

22 **1.8 Recommendations**

23 **C1. Discuss diet and fluid intake with the person (and their family or carers, as 24 appropriate), and advise:**

- 25 • adults to drink 2.5 to 3 litres of water per day and children and young people
26 (depending on their age) 1 to 2 litres
- 27 • adding fresh lemon juice to drinking water
- 28 • avoiding carbonated drinks
- 29 • adults to have a daily salt intake of no more than 6 g and children and young
30 people (depending on their age) 2 to 6 g
- 31 • adults to have a daily calcium intake of 700 to 1,200 mg and children and young
32 people (depending on their age) 350 to 1,000 mg

33 **C2. Follow the recommendations on maintaining a healthy lifestyle in the NICE 34 guideline on [preventing excess weight gain](#).**

35 **1.9 Rationale and impact**

36 **1.9.1 Why the committee made the recommendations**

37 Some evidence showed a benefit of a high water intake in reducing stone recurrence in
38 adults. Limited evidence from a single study in adults showed a benefit of lemon juice in
39 terms of urine calcium and pH but no difference in urine oxalate. Lemon juice is high in
40 citrate leading to higher concentrations of citrate in urine. This may stop calcium from binding
41 to other stone constituents and so prevent stone formation and recurrence. The committee
42 agreed to recommend a high water intake and adding lemon juice to water. Evidence

1 showed a benefit of avoiding carbonated drinks in terms of stone recurrence, and so the
2 committee agreed to recommend that these should be avoided.

3 Evidence on diet was mixed but the committee agreed that an adequate calcium intake and a
4 low salt intake may help to prevent stone recurrence. Evidence on avoiding a high protein
5 diet was inconclusive, but the committee acknowledged that this is the advice currently
6 given.

7 **1.9.2 Impact of the recommendations on practice**

8 The recommendations on diet broadly reflect current practice . They emphasise the
9 importance of dietary advice in preventing further stone episodes. Dietary advice should be
10 given in conjunction with lifestyle advice.

11 **1.10 The committee's discussion of the evidence**

12 **1.10.1 Interpreting the evidence**

13 **1.10.1.1 The outcomes that matter most**

14 The committee agreed that the outcomes that were critical for decision making were new
15 stone formation/incidence of stones/recurrence rate, change in urine metabolic tests (urine
16 calcium, urine pH, urine oxalate, urine sodium), change in stone risk score, use of healthcare
17 services/retreatment rate, quality of life and adverse events were. Compliance/adherence
18 and kidney function were also considered as important outcomes.

19 There was no evidence for change in stone risk score, use of healthcare
20 services/retreatment rate, quality of life, adverse events, compliance/adherence and kidney
21 function.

22 **1.10.1.2 The quality of the evidence**

23 For the majority of evidence in this review, the quality ranged from a GRADE rating of
24 moderate to very low. This was due to lack of blinding, and presence of selection bias,
25 resulting in a high or very high risk of bias rating. Additionally, the imprecise nature of the
26 results extracted and analysed in this review and sometimes the presence of heterogeneity
27 for some outcomes further downgraded the quality of the evidence.

28 **1.10.1.3 Benefits and harms**

29 Evidence for adults and children and young people, and for those with symptomatic and
30 asymptomatic stones was searched for. However, no evidence was identified for children
31 and young people, or for people with asymptomatic stones. The committee agreed that the
32 recommendations should include children and young people, and be based on government
33 nutritional advice and healthy eating messages aimed at the general population. They did not
34 feel that the evidence could be extrapolated to the asymptomatic population, and therefore
35 agreed that all recommendations would apply to those with symptomatic stones only.

36 *High water intake versus normal water intake*

37 The committee considered the evidence for water intake and noted that in terms of stone
38 recurrence, there was a clinical benefit of high water intake. They noted that advice to
39 increase water intake is part of current practice and took the view that it made clinical sense.

40 *Lemon juice versus diet*

41 The committee noted that there was a benefit of lemon juice in terms of urine calcium level
42 and urine pH, but there was no difference in terms of urine oxalate. Lemon juice is high in

1 natural citrate and may offer protection from forming stones due to citrate in the urine
2 preventing calcium from binding with other constituents that contribute to stone formation.
3 The committee also commented that those in the diet group were following a moderate
4 protein, low salt, normal calcium diet, and that both groups received advice to increase water
5 intake to 3 litres per day. As both groups received advice to increase water intake, the
6 committee could be sure that the benefits seen in the lemon group were due to the lemon
7 juice intervention and not the increase in water. However, it was noted that the exact water
8 intake of each group was not known. The committee also noted that the evidence came from
9 a single, very small study of low and very low quality.

10 *Mineral (low calcium) water versus tap water*

11 The evidence suggests a clinical benefit of mineral (low calcium) water in terms of recurrence
12 rate; however, the committee noted that the overall calcium content through diet was the
13 same for both comparison groups. The committee commented that the results of this
14 comparison were contrary to other non-randomised evidence they were aware of. Overall,
15 the committee agreed that the evidence was insufficient to draw a conclusion regarding
16 mineral or tap water, and therefore they felt that mineral water could be included as part of
17 general fluid intake, rather than specifying mineral water or tap water.

18 *Carbonated drinks versus non-carbonated drinks*

19 The committee noted that there was a clinical benefit of avoiding carbonated drinks in terms
20 of recurrence rate. The committee discussed the fact that there was no information provided
21 on the diets of the participants, and therefore they could not be certain that this result was
22 due to the intervention alone. However, they noted that advice not to drink carbonated drinks
23 reflects current practice, and also considered that it is unlikely for there to be a harm
24 associated with avoiding carbonated drinks.

25 *Low calcium diet versus normal calcium diet*

26 The committee noted that there was a clinical benefit of normal calcium diet in terms of
27 recurrence rate. A normal calcium intake would be around 700 mg per day for adults. The
28 committee commented that in the normal calcium group, people were also following a low
29 protein, low salt diet, which reduced the committee's confidence that the results were due to
30 the intervention alone, and were not impacted by the other aspects of the participants' diets.
31 However, the committee observed that this evidence is consistent with their knowledge
32 regarding the effect of low calcium intake on oxalate absorption. A low calcium intake
33 reduces amount of calcium available to bind with dietary oxalate, increasing the amount of
34 oxalate absorption from the gut and consequently excretion into the urine. This results in
35 increased oxalate concentrations in the urine allowing crystallisation and stone formation.
36 Based on this evidence and the expertise of the committee, the committee agreed that, a
37 normal calcium diet should be advised.

38 *DASH (dietary approaches to stop hypertension) versus low oxalate diet*

39 The committee noted that there was no clinical benefit of one diet over the other for most
40 urinary parameters (calcium, sodium and pH), but there might be a slight benefit in terms of
41 urine oxalate.

42 The committee commented that the DASH diet is a holistic approach, which, in addition to
43 unrestricted oxalate intake, includes a high intake of fruit and vegetables and low-fat dairy
44 products, and a low intake of saturated and total fat, and cholesterol; it also includes an
45 exercise regimen. Therefore, it is difficult to draw a conclusion by comparing two different
46 dietary approaches to each other. The committee also noted that the duration of the
47 intervention was 8 weeks, and discussed whether this is a sufficient time-frame in which to
48 expect to see any significant changes in the outcomes.

49 *Low animal protein diet versus high fibre diet*

1 There was conflicting evidence for this comparison. There was a benefit of low animal protein
2 diet in terms of stone recurrence rate, a benefit of high fibre diet in terms of urine sodium and
3 calcium, and no difference for urine oxalate. As with the above comparison, the committee
4 felt that comparisons of two types of diets was not as helpful as comparing a diet to no diet.
5 The committee discussed that on the balance of evidence considered, avoiding a high
6 protein intake appeared to be beneficial. The committee noted that in current practice people
7 with renal or ureteric stones are often given advice to reduce animal protein intake.

8 *Low animal protein diet versus no intervention*

9 The evidence suggested a clinical benefit of no intervention for recurrence rate and urine
10 calcium, and no clinical difference for urine sodium and oxalate.

11 The committee considered all of the evidence for protein compared to high fibre and no
12 intervention, and agreed that the evidence is conflicting and difficult to draw conclusions
13 from. They noted concerns about the quality of the evidence, and that the evidence was
14 mainly based on small, single studies.. It was also noted that in current practice many people
15 are advised to reduce animal protein intake. However, overall the committee agreed that the
16 evidence was too conflicting and not convincing enough to warrant a recommendation.

17 *High fibre diet versus no intervention*

18 There was conflicting evidence for this comparison, suggesting clinical benefit of no
19 intervention for recurrence rate, clinical benefit of high fibre diet for urine sodium, and no
20 difference for urine calcium and oxalate.

21 *Low salt diet versus no intervention*

22 The committee noted that there was a clinical benefit of low sodium diet for urine sodium,
23 calcium and oxalate, and no difference for urine pH, and agreed that a low dietary salt intake
24 should be recommended.

25 **1.10.2 Cost effectiveness and resource use**

26 No economic evidence was identified for this question.

27 There are not likely to be any direct costs of the interventions themselves, as the
28 recommendations are about giving the patient dietary advice and information so they can
29 follow the advice. This may involve some staff time, and some printed information for
30 example. However it is likely that this discussion would take place as part of a consultation
31 that would already occur, as all patients are currently given advice, such as to drink more
32 fluid following a renal stone. Therefore the resources involved with these interventions are
33 likely to be negligible.

34 If the dietary interventions are effective in terms of reducing recurrence of events, or even
35 slowing down the recurrence of events, this is likely to lead to a cost saving because of
36 interventions avoided (or deferred) that might be needed to treat the stones, which can be
37 expensive.

38 The committee reviewed the clinical evidence and made recommendations listing specific
39 advice where they felt the evidence was strong enough, but also used their own consensus
40 regarding appropriate daily intake of specific dietary interventions.

41 **1.10.3 Other factors the committee took into account**

42 A committee member was aware of epidemiological data from a large, indirect population of
43 men who have not formed stones before, that demonstrated a relationship between a high
44 dietary calcium intake and a reduced risk of symptomatic kidney stones (Curhan 1993¹⁹).
45 The committee member was also aware that further non-comparative data from a very large

- 1 number of participants suggested that lifestyle changes such as reducing animal protein
2 intake, showed some benefit in preventing stone formation (Turney 2014⁹⁴).
- 3 The committee noted current published government dietary recommendations⁷⁴ and advice
4 on healthy eating such as the Eatwell Guide⁸³ aimed at the general population, and
5 acknowledged this guidance to be relevant for a renal stone population.
6

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3 response meta-analysis of observational studies. *Medicine*. 2015; 94(27):e1042
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7 potassium-magnesium citrate during 5 weeks of bed rest. *Journal of Urology*. 2007;
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1 Appendices

2 Appendix A: Review protocols

3 **Table 13: Review protocol: dietary interventions**

Field	Content
Review question	What is the clinical and cost-effectiveness of dietary interventions to reduce the risk of future stones in people who have had renal stones?
Type of review question	Intervention review A review of health economic evidence related to the same review question was conducted in parallel with this review. For details see the health economic review protocol for this NICE guideline.
Objective of the review	To find the most effective dietary interventions for people who have had renal stones
Eligibility criteria – population / disease / condition / issue / domain	People (adults, children and young people) with symptomatic and asymptomatic renal or ureteric stones
Eligibility criteria – intervention(s) / exposure(s) / prognostic factor(s)	<ul style="list-style-type: none"> • Type of Fluid (soft drinks, fluid in general, water, lemonade, orange juice, cranberry juice, fizzy drinks, coffee, tea, alcohol) • Salt • Diet rich in Citrate (fruit and veg,) • Protein /purines intake (animal protein intake) • Calcium • Magnesium • Fibre • Acid ash • Oxalate • Vitamin C
Eligibility criteria – comparator(s) / control or reference (gold) standard	<ul style="list-style-type: none"> • To each other • No treatment • Placebo • To fluid (gold standard) • DASH (dietary approaches to stop hypertension) diet • Within intervention comparisons: fluid volume
Outcomes and prioritisation	<p>Critical outcomes:</p> <ul style="list-style-type: none"> • New stone formation/incidence of stones/recurrence rate • Change in metabolic test (urine calcium, urine pH, urine oxalate, urine sodium) • Change in stone risk score • Use of healthcare services/retreatment rate • Quality of life • Adverse events <p>Important outcomes:</p> <ul style="list-style-type: none"> • Compliance/adherence • Kidney function
Eligibility criteria – study design	Randomised controlled trials (RCTs), systematic reviews of RCTs. If no RCT evidence is available, search for observational studies (for children)
Other inclusion exclusion criteria	Bladder stones Open surgery for renal (kidney and ureteric) stones

	Non-English language studies
Proposed sensitivity / subgroup analysis, or meta-regression	<p>Strata:</p> <ul style="list-style-type: none"> • Adults (≥16 years) • Children and young people (<16 years) • People with specific metabolic abnormalities <p>Subgroups:</p> <ul style="list-style-type: none"> • Initial stone formers • Recurrent stone formers • Pregnant women • People who are HIV positive and having treatment with protease inhibitors
Selection process – duplicate screening / selection / analysis	Studies are sifted by title and abstract. Potentially significant publications obtained in full text are then assessed against the inclusion criteria specified in this protocol.
Data management (software)	<ul style="list-style-type: none"> • Pairwise meta-analyses performed using Cochrane Review Manager (RevMan5). • GRADEpro used to assess the quality of evidence for each outcome • Endnote for bibliography, citations, sifting and reference management • Data extractions performed using EviBase, a platform designed and maintained by the National Guideline Centre (NGC)
Information sources – databases and dates	<p>Clinical search databases to be used: Medline, Embase, Cochrane Library Date: all years</p> <p>Health economics search databases to be used: Medline, Embase, NHSEED, HTA Date: Medline, Embase from 2014 NHSEED, HTA – all years</p> <p>Language: Restrict to English only Supplementary search techniques: backward citation searching</p> <p>Key papers: Not known</p>
Identify if an update	Not applicable
Author contacts	https://www.nice.org.uk/guidance/indevelopment/gid-ng10033
Highlight if amendment to previous protocol	For details please see section 4.5 of Developing NICE guidelines: the manual.
Search strategy – for one database	For details please see appendix B
Data collection process – forms / duplicate	A standardised evidence table format will be used, and published as appendix D of the evidence report.
Data items – define all variables to be collected	For details please see evidence tables in Appendix D (clinical evidence tables) or H (health economic evidence tables).
Methods for assessing bias at outcome / study level	<p>Standard study checklists were used to critically appraise individual studies. For details please see section 6.2 of Developing NICE guidelines: the manual</p> <p>The risk of bias across all available evidence was evaluated for each outcome using an adaptation of the ‘Grading of Recommendations Assessment, Development and Evaluation (GRADE) toolbox’ developed by the international GRADE working group http://www.gradeworkinggroup.org/</p>

