National Institute for Health and Care Excellence

Final

Renal and ureteric stones: assessment and management

Dietary interventions

NICE guideline NG118

Intervention evidence review (C)

January 2019

Final

This evidence review was developed by the National Guideline Centre

Disclaimer

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

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

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 All NICE guidance is subject to regular review and may be updated or withdrawn.

ISBN: 978-1-4731-3190-3

Contents

1 Dietary interventions 5

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? 5

1.2 Introduction 5

1.3 PICO table 5

1.4 Clinical evidence 6

1.4.1 Included studies 6

1.4.2 Excluded studies 6

1.4.3 Summary of clinical studies included in the evidence review 7

1.4.4 Quality assessment of clinical studies included in the evidence review 10

1.5 Economic evidence 18

1.5.1 Included studies 18

1.5.2 Excluded studies 18

1.6 Resource costs 18

1.7 Evidence statements 18

1.7.1 Clinical evidence statements 18

1.7.2 Health economic evidence statements 19

1.8 The committee's discussion of the evidence 19

1.8.1 Interpreting the evidence 19

1.8.2 Cost effectiveness and resource use 21

1.8.3 Other factors the committee took into account 22

References 23

Appendices 31

Appendix A: Review protocols 31

Appendix B: Literature search strategies 35

Appendix C: Clinical evidence selection 44

Appendix D: Clinical evidence tables 45

Appendix E: Forest plots 61

Appendix F: GRADE tables 67

Appendix G: Health economic evidence selection 75

Appendix H: Health economic evidence tables 78

Appendix I: Excluded studies 79

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	• 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	• To each other • No treatment • Placebo • To fluid (gold standard) • DASH (dietary approaches to stop hypertension) diet • Within intervention comparisons: fluid volume
Outcomes	Critical outcomes: • 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 Important outcomes: • Compliance/adherence

	• Kidney function
Study design	Randomised controlled trials (RCTs), systematic reviews of RCTs. If no RCT evidence is available, search for observational studies (for children)

1.4 Clinical evidence

1.4.1 Included studies

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

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

1.4.2 Excluded studies

See the excluded studies list in appendix I.

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]	Intervention (n=10): Fresh lemon juice (85 cc) per day (containing 60 mEq of citrate) Comparison (n=10): Diet group: water 3L/day, calcium 1200 mg/day, NaCl 5 g/day, protein intakes 1.0 g/kg/day Concurrent care: advised to increase water intake to 3L/day	n=20 People with hypocitraturic urinary calcium stones Age (mean, SD): lemon juice group 36.8 (14.28); diet group 38.7 (12.01) Gender not reported Turkey	Urine calcium (3 months) Urine pH (3 months) Urine oxalate (3 months)	Duration: 3 months
Borghi 1996[11]	Intervention (n=99): High water intake (to give a urine volume ≥2 l/day) Comparison (n=100): No intervention (not necessary to follow any special procedures) Concurrent care: not reported	n=199 People with idiopathic calcium nephrolithiasis Age (mean, SD): water group 42.2 (11.6); no intervention 40.4 (13.2) Male to female ratio 134:65 Italy	Recurrence (5 years): defined as stone expulsion during follow up or silent calculus on x-ray or echography	Duration: 5 years
Borghi 2002[12]	Intervention (n=60): Low calcium diet (approx. 10 mmol/day) Comparison (n=60): Normal-to-high calcium (30 mmol/day)	n=120 People with idiopathic hypercalcuria	Recurrence (5 years): defined as presence of a radiographically identified stone	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	⊕⊕⊖⊖ LOW1,2 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)	⨁⨁⊖⊖ LOW1,2 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	⨁⨁⊖⊖ LOW1,2 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 LOW1,2 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					

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 LOW1,2 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	⊕⊕⊖⊖ LOW1,2 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	⊕⊕⊖⊖ LOW1,2 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	⊕⊕⊖⊖ LOW1,2 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	⊕⊕⊕⊖ MODERATE2 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	⊕⊕⊕⊖ MODERATE2 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	⊕⊕⊖⊖ LOW2 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	⊕⊕⊕⊖ MODERATE1 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	⊕⊕⊕⊖ MODERATE1 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.

1.5 Economic evidence

1.5.1 Included studies

No relevant health economic studies were identified.

1.5.2 Excluded studies

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

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

1.6 Resource costs

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

1.7 Evidence statements

1.7.1 Clinical evidence statements

Fluid

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

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

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

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

Calcium

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

DASH/oxalate

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

Protein/fibre

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

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

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

Salt

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

1.7.2 Health economic evidence statements

- No relevant economic evaluations were identified.