Criteria for quantitative synthesis	For details please see section 6.4 of Developing NICE guidelines: the manual.
Methods for quantitative analysis – combining studies and exploring (in)consistency	For details please see the separate Methods report for this guideline.
Meta-bias assessment – publication bias, selective reporting bias	For details please see section 6.2 of Developing NICE guidelines: the manual.
Confidence in cumulative evidence	For details please see sections 6.4 and 9.1 of Developing NICE guidelines: the manual.
Rationale / context – what is known	For details please see the introduction to the evidence review.
Describe contributions of authors and guarantor	A multidisciplinary committee developed the evidence review. The committee was convened by the National Guideline Centre (NGC) and chaired by Andrew Dickinson in line with section 3 of Developing NICE guidelines: the manual. Staff from NGC undertook systematic literature searches, appraised the evidence, conducted meta-analysis and cost-effectiveness analysis where appropriate, and drafted the evidence review in collaboration with the committee. For details please see Developing NICE guidelines: the manual.
Sources of funding / support	NGC is funded by NICE and hosted by the Royal College of Physicians.
Name of sponsor	NGC is funded by NICE and hosted by the Royal College of Physicians.
Roles of sponsor	NICE funds NGC to develop guidelines for those working in the NHS, public health and social care in England.
PROSPERO registration number	Not registered

1

Table 14: Health economic review protocol

Review question	All questions – health economic evidence
Objectives	To identify economic studies relevant to any of the review questions.
Search criteria	<ul style="list-style-type: none"> • Populations, interventions and comparators must be as specified in the individual review protocol above. • Studies must be of a relevant economic study design (cost-utility analysis, cost-effectiveness analysis, cost-benefit analysis, cost-consequences analysis, comparative cost analysis). • Studies must not be a letter, editorial or commentary, or a review of economic evaluations. (Recent reviews will be ordered although not reviewed. The bibliographies will be checked for relevant studies, which will then be ordered.) • Unpublished reports will not be considered unless submitted as part of a call for evidence. • Studies must be in English.
Search strategy	An economic study search will be undertaken using population-specific terms and an economic study filter – see Appendix G [<i>in the Full guideline</i>].
Review strategy	Studies not meeting any of the search criteria above will be excluded. Studies published before 2002, abstract-only studies and studies from non-OECD countries or the USA will also be excluded.

Each remaining study will be assessed for applicability and methodological limitations using the NICE economic evaluation checklist which can be found in Appendix G of the 2014 NICE guidelines manual.⁶⁹

Inclusion and exclusion criteria

- If a study is rated as both 'Directly applicable' and with 'Minor limitations' then it will be included in the guideline. An economic evidence table will be completed and it will be included in the economic evidence profile.
- If a study is rated as either 'Not applicable' or with 'Very serious limitations' then it will usually be excluded from the guideline. If it is excluded then an economic evidence table will not be completed and it will not be included in the economic evidence profile.
- If a study is rated as 'Partially applicable', with 'Potentially serious limitations' or both then there is discretion over whether it should be included.

Where there is discretion

The health economist will make a decision based on the relative applicability and quality of the available evidence for that question, in discussion with the Committee if required. The ultimate aim is to include economic studies that are helpful for decision-making in the context of the guideline and the current NHS setting. If several studies are considered of sufficiently high applicability and methodological quality that they could all be included, then the health economist, in discussion with the Committee if required, may decide to include only the most applicable studies and to selectively exclude the remaining studies. All studies excluded on the basis of applicability or methodological limitations will be listed with explanation as excluded economic studies in Appendix M.

The health economist will be guided by the following hierarchies.

Setting:

- UK NHS (most applicable).
- OECD countries with predominantly public health insurance systems (for example, France, Germany, Sweden).
- OECD countries with predominantly private health insurance systems (for example, Switzerland).
- Studies set in non-OECD countries or in the USA will have been excluded before being assessed for applicability and methodological limitations.

Economic study type:

- Cost-utility analysis (most applicable).
- Other type of full economic evaluation (cost-benefit analysis, cost-effectiveness analysis, cost-consequences analysis).
- Comparative cost analysis.
- Non-comparative cost analyses including cost-of-illness studies will have been excluded before being assessed for applicability and methodological limitations.

Year of analysis:

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

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

- The more closely the clinical effectiveness data used in the economic analysis matches with the outcomes of the studies included in the clinical review the more useful the analysis will be for decision-making in the guideline.

Appendix B: Literature search strategies

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

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

B.1 Clinical search literature search strategy

Searches were constructed using a PICO framework where population (P) terms were combined with Intervention (I) and in some cases Comparison (C) terms. Outcomes (O) are rarely used in search strategies for interventions as these concepts may not be well described in title, abstract or indexes and therefore difficult to retrieve. Search filters were applied to the search where appropriate.

Table 15: Database date parameters and filters used

Database	Dates searched	Search filter used
Medline (OVID)	1946 – 5 June 2017	Exclusions Randomised controlled trials Systematic review studies
Embase (OVID)	1974 – 5 June 2017	Exclusions Randomised controlled trials Systematic review studies
The Cochrane Library (Wiley)	Cochrane Reviews to 2017 Issue 6 of 12 CENTRAL to 2017 Issue 5 of 12 DARE, and NHSEED to 2015 Issue 2 of 4 HTA to 2016 Issue 4 of 4	None

Medline (Ovid) search terms

1.	exp urolithiasis/
2.	(nephrolithiasis or nephrolith or nephroliths or urolithias?s or ureterolithias?s).ti,ab.
3.	((renal or kidney* or urinary or ureter* or urethra*) adj3 (stone* or calculi or calculus or calculosis or lithiasis or c?olic*)).ti,ab.
4.	stone disease*.ti,ab.
5.	((calculi or calculus or calcium oxalate or cystine) adj3 (crystal* or stone* or lithiasis)).ti,ab.
6.	or/1-5
7.	letter/
8.	editorial/
9.	news/
10.	exp historical article/
11.	Anecdotes as Topic/
12.	comment/
13.	case report/
14.	(letter or comment*).ti.
15.	or/7-14

16.	randomized controlled trial/ or random*.ti,ab.
17.	15 not 16
18.	animals/ not humans/
19.	exp Animals, Laboratory/
20.	exp Animal Experimentation/
21.	exp Models, Animal/
22.	exp Rodentia/
23.	(rat or rats or mouse or mice).ti.
24.	or/17-23
25.	6 not 24
26.	limit 25 to English language
27.	exp Diet/
28.	Sodium, Dietary/
29.	Calcium, Dietary/
30.	exp Diet Therapy/
31.	exp diet, protein-restricted/ or exp diet, reducing/ or exp diet, sodium-restricted/
32.	exp Ascorbic Acid/
33.	exp citric acid/
34.	exp Purines/
35.	exp "diet, food, and nutrition"/
36.	exp Oxalic Acid/
37.	Drinking/
38.	exp Drinking Water/
39.	exp Carbonated Beverages/
40.	((fluid* or liquid*) adj2 (low* or reduc* or avoid* or misus* or stop* or high* or percent* or increas* or benefit* or intake* or ingest* or drink* or imbib* or consume* or manage* or hydrat* or has or have or take or taking or taken or took)).ti,ab.
41.	(drink* or beverage* or water* or H2O or juice* or lemon* or citr* or orange* or cranberr* or coffee* or tea* or fizzy or carbonated or cola* or soda* or Coke or Coca Cola or Kola or 7Up or Sprite or Dr Pepper or Pepsi or Red Bull or Mountain Dew or Fanta or Crush or Sunkist or Fresca or Lucozade or Irn-Bru or J2O or Schweppes or Tango or Ribena or Lilt or beer* or bitter* or ale* or lager* or wine* or alcohol* or sparkling or milk or fruit* or grapefruit* or punch* or smooth* or phosphoric or lime*).ti,ab.
42.	((diet* or low* or reduc* or decreas* or avoid* or misus* or abus* or withdr* or high* or percent* or consum* or intak* or benefit* or increas* or raise*) adj3 (calcium or Ca or salt or NaCl or sodium or sodium chloride or sodium glutamate or citrate or citric or protein* or purine* or magnesium or Mg or fiber or fibre or oxalic or oxalate* or ascorbic or vit* c)).ti,ab.
43.	(dairy or non dairy or cheese* or yogurt* or meat* or flesh* or game or veal or lamb or beef or steak* or burger* or hamburger* or pork or ham* or bacon or poultry or chicken or turkey or duck or fish or herring or mackerel or tuna or salmon or seafood* or shrimp* or lobster or scallop* or vegetable* or legume* or salad* or green* or plant* or avocado* or potato* or banana* or seed* or almond* or flaxseed or sunflower or spinach or beet* or berries or berry or bean* or pulses or soybean* or nuts or peanut* or walnut* or chocolate* or wholegrain* or wholemeal or rice or bran or oat* or porridge*).ti,ab.
44.	exp Exercise/
45.	exercise*.ti,ab.
46.	(physical* adj2 (activit* or train* or program* or therap*)).ti,ab.

47.	Weight Loss/
48.	(weight adj3 (loss* or lose or reduc* or percent*)).ti,ab.
49.	or/27-48
50.	randomized controlled trial.pt.
51.	controlled clinical trial.pt.
52.	randomi#ed.ti,ab.
53.	placebo.ab.
54.	randomly.ti,ab.
55.	Clinical Trials as topic.sh.
56.	trial.ti.
57.	or/50-56
58.	Meta-Analysis/
59.	exp Meta-Analysis as Topic/
60.	(meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
61.	((systematic* or evidence*) adj3 (review* or overview*)).ti,ab.
62.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
63.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
64.	(search* adj4 literature).ab.
65.	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
66.	cochrane.jw.
67.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
68.	or/58-67
69.	26 and 49
70.	57 or 68
71.	69 and 70

1

Embase (Ovid) search terms

1.	exp urolithiasis/
2.	(nephrolithiasis or nephrolith or nephroliths or urolithias?s or ureterolithias?s).ti,ab.
3.	((renal or kidney* or urinary or ureter* or urethra*) adj3 (stone* or calculi or calculus or calculosis or lithiasis or c?olic*)).ti,ab.
4.	stone disease*.ti,ab.
5.	((calculi or calculus or calcium oxalate or cystine) adj3 (crystal* or stone* or lithiasis)).ti,ab.
6.	or/1-5
7.	letter.pt. or letter/
8.	note.pt.
9.	editorial.pt.
10.	case report/ or case study/
11.	(letter or comment*).ti.
12.	or/7-11
13.	randomized controlled trial/ or random*.ti,ab.
14.	12 not 13
15.	animal/ not human/

16.	nonhuman/
17.	exp Animal Experiment/
18.	exp Experimental Animal/
19.	animal model/
20.	exp Rodent/
21.	(rat or rats or mouse or mice).ti.
22.	or/14-21
23.	6 not 22
24.	limit 23 to English language
25.	*diet/
26.	*sodium intake/
27.	*calcium intake
28.	*diet therapy
29.	protein restriction/ or sodium restriction/ or low calory diet/
30.	*ascorbic acid/
31.	*citric acid/
32.	"purines and purine derivatives"/
33.	*nutrition/
34.	oxalic acid/
35.	*drinking/
36.	*drinking water/
37.	*carbonated beverage/
38.	((fluid* or liquid*) adj2 (low* or reduc* or avoid* or misus* or stop* or high* or percent* or increas* or benefit* or intake* or ingest* or drink* or imbib* or consume* or manage* or hydrat* or has or have or take or taking or taken or took)).ti,ab.
39.	(drink* or beverage* or water* or H2O or juice* or lemon* or citr* or orange* or cranberr* or coffee* or tea* or fizzy or carbonated or cola* or soda* or Coke or Coca Cola or Kola or 7Up or Sprite or Dr Pepper or Pepsi or Red Bull or Mountain Dew or Fanta or Crush or Sunkist or Fresca or Lucozade or Irn-Bru or J2O or Schweppes or Tango or Ribena or Lilt or beer* or bitter* or ale* or lager* or wine* or alcohol* or sparkling or milk or fruit* or grapefruit* or punch* or smooth* or phosphoric or lime*).ti,ab.
40.	((diet* or low* or reduc* or decreas* or avoid* or misus* or abus* or withdr* or high* or percent* or consum* or intak* or benefit* or increas* or raise*) adj3 (calcium or Ca or salt or NaCl or sodium or sodium chloride or sodium glutamate or citrate or citric or protein* or purine* or magnesium or Mg or fiber or fibre or oxalic or oxalate* or ascorbic or vit* c)).ti,ab.
41.	(dairy or non dairy or cheese* or yogurt* or meat* or flesh* or game or veal or lamb or beef or steak* or burger* or hamburger* or pork or ham* or bacon or poultry or chicken or turkey or duck or fish or herring or mackerel or tuna or salmon or seafood* or shrimp* or lobster or scallop* or vegetable* or legume* or salad* or green* or plant* or avocado* or potato* or banana* or seed* or almond* or flaxseed or sunflower or spinach or beet* or berries or berry or bean* or pulses or soybean* or nuts or peanut* or walnut* or chocolate* or wholegrain* or wholemeal or rice or bran or oat* or porridge*).ti,ab.
42.	exercise/
43.	exercise*.ti,ab.
44.	(physical* adj2 (activit* or train* or program* or therap*)).ti,ab.
45.	*weight reduction/
46.	(weight adj3 (loss* or lose or reduc* or percent*)).ti,ab.

47.	or/25-46
48.	random*.ti,ab.
49.	factorial*.ti,ab.
50.	(crossover* or cross over*).ti,ab.
51.	((doubl* or singl*) adj blind*).ti,ab.
52.	(assign* or allocat* or volunteer* or placebo*).ti,ab.
53.	crossover procedure/
54.	single blind procedure/
55.	randomized controlled trial/
56.	double blind procedure/
57.	or/48-56
58.	systematic review/
59.	meta-analysis/
60.	(meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
61.	((systematic* or evidence*) adj3 (review* or overview*)).ti,ab.
62.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
63.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
64.	(search* adj4 literature).ab.
65.	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
66.	cochrane.jw.
67.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
68.	or/58-67
69.	24 and 47
70.	57 or 68
71.	69 and 70

1

Cochrane Library (Wiley) search terms

#1.	MeSH descriptor: [Urolithiasis] explode all trees
#2.	(nephrolithiasis or nephrolith or urolithiasis):ti,ab
#3.	((renal or kidney or urinary or ureteric or ureteral or ureter) near/2 (stone* or calculi or calculus or calculosis or lithiasis or colic)):ti,ab
#4.	(stone disease*):ti,ab
#5.	((calculi or calculus or calcium oxalate or cystine) near/2 (crystal* or stone* or lithiasis)):ti,ab
#6.	(or #1-#5)
#7.	MeSH descriptor: [Diet] explode all trees
#8.	MeSH descriptor: [Sodium, Dietary] this term only
#9.	MeSH descriptor: [Calcium, Dietary] this term only
#10.	MeSH descriptor: [Diet Therapy] explode all trees
#11.	MeSH descriptor: [Ascorbic Acid] explode all trees
#12.	MeSH descriptor: [Citric Acid] explode all trees
#13.	MeSH descriptor: [Purines] explode all trees
#14.	MeSH descriptor: [Diet, Food, and Nutrition] explode all trees
#15.	MeSH descriptor: [Oxalates] explode all trees

#16.	MeSH descriptor: [Drinking] this term only
#17.	MeSH descriptor: [Drinking Water] explode all trees
#18.	MeSH descriptor: [Carbonated Beverages] explode all trees
#19.	((fluid* or liquid*) near/2 (low* or reduc* or avoid* or misus* or stop* or high* or percent* or increas* or benefit* or intake* or ingest* or drink* or imbib* or consume* or manage* or hydrat* or has or have or take or taking or taken or took)):ti,ab
#20.	(drink* or beverage* or water* or H2O or juice* or lemon* or citr* or orange* or cranberr* or coffee* or tea* or fizzy or carbonated or cola* or soda* or Coke or Coca Cola or Kola or 7Up or Sprite or Dr Pepper or Pepsi or Red Bull or Mountain Dew or Fanta or Crush or Sunkist or Fresca or Lucozade or Irn-Bru or J2O or Schweppes or Tango or Ribena or Lilt or beer* or bitter* or ale* or lager* or wine* or alcohol* or sparkling or milk or fruit* or grapefruit* or punch* or smooth* or phosphoric or lime*):ti,ab
#21.	((diet* or low* or reduc* or decreas* or avoid* or misus* or abus* or withdr* or high* or percent* or consum* or intak* or benefit* or increas* or raise*) near/3 (calcium or Ca or salt or NaCl or sodium or sodium chloride or sodium glutamate or citrate or citric or protein* or purine* or magnesium or Mg or fiber or fibre or oxalic or oxalate* or ascorbic or vit* c)):ti,ab
#22.	(dairy or non dairy or cheese* or yogurt* or meat* or flesh* or game or veal or lamb or beef or steak* or burger* or hamburger* or pork or ham* or bacon or poultry or chicken or turkey or duck or fish or herring or mackerel or tuna or salmon or seafood* or shrimp* or lobster or scallop* or vegetable* or legume* or salad* or green* or plant* or avocado* or potato* or banana* or seed* or almond* or flaxseed or sunflower or spinach or beet* or berries or berry or bean* or pulses or soybean* or nuts or peanut* or walnut* or chocolate* or wholegrain* or wholemeal or rice or bran or oat* or porridge*):ti,ab
#23.	MeSH descriptor: [Exercise] explode all trees
#24.	exercise*:ti,ab
#25.	(physical* near/2 (activit* or train* or program* or therap*)):ti,ab
#26.	MeSH descriptor: [Weight Loss] this term only
#27.	(weight near/3 (loss* or lose or reduc* or percent*)):ti,ab
#28.	(or #7-#27)
#29.	#6 and #28

1 B.2 Health Economics literature search strategy

2 Health economic evidence was identified by conducting a broad search relating to renal and
3 ureteric stones population in NHS Economic Evaluation Database (NHS EED – this ceased
4 to be updated after March 2015) and the Health Technology Assessment database (HTA)
5 with no date restrictions. NHS EED and HTA databases are hosted by the Centre for
6 Research and Dissemination (CRD). Additional searches were run on Medline and Embase
7 for health economics studies.

8 **Table 16: Database date parameters and filters used**

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

1

Medline (Ovid) search terms

1.	exp urolithiasis/
2.	(nephrolithiasis or nephrolith or nephroliths or urolithias?s or ureterolithias?s).ti,ab.
3.	((renal or kidney* or urinary or ureter* or urethra*) adj3 (stone* or calculi or calculus or calculosis or lithiasis or c?olic*)).ti,ab.
4.	stone disease*.ti,ab.
5.	((calculi or calculus or calcium oxalate or cystine) adj3 (crystal* or stone* or lithiasis)).ti,ab.
6.	or/1-5
7.	letter/
8.	editorial/
9.	news/
10.	exp historical article/
11.	Anecdotes as Topic/
12.	comment/
13.	case report/
14.	(letter or comment*).ti.
15.	or/7-14
16.	randomized controlled trial/ or random*.ti,ab.
17.	15 not 16
18.	animals/ not humans/
19.	exp Animals, Laboratory/
20.	exp Animal Experimentation/
21.	exp Models, Animal/
22.	exp Rodentia/
23.	(rat or rats or mouse or mice).ti.
24.	or/17-23
25.	6 not 24
26.	limit 25 to English language
27.	Economics/
28.	Value of life/
29.	exp "Costs and Cost Analysis"/
30.	exp Economics, Hospital/
31.	exp Economics, Medical/
32.	Economics, Nursing/
33.	Economics, Pharmaceutical/
34.	exp "Fees and Charges"/
35.	exp Budgets/
36.	budget*.ti,ab.
37.	cost*.ti.
38.	(economic* or pharmaco?economic*).ti.
39.	(price* or pricing*).ti,ab.
40.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
41.	(financ* or fee or fees).ti,ab.

42.	(value adj2 (money or monetary)).ti,ab.
43.	or/27-42
44.	26 and 43

1

Embase (Ovid) search terms

1.	exp urolithiasis/
2.	(nephrolithiasis or nephrolith or nephroliths or urolithias?s or ureterolithias?s).ti,ab.
3.	((renal or kidney* or urinary or ureter* or urethra*) adj3 (stone* or calculi or calculus or calculosis or lithiasis or c?olic*)).ti,ab.
4.	stone disease*.ti,ab.
5.	((calculi or calculus or calcium oxalate or cystine) adj3 (crystal* or stone* or lithiasis)).ti,ab.
6.	or/1-5
7.	letter.pt. or letter/
8.	note.pt.
9.	editorial.pt.
10.	case report/ or case study/
11.	(letter or comment*).ti.
12.	or/7-11
13.	randomized controlled trial/ or random*.ti,ab.
14.	12 not 13
15.	animal/ not human/
16.	nonhuman/
17.	exp Animal Experiment/
18.	exp Experimental Animal/
19.	animal model/
20.	exp Rodent/
21.	(rat or rats or mouse or mice).ti.
22.	or/14-21
23.	6 not 22
24.	limit 23 to English language
25.	health economics/
26.	exp economic evaluation/
27.	exp health care cost/
28.	exp fee/
29.	budget/
30.	funding/
31.	budget*.ti,ab.
32.	cost*.ti.
33.	(economic* or pharmaco?economic*).ti.
34.	(price* or pricing*).ti,ab.
35.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.

36.	(financ* or fee or fees).ti,ab.
37.	(value adj2 (money or monetary)).ti,ab.
38.	or/25-37
39.	24 and 38

1

NHS EED and HTA (CRD) search terms

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

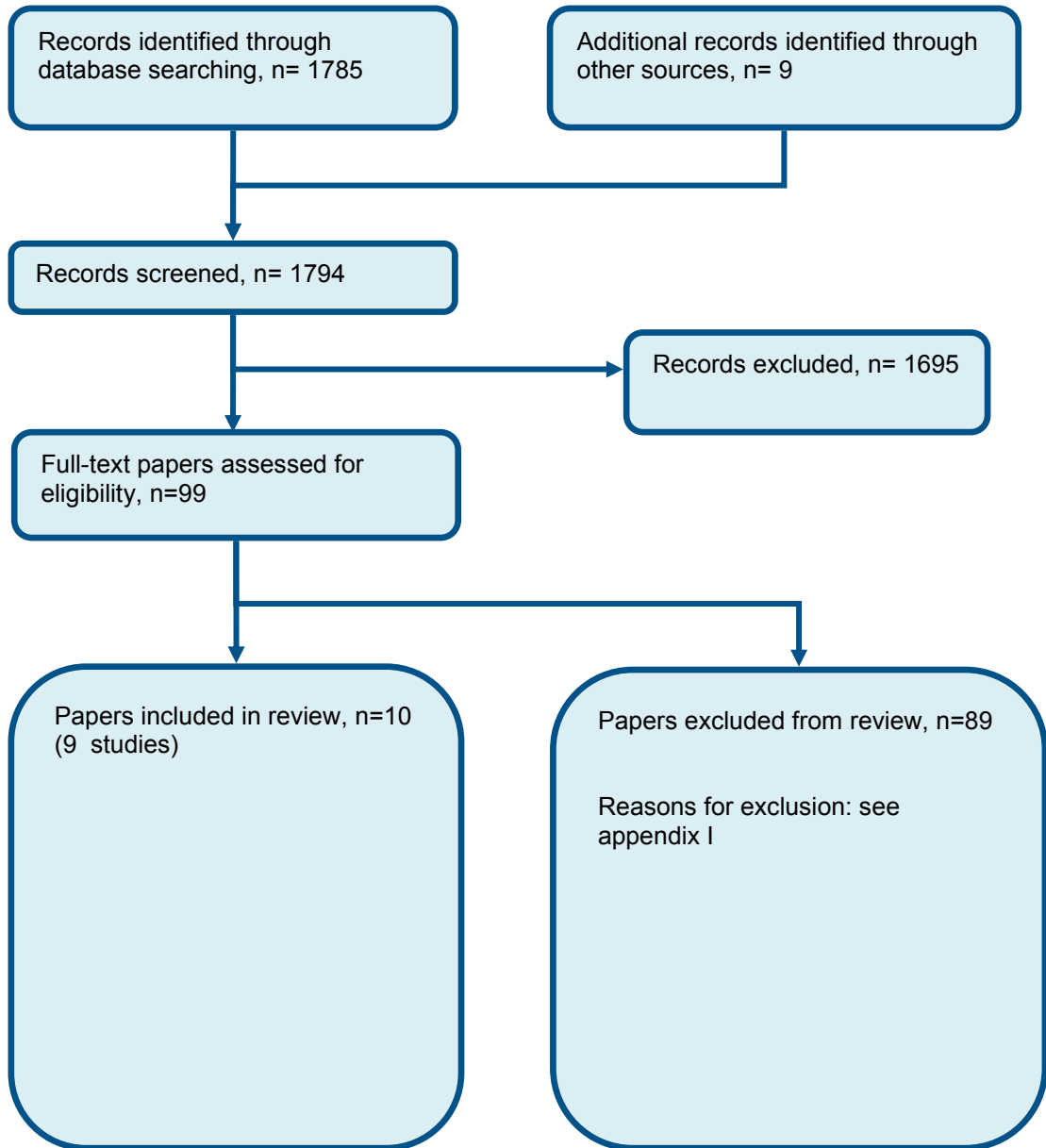
2

3

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Appendix C: Clinical evidence selection

Figure 1: Flow chart of clinical study selection for the review of dietary interventions



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Appendix D: Clinical evidence tables

Study	Aras 2008 ³
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=30)
Countries and setting	Conducted in Turkey; Setting: Outpatients
Line of therapy	1st line
Duration of study	Intervention time: 3 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Adults (≥18 years)
Subgroup analysis within study	Not applicable
Inclusion criteria	Patients with hypocitraturic urinary calcium stones
Exclusion criteria	Endocrinologic and gastrointestinal disease that could cause urinary system stones and hypocitraturia; distal renal tubular acidosis, chronic diarrhea, hyperparathyroidism, active peptic ulcers, chronic renal disease, hyperpotassemia, urinary tract infections, urinary tract anomalies; intolerance and allergy to potassium citrate
Recruitment/selection of patients	Not stated
Age, gender and ethnicity	Age - Mean (SD): 37.6±2.8. Gender (M:F): Not stated. Ethnicity: Not stated
Further population details	
Indirectness of population	No indirectness
Interventions	(n=10) Intervention 1: Fluid - Lemonade. Fresh lemon juice (85 cc) per day (containing 60 mEq of citrate). Duration 3 months. Concurrent medication/care: Increase water intake to 3 L/day. Indirectness: No indirectness (n=10) Intervention 2: Citrate - Potassium citrate. 60 mEq/day. Duration 3 months. Concurrent medication/care: Increase water intake to 3 L/day. Indirectness: No indirectness (n=10) Intervention 3: Fluid - Water. Diet group: water 3L/day, calcium 1200 mg/day, NaCl 5 g/day, protein

	intakes 1.0 g/kg/day. Duration 3 months. Concurrent medication/care: None. Indirectness: No indirectness
Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: LEMONADE versus WATER	
<p>Protocol outcome 1: Change in metabolic test: urine calcium at Define - Actual outcome for Adults (≥18 years): Calcium level (mg/day) at 3 months; Group 1: mean 118.3 mg/day (SD 86.16); n=10, Group 2: mean 185.6 mg/day (SD 61.63); n=10 Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:</p>	
<p>Protocol outcome 2: Change in metabolic test: urine pH at Define - Actual outcome for Adults (≥18 years): pH at 3 months; Group 1: mean 6 (SD 0.3); n=10, Group 2: mean 5.8 (SD 0.3); n=10 Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:</p>	
<p>Protocol outcome 3: Change in metabolic test: urine oxalate at Define - Actual outcome for Adults (≥18 years): Oxalate level (mg/day) at 3 months; Group 1: mean 25.45 mg/day (SD 19.98); n=10, Group 2: mean 22.6 mg/day (SD 12.43); n=10 Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:</p>	
Protocol outcomes not reported by the study	Quality of life at Define; Use of healthcare services/retreatment rate at Define; Adverse events at Define; Kidney function at Define; Change in metabolic test: urine sodium at Define; Change in stone risk score at Define; Compliance/adherence at Define; New stone formation/incidence of stones/recurrence rate at Define

Study	Borghi 1996¹¹
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=199)
Countries and setting	Conducted in Italy; Setting: Hospital
Line of therapy	1st line
Duration of study	Intervention + follow up: 5 years
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Renal echography or x-ray. 24h urine analysis.