1.8 The committee's discussion of the evidence

1.8.1 Interpreting the evidence

1.8.1.1 The outcomes that matter most

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

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

1.8.1.2 The quality of the evidence

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

1.8.1.3 Benefits and harms

Evidence for adults and children and young people, and for those with symptomatic and asymptomatic stones was searched for. However, no evidence was identified for children and young people, or for people with asymptomatic stones. The committee agreed that the

recommendations should include children and young people, and be based on government nutritional advice and healthy eating messages aimed at the general population. They did not feel that the evidence could be extrapolated to the asymptomatic population, and therefore agreed that all recommendations would apply to those with symptomatic stones only.

High water intake versus normal water intake

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

Lemon juice versus diet

The committee noted that there was a benefit of lemon juice in terms of urine calcium level and urine pH, but there was no difference in terms of urine oxalate. Lemon juice is high in natural citrate and may offer protection from forming stones due to citrate in the urine preventing calcium from binding with other constituents that contribute to stone formation. The committee also commented that those in the diet group were following a moderate protein, low salt, normal calcium diet, and that both groups received advice to increase water intake to 3 litres per day. As both groups received advice to increase water intake, the committee could be sure that the benefits seen in the lemon group were due to the lemon juice intervention and not the increase in water. However, it was noted that the exact water intake of each group was not known. The committee also noted that the evidence came from a single, very small study of low and very low quality.

Mineral (low calcium) water versus tap water

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

Carbonated drinks versus non-carbonated drinks

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

Low calcium diet versus normal calcium diet

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

that calcium intake should not be restricted, but should be maintained within the normal range.

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

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

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

Low animal protein diet versus high fibre diet

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

Low animal protein diet versus no intervention

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

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

High fibre diet versus no intervention

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

Low salt diet versus no intervention

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

1.8.2 Cost effectiveness and resource use

No economic evidence was identified for this question.

There are not likely to be any direct costs of the interventions themselves, as the recommendations are about giving the patient dietary advice and information so they can follow the advice. This may involve some staff time, and some printed information for example. However it is likely that this discussion would take place as part of a consultation that would already occur, as all patients are currently given advice, such as to drink more

fluid following a renal stone. Therefore the resources involved with these interventions are likely to be negligible.

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

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

1.8.3 Other factors the committee took into account

A committee member was aware of epidemiological data from a large, indirect population of men who have not formed stones before, that demonstrated a relationship between a high dietary calcium intake and a reduced risk of symptomatic kidney stones (Curhan 1993[19]). The committee member was also aware that further non-comparative data from a very large number of participants suggested that lifestyle changes such as reducing animal protein intake, showed some benefit in preventing stone formation (Turney 2014[94]).

The committee noted current published government dietary recommendations[74] and advice on healthy eating such as the Eatwell Guide[83] aimed at the general population, and acknowledged this guidance to be relevant for a renal stone population.

The committee noted that people with recurrent and/or complex stones may need specific dietary/lifestyle review and advice from a multidisciplinary team, including a dietician with an interest in renal stone disease, specialist nurse, chemical pathologist.

References

1. Abdulhadi MH, Hall PM, Streem SB. Can citrate therapy prevent nephrolithiasis? Urology. 1993; 41(3):221-4

2. Allie-Hamdulay S, Rodgers AL. Prophylactic and therapeutic properties of a sodium citrate preparation in the management of calcium oxalate urolithiasis: randomized, placebo-controlled trial. Urological Research. 2005; 33(2):116-24

3. Aras B, Kalfazade N, Tuğcu V, Kemahli E, Ozbay B, Polat H et al. Can lemon juice be an alternative to potassium citrate in the treatment of urinary calcium stones in patients with hypocitraturia? A prospective randomized study. Urological Research. 2008; 36(6):313-7

4. Baia Lda C, Baxmann AC, Moreira SR, Holmes RP, Heilberg IP. Noncitrus alkaline fruit: a dietary alternative for the treatment of hypocitraturic stone formers. Journal of Endourology. 2012; 26(9):1221-6

5. Bao Y, Wei Q. Water for preventing urinary stones. Cochrane Database of Systematic Reviews 2012, Issue 6. Art. No.: CD004292. DOI: 10.1002/14651858.CD004292.pub3.