Stratum	Adults (≥18 years):
Subgroup analysis within study	Not applicable:
Inclusion criteria	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), absence of other retained calculi (renal echography and IVP) and absence of arterial hypertension or other metabolic pathology that requires regular dietary measures or drug therapy.
Exclusion criteria	Not stated
Recruitment/selection of patients	Stone patients referred to the stone centre
Age, gender and ethnicity	Age - Mean (SD): Intervention: 42.2 (11.6); control: 40.1 (13.2). Gender (M:F): 134/65. Ethnicity: Not stated
Further population details	
Indirectness of population	No indirectness
Interventions	(n=99) Intervention 1: Fluid - Water. High water intake (to give a urine volume ≥2 l/day. Duration 5 years. Concurrent medication/care: None. Indirectness: No indirectness (n=100) Intervention 2: No intervention. Not necessary to follow any special procedures. Duration 5 years. Concurrent medication/care: None. Indirectness: No indirectness
Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: WATER versus NO INTERVENTION	
<p>Protocol outcome 1: New stone formation/incidence of stones/recurrence rate at Define - Actual outcome for Adults (≥18 years): Second episode of calculosis at 5 years; Group 1: 12/99, Group 2: 27/100 Risk of bias: All domain - High, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:</p>	
Protocol outcomes not reported by the study	Quality of life at Define; Adverse events at Define; Kidney function at Define; Change in metabolic test: urine calcium at Define; Change in metabolic test: urine pH at Define; Change in metabolic test: urine oxalate at Define; Change in metabolic test: urine sodium at Define; Change in stone risk score at Define; Compliance/adherence at Define; Use of healthcare services/retreatment rate at Define

Study	Borghi 2002 ¹²
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=120)
Countries and setting	Conducted in Italy; Setting: Outpatient department
Line of therapy	Not applicable
Duration of study	Intervention + follow up: 5 years
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Idiopathic hypercalciuria and formation of at least two documented calcium oxalate stones
Stratum	Adults (≥18 years)
Subgroup analysis within study	Not applicable
Inclusion criteria	Men with idiopathic hypercalciuria (urinary calcium excretion >300mg per day [7.5mmol per day]) on an unrestricted diet, recurrent formation of calcium oxalate stones (at least 2 documented events - colic episodes with expulsion of stones or radiographic evidence of retained stones), no known condition that is commonly associated with calcium nephrolithiasis (e.g. primary hyperparathyroidism, primary hyperoxaluria, enteric hyperoxaluria, bowel resection, inflammatory bowel disease, renal tubular acidosis, sarcoidosis, or sponge kidney), no previous visit to a stone disease centre, no current treatment for the prevention of recurrent stones except for the advice to increase water intake, and residence in the area of Parma, Italy
Exclusion criteria	Not reported
Recruitment/selection of patients	Not reported
Age, gender and ethnicity	Age - Mean (SD): Low calcium group: 45.4 (10.9), normal calcium group: 44.8 (9.2). Gender (M:F): Males. Ethnicity: Not reported
Further population details	
Indirectness of population	No indirectness
Interventions	(n=60) Intervention 1: Calcium. Low calcium diet - men were instructed to avoid milk, yoghurt, and cheese so that calcium intake would be reduced to approximately 10mmol per day. Men were also advised to avoid consuming large amount of oxalate rice foods e.g. walnuts, spinach, rhubarb, parsley and chocolate. Duration 5 years. Concurrent medication/care: Not reported. Indirectness: No indirectness (n=60) Intervention 2: Calcium. Normal-to-high calcium, low protein and low salt diet. Also advised to avoid foods rich in oxalate. Moderate consumption of wine, beer, carbonated beverages and coffee were allowed. Duration 5 years. Concurrent medication/care: Not reported. Indirectness: No indirectness

Funding	Academic or government funding (Supported in part by grants from the University of Parma and the Italian Ministry for Universities for Scientific and Technological Research)
<p>RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: CALCIUM - LOW versus CALCIUM - NORMAL-HIGH</p> <p>Protocol outcome 1: New stone formation/incidence of stones/recurrence rate at Define - Actual outcome for Adults (≥18 years): Recurrence at 5 years; Group 1: 23/60, Group 2: 12/60 Risk of bias: All domain - High, Selection - Very high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 9; Group 2 Number missing: 8</p>	
Protocol outcomes not reported by the study	Quality of life at Define; Adverse events at Define; Kidney function at Define; Change in metabolic test: urine calcium at Define; Change in metabolic test: urine pH at Define; Change in metabolic test: urine oxalate at Define; Change in metabolic test: urine sodium at Define; Change in stone risk score at Define; Compliance/adherence at Define; Use of healthcare services/retreatment rate at Define

Study (subsidiary papers)	Dussol 2008 ²¹ (Rotily 2000 ⁸⁵)
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=175)
Countries and setting	Conducted in France
Line of therapy	1st line
Duration of study	Intervention + follow up: 4 years
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Adults (≥18 years)
Subgroup analysis within study	Not applicable
Inclusion criteria	Over 18 and under 70 years of age, speak French, understand dietary instructions, live close to our center and have no plan to move in the following months
Exclusion criteria	Patients with systemic disease (including primary hyperparathyroidism, sarcoidosis, vitamin D excess, bowel disease of any kind, renal tubular acidosis, primary hyperoxaluria or urinary tract infections). In addition, none had hereditary or acquired anatomical disorders of the kidney or the urinary drainage system, except medullary sponge kidney.
Age, gender and ethnicity	Age - Mean (SD): LAPD group: 44 (12); HFD group: 44 (12); control group: 45 (11); . Gender (M:F): 114/61. Ethnicity: Not stated

Further population details	
Extra comments	Some patients previously attended a stone disease center, but none of them had taken drugs or gone on diets, although during their evaluation some had received advice to increase their water intake.
Indirectness of population	No indirectness
Interventions	<p>(n=55) Intervention 1: Protein/purines intake - Animal protein. Low-animal-protein diet (LAPD). The LAPD group was instructed to decrease their intake of animal protein by limiting their consumption of meat and fish to 3 servings per week and to not exceed 100 g/day of milk products (milk, cheese and yogurt). The target was to obtain a daily contribution of protein to energy of < 13%. Instead of protein, patients were counselled to eat refined cereals (pasta and rice).. Duration 4 years. Concurrent medication/care: All participants were advised to maintain a high water intake and to have a calcium intake between 800 and 1,000 mg per day. They were given a leaflet with information about the benefits of daily water intake and how to increase it by drinking 8 glasses of tap water (2 litres/day) at fixed times. The calcium content of tap water available in the Marseille area is 100 mg/l. The attending physician did not recommend any modification of dietary habits but did insist on an increase in fluid intake. No advice was given for sodium intake.. Indirectness: No indirectness</p> <p>(n=60) Intervention 2: Fibre. High-fiber diet (HFD). The HFD group was instructed to increase their intake of fruits and vegetables and to substitute their usual cereals with whole grain dietary products in order to limit the increase in energy. The target was to obtain a 25-g/day increase in fiber intake. They were not instructed to exclude fruits and vegetables particularly rich in oxalate.. Duration 4 years. Concurrent medication/care: All participants were advised to maintain a high water intake and to have a calcium intake between 800 and 1,000 mg per day. They were given a leaflet with information about the benefits of daily water intake and how to increase it by drinking 8 glasses of tap water (2 litres/day) at fixed times. The calcium content of tap water available in the Marseille area is 100 mg/l. The attending physician did not recommend any modification of dietary habits but did insist on an increase in fluid intake. No advice was given for sodium intake.. Indirectness: No indirectness</p> <p>(n=60) Intervention 3: No intervention. Control group. Duration 4 years. Concurrent medication/care: All participants were advised to maintain a high water intake and to have a calcium intake between 800 and 1,000 mg per day. They were given a leaflet with information about the benefits of daily water intake and how to increase it by drinking 8 glasses of tap water (2 litres/day) at fixed times. The calcium content of tap water available in the Marseille area is 100 mg/l. The attending physician did not recommend any modification of dietary habits but did insist on an increase in fluid intake. No advice was given for sodium intake.. Indirectness: No indirectness</p>
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: ANIMAL PROTEIN versus FIBRE

Protocol outcome 1: New stone formation/incidence of stones/recurrence rate at Define

- Actual outcome for Adults (≥18 years): Recurrence at 4 years; Group 1: 11/23, Group 2: 17/27

Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 32, Reason: 59 loss to follow up, 39 unwilling to complete the study because of the proposed diet, 4 withdrew because of medical conditions requiring treatment not allowed in the study (thiazides, allopurinol, anti-osteoporotic drugs); Group 2 Number missing: 33

Protocol outcome 2: Change in metabolic test: urine calcium at Define

- Actual outcome for Adults (≥18 years): Calcium (mmol/day) at 4 years; Group 1: mean 7.7 mmol/day (SD 4.5); n=23, Group 2: mean 5.3 mmol/day (SD 3.5); n=27

Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 32, Reason: 59 loss to follow up, 39 unwilling to complete the study because of the proposed diet, 4 withdrew because of medical conditions requiring treatment not allowed in the study (thiazides, allopurinol, anti-osteoporotic drugs); Group 2 Number missing: 33

Protocol outcome 3: Change in metabolic test: urine oxalate at Define

- Actual outcome for Adults (≥18 years): Oxalate (mmol/day) at 4 years; Group 1: mean 0.31 mmol/day (SD 0.2); n=23, Group 2: mean 0.31 mmol/day (SD 0.1); n=27

Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 32, Reason: 59 loss to follow up, 39 unwilling to complete the study because of the proposed diet, 4 withdrew because of medical conditions requiring treatment not allowed in the study (thiazides, allopurinol, anti-osteoporotic drugs); Group 2 Number missing: 33

Protocol outcome 4: Change in metabolic test: urine sodium at Define

- Actual outcome for Adults (≥18 years): Sodium (mmol/day) at 4 years; Group 1: mean 173 mmol/day (SD 78); n=23, Group 2: mean 133 mmol/day (SD 57); n=27

Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 32, Reason: 59 loss to follow up, 39 unwilling to complete the study because of the proposed diet, 4 withdrew because of medical conditions requiring treatment not allowed in the study (thiazides, allopurinol, anti-osteoporotic drugs); Group 2 Number missing: 33

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: ANIMAL PROTEIN versus NO INTERVENTION

Protocol outcome 1: New stone formation/incidence of stones/recurrence rate at Define

- Actual outcome for Adults (≥18 years): Recurrence at 4 years; Group 1: 11/23, Group 2: 11/23

Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 32, Reason: 59 loss to follow up, 39 unwilling to complete the study because of the proposed diet, 4 withdrew because of medical conditions requiring treatment not allowed in the study (thiazides, allopurinol, anti-osteoporotic drugs); Group 2 Number missing: 33

Protocol outcome 2: Change in metabolic test: urine calcium at Define

- Actual outcome for Adults (≥18 years): Calcium (mmol/day) at 4 years; Group 1: mean 7.7 mmol/day (SD 4.5); n=23, Group 2: mean 6.1 mmol/day (SD 2.6); n=23

Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 32, Reason: 59 loss to follow up, 39 unwilling to complete the study because of the proposed diet, 4 withdrew because of medical conditions requiring treatment not allowed in the study (thiazides, allopurinol, anti-osteoporotic drugs); Group 2 Number missing: 33

Protocol outcome 3: Change in metabolic test: urine oxalate at Define

- Actual outcome for Adults (≥18 years): Oxalate (mmol/day) at 4 years; Group 1: mean 0.31 mmol/day (SD 0.2); n=23, Group 2: mean 0.28 mmol/day (SD 0.2); n=23

Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 32, Reason: 59 loss to follow up, 39 unwilling to complete the study because of the proposed diet, 4 withdrew because of medical conditions requiring treatment not allowed in the study (thiazides, allopurinol, anti-osteoporotic drugs); Group 2 Number missing: 33

Protocol outcome 4: Change in metabolic test: urine sodium at Define

- Actual outcome for Adults (≥18 years): Sodium (mmol/day) at 4 years; Group 1: mean 173 mmol/day (SD 78); n=23, Group 2: mean 163 mmol/day (SD 66); n=23

Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 32, Reason: 59 loss to follow up, 39 unwilling to complete the study because of the proposed diet, 4 withdrew because of medical conditions requiring treatment not allowed in the study (thiazides, allopurinol, anti-osteoporotic drugs); Group 2 Number missing: 33

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: FIBRE versus NO INTERVENTION

Protocol outcome 1: New stone formation/incidence of stones/recurrence rate at Define

- Actual outcome for Adults (≥18 years): Recurrence at 4 years; Group 1: 17/27, Group 2: 11/23

Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 32, Reason: 59 loss to follow up, 39 unwilling to complete the study because of the proposed diet, 4 withdrew because of medical conditions requiring treatment not allowed in the study (thiazides, allopurinol, anti-osteoporotic drugs); Group 2 Number missing: 33

Protocol outcome 2: Change in metabolic test: urine calcium at Define

- Actual outcome for Adults (≥18 years): Calcium (mmol/day) at 4 years; Group 1: mean 5.3 mmol/day (SD 3.5); n=27, Group 2: mean 6.1 mmol/day (SD 2.6); n=23

Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 32, Reason: 59 loss to follow up, 39 unwilling to complete the study because of the proposed diet, 4 withdrew because of medical conditions requiring treatment not allowed in the study (thiazides, allopurinol, anti-osteoporotic drugs); Group 2 Number missing: 33

Protocol outcome 3: Change in metabolic test: urine oxalate at Define

- Actual outcome for Adults (≥18 years): Oxalate (mmol/day) at 4 years; Group 1: mean 0.31 mmol/day (SD 0.1); n=27, Group 2: mean 0.28 mmol/day (SD 0.2); n=23

Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 32, Reason: 59 loss to follow up, 39 unwilling to complete the study because of the proposed diet, 4 withdrew because of medical conditions requiring treatment not allowed in the study (thiazides, allopurinol, anti-osteoporotic drugs); Group 2 Number missing: 33

Protocol outcome 4: Change in metabolic test: urine sodium at Define

- Actual outcome for Adults (≥18 years): Sodium (mmol/day) at 4 years; Group 1: mean 133 mmol/day (SD 57); n=27, Group 2: mean 163 mmol/day (SD 66); n=23

Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 32, Reason: 59 loss to follow up, 39 unwilling to complete the study because of the proposed diet, 4 withdrew because of medical conditions requiring treatment not allowed in the study (thiazides, allopurinol, anti-osteoporotic drugs); Group 2 Number missing: 33

Protocol outcomes not reported by the study

Quality of life at Define; Adverse events at Define; Kidney function at Define; Change in metabolic test: urine pH at Define; Change in stone risk score at Define; Compliance/adherence at Define; Use of healthcare services/retreatment rate at Define

Study	Noori 2014 ⁷¹
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=41)
Countries and setting	Conducted in Iran; Setting:
Line of therapy	1st line
Duration of study	Intervention + follow up: 8 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Adults (≥18 years)
Subgroup analysis within study	Not applicable
Inclusion criteria	Men and women with a history of at least 2 episodes of calcium oxalate kidney stones (≥50% calcium oxalate) who also had documented hyperoxaluria (urine oxalate >40 mg/d). Patients with urinary abnormalities in addition to hyperoxaluria, including low urine volume, hypercalcinuria, hypocitraturia, and hyperuricosuria, were not excluded. Patients were included when they were taking drugs for the prevention of stone disease, including pyridoxine, thiazides, hydrochlorothiazide, or indapamide), and allopurinol, as long as there had been no changes in these prescriptions for at least 3 previous months.
Exclusion criteria	History of diabetes, inflammatory bowel disease, ileal or colonic resection, bariatric surgery, chronic kidney disease, of hepatic, thyroid, parathyroid, or immunologic disease; primary hyperoxaluria or patients treated with potassium citrate, cholestyramine, or calcium supplements.
Age, gender and ethnicity	Age - Mean (SD): 48 (13). Gender (M:F): 10/31. Ethnicity: Not stated
Further population details	
Indirectness of population	No indirectness
Interventions	(n=21) Intervention 1: DASH diet. DASH diet plan with unrestricted oxalate intake. Diet higher in fruits, vegetables, and low-fat dairy products and lower in saturated fat, total fat, and cholesterol; it contained more whole grains and fewer refined grains, sweets, and red meat. . Duration 8 weeks. Concurrent medication/care: 2L water during cold weather and 3 L water during warm or hot weather. Indirectness: No indirectness (n=20) Intervention 2: Oxalate. Low-oxalate diet (avoid very high-oxalate foods entirely and to restrict intake of high-oxalate foods). Duration 8 weeks. Concurrent medication/care: 2L water during cold weather and 3 L water during warm or hot weather. Indirectness: No indirectness
Funding	Other (Nephrology and urology research centre of Shahid Beheshti university of medical sciences)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: DASH DIET versus OXALATE

Protocol outcome 1: Change in metabolic test: urine calcium at Define

- Actual outcome for Adults (≥18 years): Calcium at 8 weeks; Group 1: mean 171.5 mg/d (SD 81.9); n=21, Group 2: mean 175.2 mg/d (SD 72.4); n=20

Risk of bias: All domain - High, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 2: Change in metabolic test: urine pH at Define

- Actual outcome for Adults (≥18 years): pH at 8 weeks; Group 1: mean 5.9 (SD 0.4); n=21, Group 2: mean 6 (SD 0.7); n=20

Risk of bias: All domain - High, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 3: Change in metabolic test: urine oxalate at Define

- Actual outcome for Adults (≥18 years): Oxalate at 8 weeks; Group 1: mean 53.9 (SD 14); n=21, Group 2: mean 47 (SD 13.4); n=20

Risk of bias: All domain - High, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 4: Change in metabolic test: urine sodium at Define

- Actual outcome for Adults (≥18 years): Sodium at 8 weeks; Group 1: mean 147.2 mEq/d (SD 73.5); n=21, Group 2: mean 159.3 mEq/d (SD 93.5); n=20

Risk of bias: All domain - High, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcomes not reported by the study

Quality of life at Define; Use of healthcare services/retreatment rate at Define; Adverse events at Define; Kidney function at Define; Change in stone risk score at Define; Compliance/adherence at Define; New stone formation/incidence of stones/recurrence rate at Define

Study	Nouvenne 2010 ⁷³
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=210)
Countries and setting	Conducted in Italy; Setting:
Line of therapy	1st line
Duration of study	Intervention + follow up: 3 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis

Stratum	Adults (≥18 years)
Subgroup analysis within study	Not applicable
Inclusion criteria	A diagnosis of idiopathic calcium-oxalate stone disease made on the basis of at least one stone expelled and analysed by infraredspectrophotometry; perfect mental and physical health, free from diabetes mellitus, no episode of renal colic in the preceding 3 months, no retained stone, no long trip or holiday away from home planned for the next 3 months, no intention of chronic use of drugs or supplements for the next 3 months, systolic blood pressure >110mmHg (measured at rest in a sitting position with a manual mercury sphygmomanometer), normal kidney function, and daily urinary excretion of >100 mmol Na and Cl/d and >300 mg Ca/d (7.5 mmol) in men and .250 mgCa/d (6.25 mmol) in women while on a free diet
Exclusion criteria	Presence of diseases known to be associated with the production of calcium stones (for example, primary hyperparathyroidism, primary hyperoxaluria, enteric hyperoxaluria, bowel resection, inflammatory bowel disease, renal tubular acidosis, sarcoidosis, sponge kidney, and hyperthyroidism); chronic use of drugs capable of increasing the risk of calcium stone formation, such as vitamin D, acetazolamide, and antiepileptic drugs
Recruitment/selection of patients	All patients were enrolled through the specialist out-patient clinic of the University Hospital of Parma (Parma, Italy), which has followed a standardized screening protocol for stone disease since 1984
Age, gender and ethnicity	Age - Mean (SD): Low sodium diet: 39 (9); No intervention: 40 (10). Gender (M:F): 150/60. Ethnicity: Not stated
Further population details	
Indirectness of population	No indirectness
Interventions	<p>(n=108) Intervention 1: Salt - Low sodium diet. Patients were recommended to eliminate the intake of kitchen salt (including salt added to foods and salt used for cooking) and to strictly limit their consumption of food with a high salt content, as specified on the instruction sheet given to them after detailed explanations and information were provided to them by a member of our team who specialized in food science. To improve food palatability, in place of kitchen salt, the patients were advised to use various herbs and spices, as detailed on the instruction sheet. Another dietary recommendation concerned the intake of calcium in amounts of 800–1000 mg/d, which was to be achieved through the consumption of milk, yogurt, and cheeses with a low salt content. Apart from these restrictions, the diet was free. Duration 3 months. Concurrent medication/care: Beverage consumption amounted to 2 L/d in the cold season (October–March) and 3 L/d in the warm season (April–September); the water that was consumed had a low sodium and calcium content (7 mg Na/L, 15.9 mg Ca/L, 6.3 mg Mg/L, 4.4 mg K/L, 81.7 mg HCO₃, 13.9 mg Cl/L, 7 mg NO₄ 2/L, 12.8 mg SiO₂/L, pH 6.8; Fiuggi 2/L, 6 mg SO₄ water; Fiuggi-Sangemini, Frosinone, Italy). Indirectness: No indirectness</p> <p>(n=102) Intervention 2: No intervention. Free diet. Duration 3 months. Concurrent medication/care: Beverage consumption amounted to 2 L/d in the cold season (October–March) and 3 L/d in the warm season (April–September); the water that was consumed had a low sodium and calcium content (7 mg Na/L, 15.9 mg</p>

	Ca/L,6.3mgMg/L, 4.4mgK/L,81.7mgHCO3 13.9 mg Cl/L, 7 mg NO4 2/L,12.8mgSiO2/L, pH 6.8; Fiuggi 2/L, 6 mg SO4 water; Fiuggi-Sangemini, Frosinone, Italy).. Indirectness: No indirectness
Funding	Funding not stated
<p>RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: LOW SODIUM DIET versus NO INTERVENTION</p> <p>Protocol outcome 1: Change in metabolic test: urine calcium at Define - Actual outcome for Adults (≥18 years): Urine calcium (mg/d) at 3 months; Group 1: mean 271 mg/d (SD 86); n=97, Group 2: mean 361 mg/d (SD 129); n=100 Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 11, Reason: Could not tolerate the low sodium diet; Group 2 Number missing: 2, Reason: Work commitment</p> <p>Protocol outcome 2: Change in metabolic test: urine pH at Define - Actual outcome for Adults (≥18 years): Urine pH at 3 months; Group 1: mean 6.01 (SD 0.42); n=97, Group 2: mean 6.01 (SD 0.47); n=100 Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 11, Reason: Could not tolerate the low sodium diet; Group 2 Number missing: 2, Reason: Work commitment</p> <p>Protocol outcome 3: Change in metabolic test: urine oxalate at Define - Actual outcome for Adults (≥18 years): Urine oxalate (mg/d) at 3 months; Group 1: mean 28 mg/d (SD 8); n=97, Group 2: mean 32 mg/d (SD 10); n=100 Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 11, Reason: Could not tolerate the low sodium diet; Group 2 Number missing: 2, Reason: Work commitment</p> <p>Protocol outcome 4: Change in metabolic test: urine sodium at Define - Actual outcome for Adults (≥18 years): Urine sodium (mmol/d) at 3 months; Group 1: mean 68 mmol/d (SD 43); n=97, Group 2: mean 200 mmol/d (SD 61); n=100 Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 11, Reason: Could not tolerate the low sodium diet; Group 2 Number missing: 2, Reason: Work commitment</p>	
Protocol outcomes not reported by the study	Quality of life at Define; Use of healthcare services/retreatment rate at Define; Adverse events at Define; Kidney function at Define; Change in stone risk score at Define; Compliance/adherence at Define; New stone formation/incidence of stones/recurrence rate at Define

Study	Shuster 1992 ⁸⁸
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=1009)
Countries and setting	Conducted in USA; Setting:
Line of therapy	1st line
Duration of study	Intervention + follow up: 3 years
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Adults (≥18 years)
Subgroup analysis within study	Not applicable
Inclusion criteria	Male, age 18-75 years, at the conclusion of a physician-confirmed urinary stone episode. All stone subtypes were included.
Exclusion criteria	Consumption of <160 ml/day of soft drinks.
Age, gender and ethnicity	Age - Mean (range): No soft drinks: 43 (35-53); soft drinks: 42 (35-52). Gender (M:F): 100% male. Ethnicity: Not stated
Further population details	
Indirectness of population	No indirectness
Interventions	(n=504) Intervention 1: Fluid - Water. Patients were asked to refrain from consuming soft drinks. Duration 3 years. Concurrent medication/care: None. Indirectness: No indirectness (n=505) Intervention 2: Fluid - Soft drinks. Consumption of soft drinks ≥160 ml/day. Duration 3 years. Concurrent medication/care: None. Indirectness: No indirectness
Funding	Other (National Institute of Health grant)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: WATER versus SOFT DRINKS

Protocol outcome 1: New stone formation/incidence of stones/recurrence rate at Define

- Actual outcome for Adults (≥18 years): New stone formation at 3 years; Group 1: 170/504, Group 2: 205/505

Risk of bias: All domain - High, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 44, Reason: 2 deaths and 42 loses to follow up; Group 2 Number missing: 28, Reason: 2 deaths and 26 loses to follow up

Protocol outcomes not reported by the study	Quality of life at Define; Adverse events at Define; Kidney function at Define; Change in metabolic test: urine calcium at Define; Change in metabolic test: urine pH at Define; Change in metabolic test: urine oxalate at Define; Change in metabolic test: urine sodium at Define; Change in stone risk score at Define; Compliance/adherence at Define; Use of healthcare services/retreatment rate at Define
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Study	Silverio 2000 ⁹⁰
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=384)
Countries and setting	Conducted in Italy; Setting:
Line of therapy	1st line
Duration of study	Intervention time: Mean: 19 months (range: 14-34 months)
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Adults (≥18 years)
Subgroup analysis within study	Not applicable
Inclusion criteria	Patients submitted to ESWL for idiopathic calcium urolithiasis and presented with episodes of recurrence (3 recurrences within the last 4 years or 2 recurrences within the last 3 years); free from clinically evident residual stones or fragments upon recruitment.
Exclusion criteria	Severe diabetes, gout or urinary infections
Age, gender and ethnicity	Age - Median (range): Males: 38.3 (24-65); females: 40.8 (24-65). Gender (M:F): 231/153. Ethnicity: Not stated
Further population details	
Indirectness of population	No indirectness
Interventions	(n=192) Intervention 1: Fluid - Mineral water. Mineral (Fiuggi) water 2 L/day. Calcium content: 15 mg/l. Duration 19 months. Concurrent medication/care: A varied diet with a mean calcium content of 600 mg/day. Indirectness: No indirectness (n=192) Intervention 2: Fluid - Tap water. Tap water (calcium content range: 55-130 mg/l). Duration 19 months. Concurrent medication/care: A varied diet with a mean calcium content of 600 mg/day. Indirectness: No indirectness
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: MINERAL WATER versus TAP WATER

Protocol outcome 1: New stone formation/incidence of stones/recurrence rate at Define

- Actual outcome for Adults (≥18 years): Recurrence at 19 months; Group 1: 32/192, Group 2: 44/192

Risk of bias: All domain - High, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:

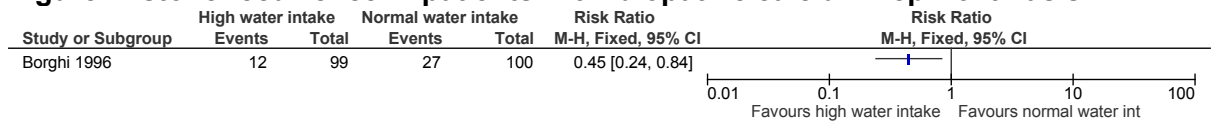
Protocol outcomes not reported by the study

Quality of life at Define; Adverse events at Define; Kidney function at Define; Change in metabolic test: urine calcium at Define; Change in metabolic test: urine pH at Define; Change in metabolic test: urine oxalate at Define; Change in metabolic test: urine sodium at Define; Change in stone risk score at Define; Compliance/adherence at Define; Use of healthcare services/retreatment rate at Define

1 Appendix E: Forest plots

2 E.1 High water intake versus normal water intake

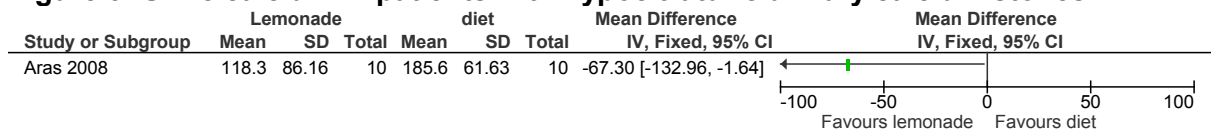
Figure 2: stone recurrence in patients with idiopathic calcium nephrolithiasis



Follow up: 5 years

3 E.2 Lemonade (fresh lemon juice in water) versus diet

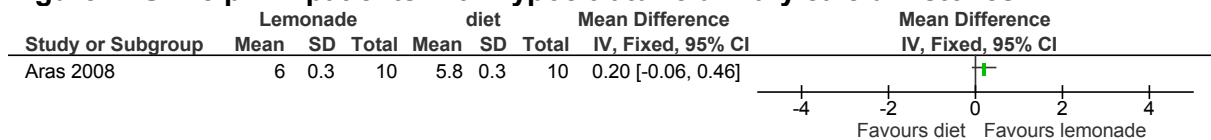
Figure 3: Urine calcium in patients with hypocitraturic urinary calcium stones



Follow up: 3 months

4

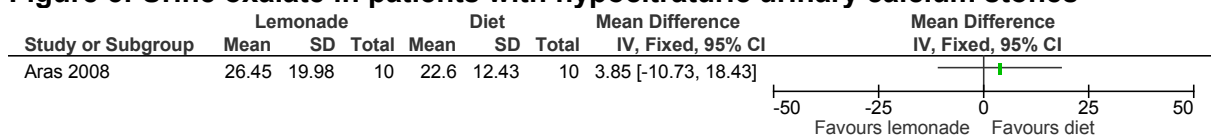
Figure 4: Urine pH in patients with hypocitraturic urinary calcium stones



Follow up: 3 months

5

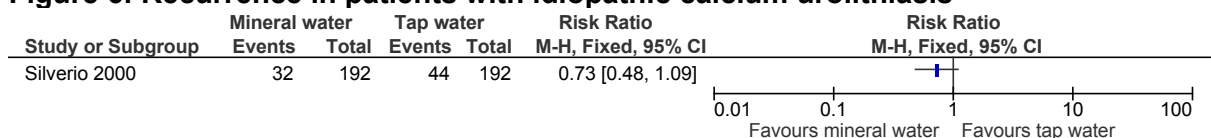
Figure 5: Urine oxalate in patients with hypocitraturic urinary calcium stones



Follow up: 3 months

6 E.3 Mineral water (low calcium content) vs tap water

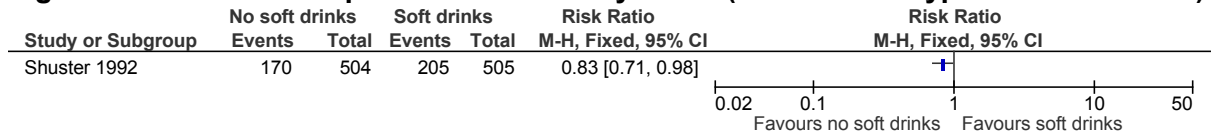
Figure 6: Recurrence in patients with idiopathic calcium urolithiasis



Follow up: 19 months

1 **E.4 No soft (carbonated) drinks vs soft (carbonated) drinks**
2 **(soda, >160 ml/day)**

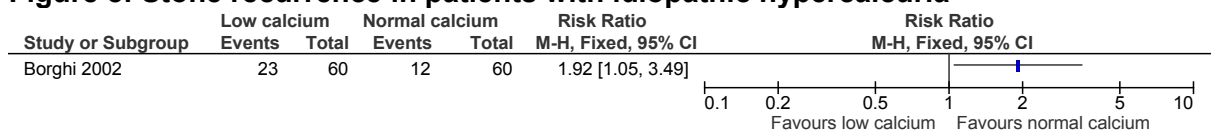
Figure 7: Recurrence in patients with urinary stone (all stone subtypes were included)



Follow up: 3 years

3 **E.5 Low calcium diet versus normal calcium diet**

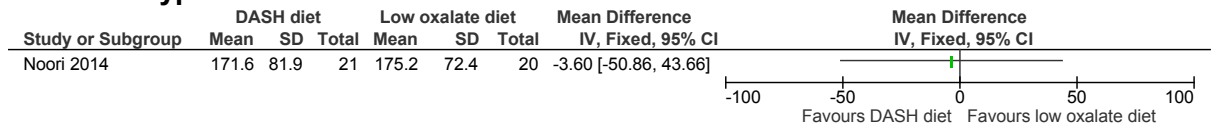
Figure 8: Stone recurrence in patients with idiopathic hypercalcaemia



Follow up: 5 years

4 **E.6 DASH diet versus low oxalate diet**

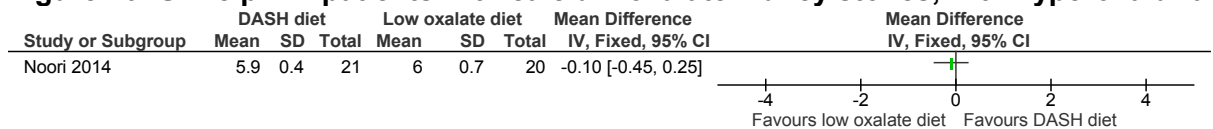
Figure 9: Urine calcium in patients with calcium oxalate kidney stones, with hyperoxaluria



Follow up: 8 weeks

5

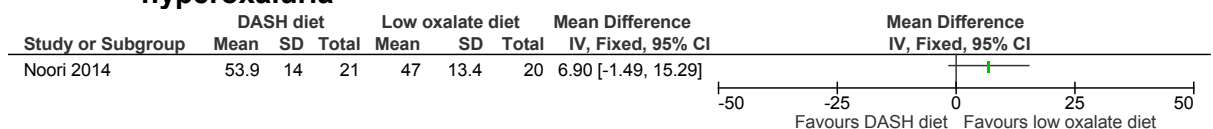
Figure 10: Urine pH in patients with calcium oxalate kidney stones, with hyperoxaluria



Follow up: 8 weeks

6

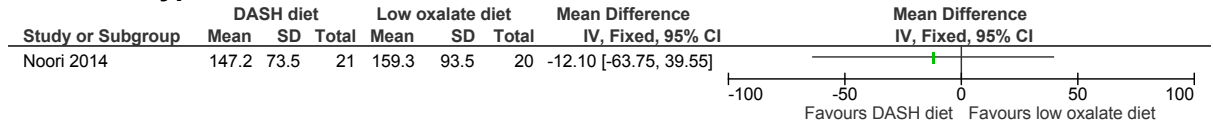
Figure 11: Urine oxalate in patients with calcium oxalate kidney stones, with hyperoxaluria



Follow up: 8 weeks

1

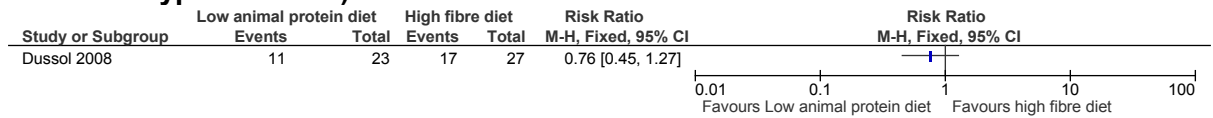
Figure 12: Urine sodium in patients with calcium oxalate kidney stones, with hyperoxaluria



Follow up: 8 weeks

2 **E.7 Low animal protein diet versus high fibre diet**

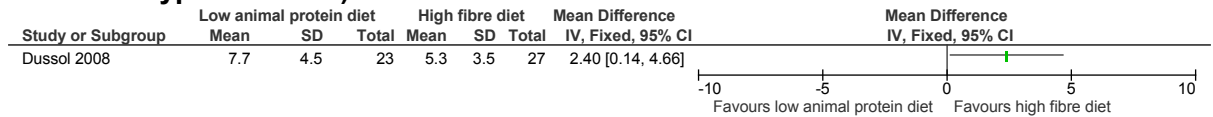
Figure 13: Recurrence in patients with idiopathic calcium stones (38% had hypercalciuria)



Follow up: 4 years

3

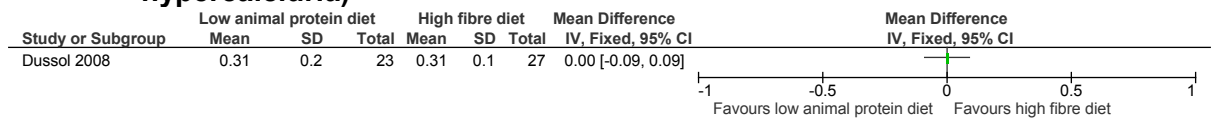
Figure 14: Urine calcium in patients with idiopathic calcium stones (38% had hypercalciuria)



Follow up: 4 years

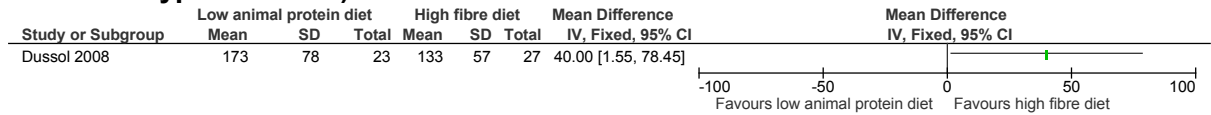
4

Figure 15: Urine oxalate in patients with idiopathic calcium stones (38% had hypercalciuria)



Follow up: 4 years

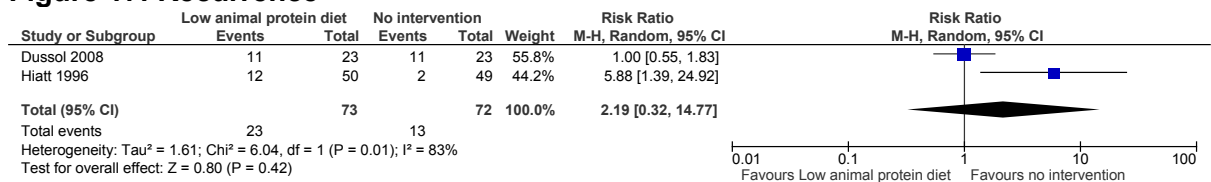
Figure 16: Urine sodium in patients with idiopathic calcium stones (38% had hypercalciuria)



Follow up: 4 years

1 E.8 Low animal protein diet versus no intervention

Figure 17: Recurrence



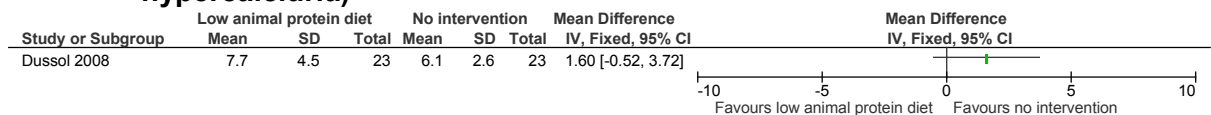
Follow up: 4 years

Dussol 2008: idiopathic calcium stones (38% had hypercalciuria)

Hiatt 1996: Calcium oxalate kidney stone (≥65%calcium oxalate)