6. Barcelo P, Wuhl O, Servitge E, Rousaud A, Pak CY. Randomized double-blind study of potassium citrate in idiopathic hypocitraturic calcium nephrolithiasis. Journal of Urology. 1993; 150(6):1761-4

7. Bellizzi V, Nicola L, Minutolo R, Russo D, Cianciaruso B, Andreucci M et al. Effects of water hardness on urinary risk factors for kidney stones in patients with idiopathic nephrolithiasis. Nephron. 1999; 81(Suppl 1):66-70

8. Berg C, Larsson L, Tiselius HG. The effects of a single evening dose of alkaline citrate on urine composition and calcium stone formation. Journal of Urology. 1992; 148(3 Pt 2):979-85

9. Bolanos-Diaz R, Regalado-Rafael R, Mezones-Holguin E. Cost-effectiveness of the preventive treatment of urolithiasis with potassium citrate (Provisional abstract). Journal of Pharmaceutical Health Services Research. 2011; 2(2):107-12

10. Borghi L. The links between water and salt intake, body weight, hypertension and kidney stones: a difficult puzzle [NCT01100580]. 2011. Available from: clinicaltrials.gov/ct2/show/NCT01100580 Last accessed: 02/08/17.

11. Borghi L, Meschi T, Amato F, Briganti A, Novarini A, Giannini A. Urinary volume, water and recurrences in idiopathic calcium nephrolithiasis: a 5-year randomized prospective study. Journal of Urology. 1996; 155(3):839-43

12. Borghi L, Schianchi T, Meschi T, Guerra A, Allegri F, Maggiore U et al. Comparison of two diets for the prevention of recurrent stones in idiopathic hypercalciuria. New England Journal of Medicine. 2002; 346(2):77-84

13. Brardi S, Imperiali P, Cevenini G, Verdacchi T, Ponchietti R. Effects of the association of potassium citrate and agropyrum repens in renal stone treatment: results of a prospective randomized comparison with potassium citrate. Archivio Italiano di Urologia, Andrologia. 2012; 84(2):61-7

14. Bren A, Kmetec A, Kveder R, Kaplan-Pavlovcic S. Magnesium hydrogen carbonate natural mineral water enriched with K(+)-citrate and vitamin B6 improves urinary abnormalities in patients with calcium oxalate nephrolithiasis. Urologia Internationalis. 1998; 60(2):105-7

15. Campoy Martínez P, Arrabal Martín M, Blasco Hernández P, Silva Mejías C, Reina Ruiz C, Espinosa Olmedo FJ et al. [Orange juice in the prevention of calcium oxalate lithiasis]. Actas Urologicas Espanolas. 1994; 18(7):738-43

16. Carvalho M, Erbano BO, Kuwaki EY, Pontes HP, Liu JW, Boros LH et al. Effect of potassium citrate supplement on stone recurrence before or after lithotripsy: systematic review and meta-analysis. Urolithiasis. 2016; 45(5):449-55

17. Cheungpasitporn W, Rossetti S, Friend K, Erickson SB, Lieske JC. Treatment effect, adherence, and safety of high fluid intake for the prevention of incident and recurrent kidney stones: a systematic review and meta-analysis. Journal of Nephrology. 2016; 29(2):211-9

18. Cicerello E, Merlo F, Gambaro G, Maccatrozzo L, Fandella A, Baggio B et al. Effect of alkaline citrate therapy on clearance of residual renal stone fragments after extracorporeal shock wave lithotripsy in sterile calcium and infection nephrolithiasis patients. Journal of Urology. 1994; 151(1):5-9

19. Curhan GC, Willett WC, Rimm EB, Stampfer MJ. A prospective study of dietary calcium and other nutrients and the risk of symptomatic kidney stones. New England Journal of Medicine. 1993; 328(12):833-8

20. De O. G. Mendonça C, Martini LA, Baxmann AC, Nishiura JL, Cuppari L, Sigulem DM et al. Effects of an oxalate load on urinary oxalate excretion in calcium stone formers. Journal of Renal Nutrition. 2003; 13(1):39-46

21. Dussol B, Iovanna C, Rotily M, Morange S, Leonetti F, Dupuy P et al. A randomized trial of low-animal-protein or high-fiber diets for secondary prevention of calcium nephrolithiasis. Nephron - Clinical Practice. 2008; 110(3):c185-94

22. El-Gamal O, El-Bendary M, Ragab M, Rasheed M. Role of combined use of potassium citrate and tamsulosin in the management of uric acid distal ureteral calculi. Urological Research. 2012; 40(3):219-24

23. Ettinger B, Pak CYC, Citron JT, Thomas C, Adams-Huet B, Vangessel A. Potassium-magnesium citrate is an effective prophylaxis against recurrent calcium oxalate nephrolithiasis. Journal of Urology. 1997; 158(6):2069-73