2

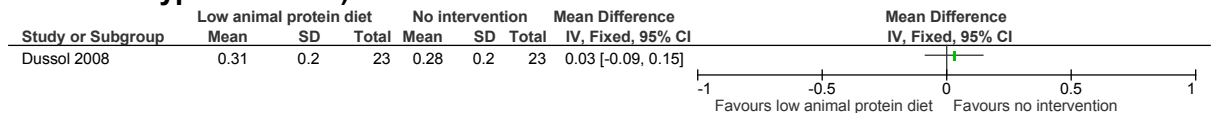
Figure 18: Urine calcium in patients with idiopathic calcium stones (38% had hypercalciuria)



Follow up: 4 years

3

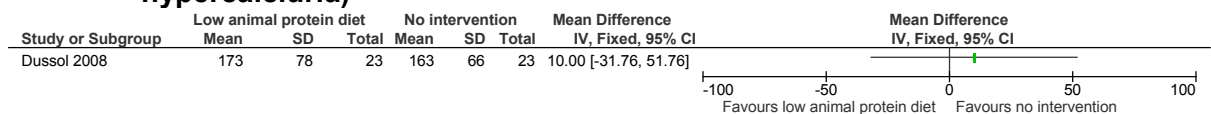
Figure 19: Urine oxalate in patients with idiopathic calcium stones (38% had hypercalciuria)



Follow up: 4 years

4

Figure 20: Urine sodium in patients with idiopathic calcium stones (38% had hypercalciuria)

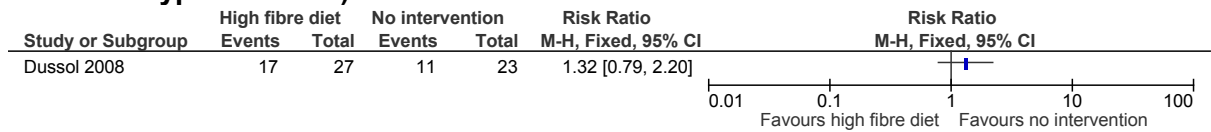


Follow up: 4 years

5

1 E.9 High fibre diet versus no intervention

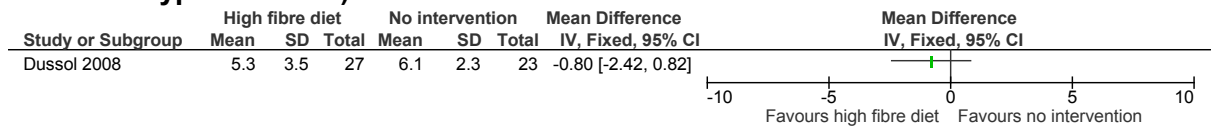
Figure 21: Recurrence in patients with idiopathic calcium stones (38% had hypercalciuria)



Follow up: 4 years

2

Figure 22: Urine calcium in patients with Idiopathic calcium stones (38% had hypercalciuria)



Follow up: 4 years

3

Figure 23: Urine oxalate in patients with idiopathic calcium stones (38% had hypercalciuria)

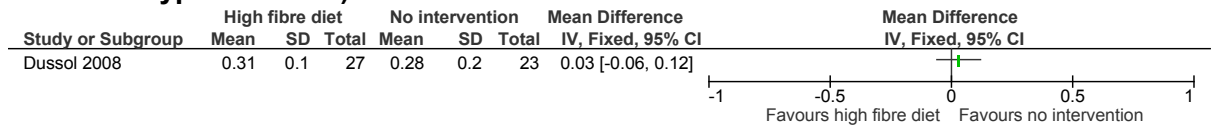
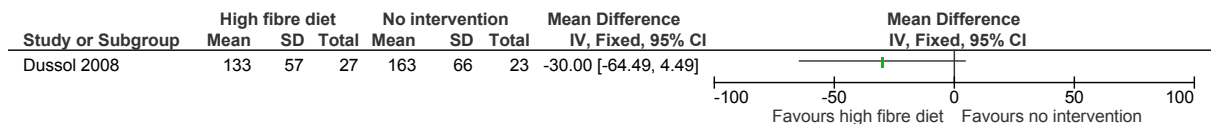


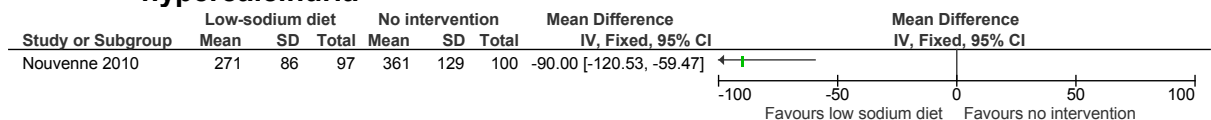
Figure 24: Urine sodium in patients with idiopathic calcium stones (38% had hypercalciuria)



Follow up: 4 years

4 E.10 Low salt diet versus no intervention

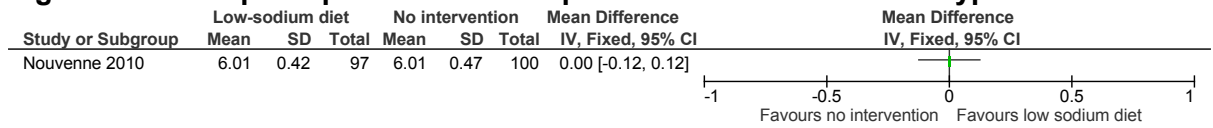
Figure 25: Urine calcium in patients with idiopathic calcium stones and hypercalciuria



Follow up: 3 months

5

Figure 26: Urine pH in patients with idiopathic calcium stones and hypercalcaemia



Follow up: 3 months

1

Figure 27: Urine oxalate in patients with idiopathic calcium stones and hypercalcaemia

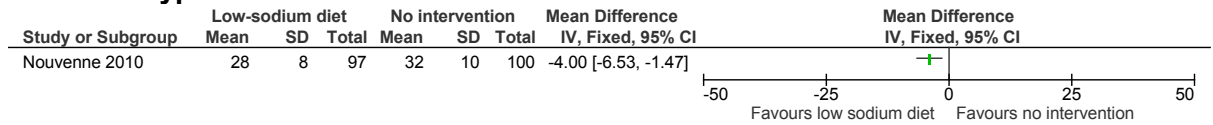
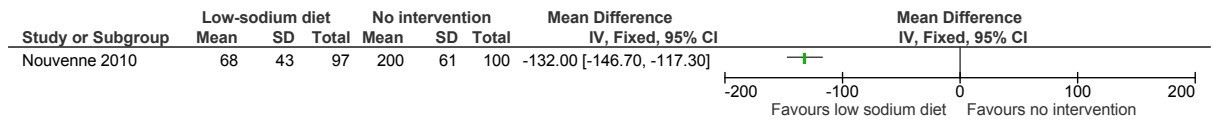


Figure 28: Urine sodium in patients with idiopathic calcium stones and hypercalcaemia



Follow up: 3 months

2

3

Appendix F: GRADE tables

Table 17: Clinical evidence profile: High water intake versus normal water intake

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	High water intake	Normal water intake	Relative (95% CI)	Absolute		
Number of stone recurrences (follow-up mean 5 years)												
1	randomised trials	serious ¹	no serious inconsistency	no serious indirectness	serious ²	none	12/99 (12.1%)	27%	RR 0.45 (0.24 to 0.84)	149 fewer per 1000 (from 43 fewer to 205 fewer)	⊕⊕⊕⊕ LOW	CRITICAL

¹ Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

² Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs.

Table 18: Clinical evidence profile: Lemonade (fresh lemon juice in water) versus water

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Lemonade	Water	Relative (95% CI)	Absolute		
Oxalate level (follow-up mean 3 months; Better indicated by lower values)												
1	randomised trials	serious ¹	no serious inconsistency	no serious indirectness	very serious ²	none	10	10	-	MD 3.85 higher (10.73 lower to 18.43 higher)	⊕⊕⊕⊕ VERY LOW	CRITICAL
Calcium level (Better indicated by lower values)												

1	randomised trials	serious ¹	no serious inconsistency	no serious indirectness	serious ²	none	10	10	-	MD 67.3 lower (132.96 to 1.64 lower)	⊕⊕⊕⊕ LOW	CRITICAL
pH (follow-up median 3 months; Better indicated by higher values)												
1	randomised trials	serious ¹	no serious inconsistency	no serious indirectness	serious ²	none	10	10	-	MD 0.2 higher (0.06 lower to 0.46 higher)	⊕⊕⊕⊕ LOW	CRITICAL

¹ Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

² Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

Table 19: Clinical evidence profile: Mineral water (low calcium content) versus tap water

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Mineral water	Tap water	Relative (95% CI)	Absolute		
Recurrence (follow-up mean 19 months)												
1	randomised trials	serious ¹	no serious inconsistency	no serious indirectness	serious ²	none	32/192 (16.7%)	22.9%	RR 0.73 (0.48 to 1.09)	62 fewer per 1000 (from 119 fewer to 21 more)	⊕⊕⊕⊕ LOW	CRITICAL

¹ Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

² Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

Table 20: Clinical evidence profile: No soft (carbonated) drinks versus soft (carbonated) drinks (soda>160 ml/day)

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	No soft drinks	Soft drinks (>160 ml/day)	Relative (95% CI)	Absolute		
Recurrence (follow-up mean 3 years)												

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1	randomised trials	serious ¹	no serious inconsistency	no serious indirectness	serious ²	none	170/504 (33.7%)	40.6%	RR 0.83 (0.71 to 0.98)	69 fewer per 1000 (from 8 fewer to 118 fewer)	⊕⊕⊕⊕ LOW	CRITICAL
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¹ Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

² 4 Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

Table 21: Clinical evidence profile: Low calcium diet versus normal calcium diet

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Low calcium diet	Normal calcium diet	Relative (95% CI)	Absolute		
Number of stone recurrences (follow-up mean 5 years)												
1	randomised trials	serious ¹	no serious inconsistency	no serious indirectness	serious ²	none	23/60 (38.3%)	20%	RR 1.92 (1.05 to 3.49)	184 more per 1000 (from 10 more to 498 more)	⊕⊕⊕⊕ LOW	CRITICAL

¹ Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

² Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

Table 22: Clinical evidence profile: DASH diet versus low oxalate diet

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	DASH diet	Low oxalate diet	Relative (95% CI)	Absolute		
Urine calcium (follow-up mean 8 weeks; Better indicated by lower values)												

1	randomised trials	serious ¹	no serious inconsistency	no serious indirectness	very serious ²	none	21	20	-	MD 3.6 lower (50.86 lower to 43.66 higher)	⊕⊕⊕⊕ VERY LOW	CRITICAL
Urine sodium (follow-up mean 8 weeks; Better indicated by lower values)												
1	randomised trials	serious ¹	no serious inconsistency	no serious indirectness	serious ²	none	21	20	-	MD 12.1 lower (63.75 lower to 39.55 higher)	⊕⊕⊕⊕ LOW	CRITICAL
Urine oxalate (follow-up mean 8 weeks; Better indicated by lower values)												
1	randomised trials	serious ¹	no serious inconsistency	no serious indirectness	serious ²	none	21	20	-	MD 6.9 higher (1.49 lower to 15.29 higher)	⊕⊕⊕⊕ LOW	CRITICAL
pH (follow-up mean 8 weeks; Better indicated by higher values)												
1	randomised trials	serious ¹	no serious inconsistency	no serious indirectness	serious ²	none	21	20	-	MD 0.1 lower (0.45 lower to 0.25 higher)	⊕⊕⊕⊕ LOW	CRITICAL

¹ Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

² Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

Table 23: Clinical evidence profile: Low animal protein diet versus high fibre diet

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Low animal protein diet	High fibre diet	Relative (95% CI)	Absolute		
Recurrence (follow-up mean 4 years)												

1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious ¹	none	11/23 (47.8%)	63%	RR 0.76 (0.45 to 1.27)	151 fewer per 1000 (from 347 fewer to 170 more)	⊕⊕⊕⊕ LOW	CRITICAL
Urine sodium (follow-up mean 4 years; Better indicated by lower values)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious ¹	none	23	27	-	MD 40 higher (1.55 to 78.45 higher)	⊕⊕⊕⊕ MODERATE	CRITICAL
Urine calcium (follow-up mean 4 years; Better indicated by lower values)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious ¹	none	23	27	-	MD 2.4 higher (0.14 to 4.66 higher)	⊕⊕⊕⊕ MODERATE	CRITICAL
Urine oxalate (follow-up mean 4 years; Better indicated by lower values)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious ¹	none	23	27	-	MD 0 higher (0.09 lower to 0.09 higher)	⊕⊕⊕⊕ LOW	CRITICAL

¹ Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

Table 24: Clinical evidence profile: Low animal protein diet versus no intervention

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Low animal protein diet	No intervention	Relative (95% CI)	Absolute		
Recurrence (follow-up mean 4 years)												
2	randomised trials	no serious risk of bias	very serious ¹	no serious indirectness	serious ²	none	23/73 (31.5%)	18.1%	RR 2.19 (0.32 to 14.77)	309 more per 1000 (from 177 fewer to 1000 more)	⊕⊕⊕⊕ VERY LOW	CRITICAL
Urine sodium (follow-up mean 4 years; Better indicated by lower values)												

1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious ²	none	23	23	-	MD 10 higher (31.76 lower to 51.76 higher)	⊕⊕⊕⊕ LOW	CRITICAL
Urine calcium (follow-up mean 4 years; Better indicated by lower values)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious ²	none	23	23	-	MD 1.6 higher (0.52 lower to 3.72 higher)	⊕⊕⊕⊕ MODERATE	CRITICAL
Urine oxalate (follow-up mean 4 years; Better indicated by lower values)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious ²	none	23	23	-	MD 0.03 higher (0.09 lower to 0.15 higher)	⊕⊕⊕⊕ MODERATE	CRITICAL

¹ Downgraded by 1 or 2 increments because heterogeneity, I²= 83%, p= > 0.1, unexplained by subgroup analysis

² Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

Table 25: Clinical evidence profile: High fibre diet versus no intervention

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	High fibre diet	No intervention	Relative (95% CI)	Absolute		
Recurrence (follow-up mean 4 years)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious ¹	none	17/27 (63%)	47.8%	RR 1.32 (0.79 to 2.2)	153 more per 1000 (from 100 fewer to 574 more)	⊕⊕⊕⊕ MODERATE	CRITICAL
Urine sodium (follow-up mean 4 years; Better indicated by lower values)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious ¹	none	27	23	-	MD 30 lower (64.49 lower to 4.49 higher)	⊕⊕⊕⊕ MODERATE	CRITICAL
Urine calcium (follow-up mean 4 years; Better indicated by lower values)												

1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious ¹	none	27	23	-	MD 0.8 lower (2.42 lower to 0.82 higher)	⊕⊕⊕○ MODERATE	CRITICAL
Urine oxalate (follow-up mean 4 years; Better indicated by lower values)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious ¹	none	27	23	-	MD 0.03 higher (0.06 lower to 0.12 higher)	⊕⊕⊕○ MODERATE	CRITICAL

¹ Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

Table 26: Clinical evidence profile: Low salt diet versus no intervention

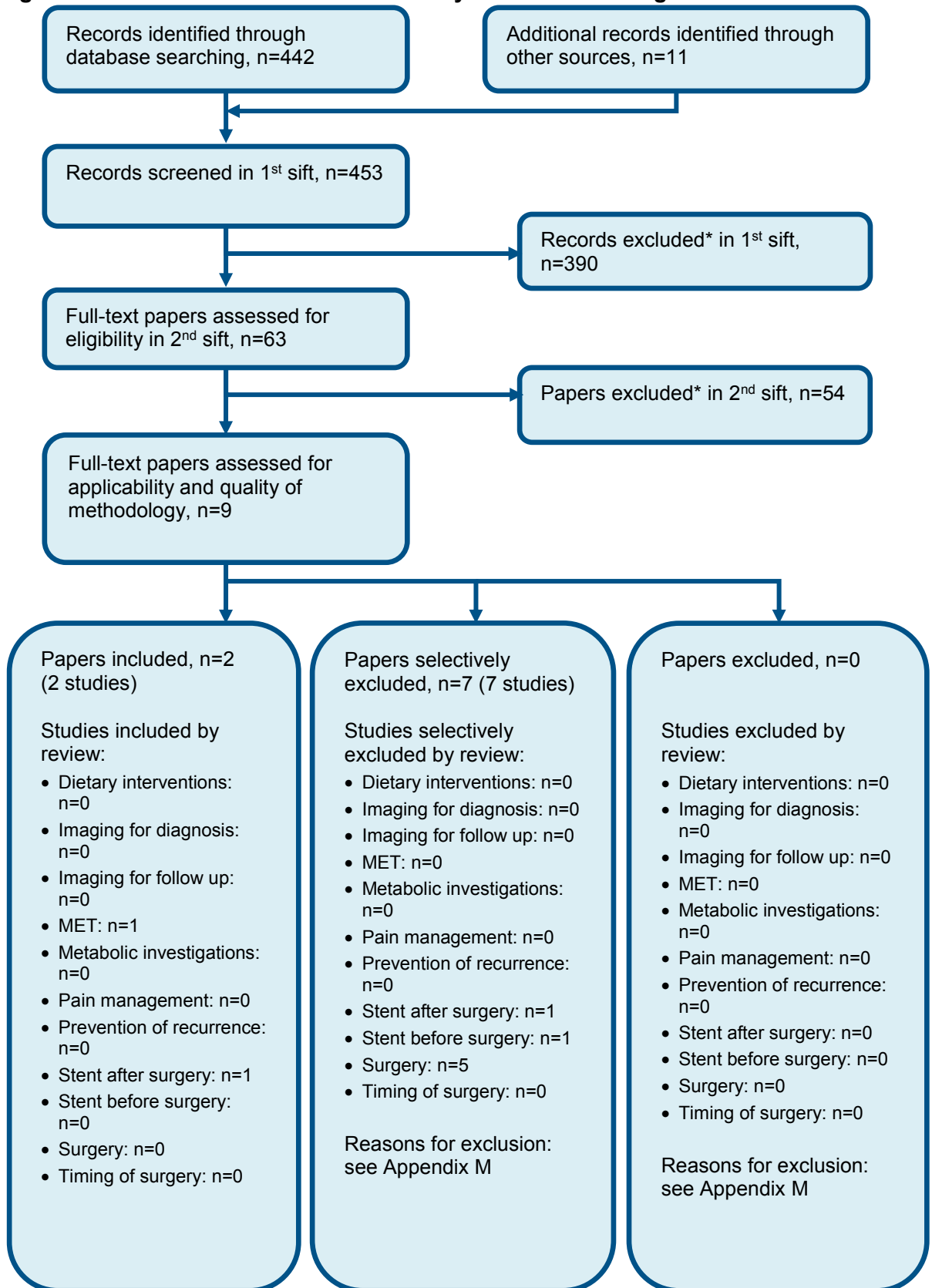
Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Low salt diet	No intervention	Relative (95% CI)	Absolute		
Urine sodium (follow-up mean 3 months; Better indicated by lower values)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	97	100	-	MD 132 lower (146.7 to 117.3 lower)	⊕⊕⊕⊕ HIGH	CRITICAL
Urine calcium (follow-up mean 3 months; Better indicated by lower values)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious ¹	none	97	100	-	MD 90 lower (120.53 to 59.47 lower)	⊕⊕⊕○ MODERATE	CRITICAL
Urine oxalate (follow-up mean 3 months; Better indicated by lower values)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious ¹	none	97	100	-	MD 4 lower (6.53 to 1.47 lower)	⊕⊕⊕○ MODERATE	CRITICAL
Urine pH (follow-up mean 3 months; Better indicated by higher values)												

1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	97	100	-	MD 0 higher (0.12 lower to 0.12 higher)	⊕⊕⊕⊕ HIGH	CRITICAL
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¹ Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

1 **Appendix G: Health economic evidence**
2 **selection**

Figure 29: Flow chart of economic study selection for the guideline



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

Appendix H: Health economic evidence tables

None

Appendix I: Excluded studies

I.1 Excluded clinical studies

Table 27: Studies excluded from the clinical review

Reference	Reason for exclusion
Abdulhadi 1993 ¹	Incorrect study design (case-control)
Allie-Hamdulay 2005 ²	Incorrect population (includes 50% of healthy subjects, not specific for renal stones)
Baia Lda 2012 ⁴	No relevant outcomes
Bao 2012 ⁵	Incorrect population (All patients with or without a history of urinary stones (all types))
Barcelo 1993 ⁶	Incorrect intervention (citrate supplement)
Bellizzi 1999 ⁷	Incorrect study design (cross-over)
Berg 1992 ⁸	Incorrect population (includes people (50%) with no previous history of renal stones); incorrect study design (non-randomised)
Bolanos-Diaz 2011 ⁹	Incorrect study design (cost effectiveness analysis, no clinical data)
Borghi 2011 ¹⁰	Citation only
Brardi 2012 ¹³	Not in English
Bren 1998 ¹⁴	Incorrect study design (non-randomised)
C 2003 ²⁰	Incorrect study design (non-randomised)
Campoy Martínez 1994 ¹⁵	Not in English
Carvalho 2016 ¹⁶	SR with different protocol (excludes pregnant women and children). References checked.
Cheungpasitporn 2016 ¹⁷	SR with different protocol (includes observational studies)
Cicerello 1994 ¹⁸	Incorrect intervention (citrate supplement)
El-Gamal 2012 ²²	Incorrect intervention (citrate supplement)
Ettinger 1997 ²³	Incorrect intervention (citrate supplement)
Faassen 1998 ²⁴	Incorrect intervention (citrate supplement)
Fabris 2009 ²⁵	Incorrect study design (retrospective cohort)
Fabris 2010 ²⁶	Incorrect study design (retrospective cohort)
Ferraro 2017 ²⁷	Systematic review of different dietary changes and drug interventions
Ferroni 2017 ²⁸	Incorrect comparison (two different doses of vitamin D supplement)
Fink 2009 ²⁹	Systematic review of different dietary changes and drug interventions
Friedman 2012 ³⁰	Incorrect population (people with no previous history of renal stones)
Gallagher 2014 ³¹	Incorrect population (menopausal women, not specific for renal stones)
Gao 2010 ³²	Citrate supplement
Garg 1990 ³³	Incorrect population (people with no previous history of renal stones)
Gettman 2005 ³⁴	Incorrect population (includes people [50%] with no previous history of renal stones)

Reference	Reason for exclusion
Ginde 2016 ³⁵	Incorrect population (general population not specific for renal stones)
Gökta 2012 ³⁶	Incorrect intervention (citrate as adjunctive to SWL)
Goldfarb 2001 ³⁷	Incorrect population (people with no previous history of renal stones); incorrect study design (non-randomised study)
Goodman 2009 ³⁸	Incorrect population (general population not specific for renal stones); incorrect study design (cross-over trial)
Guéronnière 2011 ³⁹	Incorrect population (people with no previous history of renal stones)
Guéronnière 2011 ³⁹	Incorrect population (healthy subjects, not specific for renal stones)
Hauser 1990 ⁴⁰	Incorrect study design (non-randomised study); incorrect comparison (intermittent versus continuous alkali citrate)
Herrmann 1992 ⁴¹	Incorrect study design (cohort study)
Hofbauer 1994 ⁴³	Incorrect intervention (citrate supplement)
Jaipakdee 2004 ⁴⁴	Incorrect intervention (citrate supplement)
Jiménez Verdejo 2001 ⁴⁵	Not in English
Karagulle 2007 ⁴⁶	Incorrect study design (cross-over)
Kato 2004 ⁴⁷	Incorrect population (people without a history renal stones); incorrect study design (non-randomised cross-over trial)
Kessler 2000 ⁴⁸	Incorrect population (people with no previous history of urinary calculi)
Khan 2015 ⁴⁹	Incorrect intervention (diet as primary treatment of stones, not for preventions of recurrence)
Kocvara 1999 ⁵⁰	Incorrect intervention (5 different dietary interventions for 5 subgroups, but results not analysed separately)
Koff 2007 ⁵¹	Incorrect study design (cross-over trial)
Kozyrakis 2017 ⁵²	Incorrect population (healthy subjects, not specific for renal stones)
Krishna Reddy 2014 ⁵³	Incorrect study design (case-control study)
Lieske 2017 ⁵⁴	Review of probiotics for hyperoxaluria. Incorrect population (includes non-stone patients)
Lieske 2010 ⁵⁵	Incorrect interventions (addition of probiotics to a low oxalate diet)
Lojanapiwat 2011 ⁵⁶	Incorrect intervention (citrate supplement)
Lotan 2013 ⁵⁷	Incorrect study design (cost-effectiveness analysis, no clinical data)
Malihi 2016 ⁵⁸	Systematic review includes people with no history of kidney stones
Massey 1998 ⁶⁰	Incorrect study design (cross-over trial)
Massey 2001 ⁶¹	Incorrect study design (cross-over trial)
Massey 2005 ⁶²	Incorrect population (includes people with no previous history of kidney stones)
Massey 2005 ⁵⁹	Incorrect population (people without renal stones)
Matsumoto 2006 ⁶³	Incorrect study design (cross-over); incorrect study population (healthy subjects)
Mattle 2005 ⁶⁴	SR with different inclusion criteria (includes non-randomised studies)
McHarg 2003 ⁶⁵	Incorrect population (people with no previous history of kidney stones)

Reference	Reason for exclusion
Mechlin 2011 ⁶⁶	Incorrect population (people without renal stones); incorrect intervention (potassium citrate vs potassium citrate + Splenda); incorrect study design (cross-over trial)
Miao 1984 ⁶⁷	Not in English
Moyad 2009 ⁶⁸	Incorrect population (people with no previous history of kidney stones)
Nomura 1995 ⁷⁰	Incorrect study design (non-randomised); incorrect intervention (dietary counselling vs non-counselling)
Nouvenne 2009 ⁷²	Incorrect study design (case-control study)
Odvin 2006 ⁷⁵	Incorrect population (includes people without renal stones)
Osorio 1997 ⁷⁶	Incorrect population (children with idiopathic hypercalciuria, not specific for renal stones). Incorrect design (non-RCT)
Osther 2006 ⁷⁷	Incorrect population: 50% are healthy subjects (not specific for renal stones)
Parivar 1996 ⁷⁸	Incorrect study design (narrative review)
Phillips 2015 ⁷⁹	Incorrect population (includes primary prevention of stones)
Pinheiro 2013 ⁸⁰	Incorrect study design (cross-over trial)
Prasetyo 2013 ⁸¹	Systematic review includes non-RCT studies
Prieto 2010 ⁸²	Incorrect population (general population, not specific for renal stones)
Rodgers 1998 ⁸⁴	Incorrect population (includes people with no previous history of kidney stones)
Sakhaee 2004 ⁸⁶	Incorrect population (people with no previous history of renal stones)
Sarica 2006 ⁸⁷	Incorrect intervention (citrate supplement)
Silverio 1994 ⁸⁹	Not in English
Soygür 2002 ⁹¹	Incorrect intervention (citrate supplement)
Tosukhowong 2008 ⁹²	Incorrect intervention (citrate supplement)
Tracy 2014 ⁹³	Incorrect population (people with no previous history of kidney stones)
Valli 2000 ⁹⁵	Not in English
Vescini 2005 ⁹⁶	Incorrect study design (cohort study)
Wabner 1993 ⁹⁷	Incorrect study design (cross-over study)
Wallace 2011 ⁹⁸	Incorrect population (post menopausal women with no previous history of kidney stones)
Whalley 1996 ⁹⁹	Incorrect study design (non-randomised study)
Worster 2012 ¹⁰⁰	Systematic review (to cure acute episodes, not prevention of recurrence)
Xu 2015 ¹⁰¹	Systematic review of non-randomised studies
Yatzidis 1985 ¹⁰²	Incorrect study design (non-randomised study)
Zerwekh 2007 ¹⁰³	Incorrect population (people with no previous history of kidney stones)

1 I.2 Excluded health economic studies

2 None