24. Faassen A, Ploeg EM, Habets HM, Meer R, Hermus RJ, Janknegt RA. The effects of the calcium-restricted diet of urolithiasis patients with absorptive hypercalciuria type II on risk factors for kidney stones and osteopenia. Urological Research. 1998; 26(1):65-9

25. Fabris A, Bernich P, Abaterusso C, Marchionna N, Canciani C, Nouvenne A et al. Bone disease in medullary sponge kidney and effect of potassium citrate treatment. Clinical Journal of the American Society of Nephrology. 2009; 4(12):1974-9

26. Fabris A, Lupo A, Bernich P, Abaterusso C, Marchionna N, Nouvenne A et al. Long-term treatment with potassium citrate and renal stones in medullary sponge kidney. Clinical Journal of the American Society of Nephrology. 2010; 5(9):1663-8

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

28. Ferroni MC, Rycyna KJ, Averch TD, Semins MJ. Vitamin D repletion in kidney stone formers: a randomized controlled trial. Journal of Urology. 2017; 197(4):1079-83

29. Fink HA, Akornor JW, Garimella PS, MacDonald R, Cutting A, Rutks IR et al. Diet, fluid, or supplements for secondary prevention of nephrolithiasis: a systematic review and meta-analysis of randomized trials. European Urology. 2009; 56(1):72-80

30. Friedman AN, Ogden LG, Foster GD, Klein S, Stein R, Miller B et al. Comparative effects of low-carbohydrate high-protein versus low-fat diets on the kidney. Clinical Journal of the American Society of Nephrology. 2012; 7(7):1103-11

31. Gallagher JC, Smith LM, Yalamanchili V. Incidence of hypercalciuria and hypercalcemia during vitamin D and calcium supplementation in older women. Menopause. 2014; 21(11):1173-80

32. Gao J, Shen Y, Sun N, Jia LQ, Pan YS, Sun Q. Therapeutic effects of potassium sodium hydrogen citrate on melamine-induced urinary calculi in China. Chinese Medical Journal. 2010; 123(9):1112-6

33. Garg A, Bonanome A, Grundy SM, Unger RH, Breslau NA, Pak CY. Effects of dietary carbohydrates on metabolism of calcium and other minerals in normal subjects and patients with noninsulin-dependent diabetes mellitus. Journal of Clinical Endocrinology and Metabolism. 1990; 70(4):1007-13

34. Gettman MT, Ogan K, Brinkley LJ, Adams-Huet B, Pak CY, Pearle MS. Effect of cranberry juice consumption on urinary stone risk factors. Journal of Urology. 2005; 174(2):590-4; quiz 801

35. Ginde AA, Blatchford P, Breese K, Zarrabi L, Linnebur SA, Wallace JI et al. High-dose monthly vitamin D for prevention of acute respiratory infection in older long-term care residents: a randomized clinical trial. Journal of the American Geriatrics Society. 2016; 65(3):496-503

36. Gökta C, Horuz R, Akça O, Cetinel CA, Cangüven O, Kafkasl A et al. The effect of citrate replacement in hypocitraturic cases on the results of SWL: a preliminary prospective randomized study. International Urology and Nephrology. 2012; 44(5):1357-62

37. Goldfarb DS, Asplin JR. Effect of grapefruit juice on urinary lithogenicity. Journal of Urology. 2001; 166(1):263-7

38. Goodman JW, Asplin JR, Goldfarb DS. Effect of two sports drinks on urinary lithogenicity. Urological Research. 2009; 37(1):41-6

39. Guéronnière V, Bellego L, Jimenez IB, Dohein O, Tack I, Daudon M. Increasing water intake by 2 liters reduces crystallization risk indexes in healthy subjects. Archivio Italiano di Urologia, Andrologia. 2011; 83(1):43-50

40. Hauser W, Frick J, Kunit G. Alkali citrate for preventing recurrence of calcium oxalate stones. European Urology. 1990; 17(3):248-51

41. Herrmann U, Schwille PO, Schwarzlaender H, Berger I, Hoffmann G. Citrate and recurrent idiopathic calcium urolithiasis. A longitudinal pilot study on the metabolic effects of oral potassium sodium citrate administered as short-, medium- and long-term to male stone patients. Urological Research. 1992; 20(5):347-53

42. Hiatt RA, Ettinger B, Caan B, Quesenberry CP, Duncan D, Citron JT. Randomized controlled trial of a low animal protein, high fiber diet in the prevention of recurrent calcium oxalate kidney stones. American Journal of Epidemiology. 1996; 144(1):25-33

43. Hofbauer J, Höbarth K, Szabo N, Marberger M. Alkali citrate prophylaxis in idiopathic recurrent calcium oxalate urolithiasis--a prospective randomized study. British Journal of Urology. 1994; 73(4):362-5

44. Jaipakdee S, Prasongwatana V, Premgamone A, Reungjui S, Tosukhowong P, Tungsanga K et al. The effects of potassium and magnesium supplementations on urinary risk factors of renal stone patients. Journal of the Medical Association of Thailand. 2004; 87(3):255-63

45. Jiménez Verdejo A, Arrabal Martín M, Miján Ortiz JL, Hita Rosino E, Palao Yago F, Zuluaga Gómez A. [Effect of potassium citrate in the prophylaxis of urinary lithiasis]. Archivos Españoles de Urología. 2001; 54(9):1036-46

46. Karagulle O, Smorag U, Candir F, Gundermann G, Jonas U, Becker AJ et al. Clinical study on the effect of mineral waters containing bicarbonate on the risk of urinary stone formation in patients with multiple episodes of CaOx-urolithiasis. World Journal of Urology. 2007; 25(3):315-23

47. Kato Y, Yamaguchi S, Yachiku S, Nakazono S, Hori J, Wada N et al. Changes in urinary parameters after oral administration of potassium-sodium citrate and magnesium oxide to prevent urolithiasis. Urology. 2004; 63(1):7-12

48. Kessler T, Hesse A. Cross-over study of the influence of bicarbonate-rich mineral water on urinary composition in comparison with sodium potassium citrate in healthy male subjects. British Journal of Nutrition. 2000; 84(6):865-71

49. Khan MM, Khan MW, Qadir I, Ali Ch Z, Liaquat H. A study regarding citrus juices effect (lemonade & orange juices only) in urolithiasis when compared to plain drinking water. Pakistan Journal of Medical and Health Sciences. 2015; 9(1):239-42

50. Kocvara R, Plasgura P, Petrík A, Louzenský G, Bartonícková K, Dvorácek J. A prospective study of nonmedical prophylaxis after a first kidney stone. BJU International. 1999; 84(4):393-8

51. Koff SG, Paquette EL, Cullen J, Gancarczyk KK, Tucciarone PR, Schenkman NS. Comparison between lemonade and potassium citrate and impact on urine pH and 24-hour urine parameters in patients with kidney stone formation. Urology. 2007; 69(6):1013-6

52. Kozyrakis D, Paridis D, Karatzas A, Soukias G, Dailiana Z. Do calcium supplements predispose to urolithiasis? Current Urology Reports. 2017; 18(3):17

53. Krishna Reddy S, Shaik AB, Bokkisam S. Effect of potassium magnesium citrate and vitamin B-6 prophylaxis for recurrent and multiple calcium oxalate and phosphate urolithiasis. Korean Journal of Urology. 2014; 55(6):411-6

54. Lieske JC. Probiotics for prevention of urinary stones. Annals of Translational Medicine. 2017; 5(2):29

55. Lieske JC, Tremaine WJ, Simone C, O'Connor HM, Li X, Bergstralh EJ et al. Diet, but not oral probiotics, effectively reduces urinary oxalate excretion and calcium oxalate supersaturation. Kidney International. 2010; 78(11):1178-85

56. Lojanapiwat B, Tanthanuch M, Pripathanont C, Ratchanon S, Srinualnad S, Taweemonkongsap T et al. Alkaline citrate reduces stone recurrence and regrowth after shockwave lithotripsy and percutaneous nephrolithotomy. International Brazilian Journal of Urology. 2011; 37(5):611-6

57. Lotan Y, Buendia Jimenez I, Lenoir-Wijnkoop I, Daudon M, Molinier L, Tack I et al. Increased water intake as a prevention strategy for recurrent urolithiasis: major impact of compliance on cost-effectiveness. Journal of Urology. 2013; 189(3):935-9

58. Malihi Z, Wu Z, Stewart AW, Lawes CM, Scragg R. Hypercalcemia, hypercalciuria, and kidney stones in long-term studies of vitamin D supplementation: a systematic review and meta-analysis. American Journal of Clinical Nutrition. 2016; 104(4):1039-51

59. Massey LK. Effect of dietary salt intake on circadian calcium metabolism, bone turnover, and calcium oxalate kidney stone risk in postmenopausal women. Nutrition Research. 2005; 25(10):891-903

60. Massey LK, Kynast-Gales SA. Substituting milk for apple juice does not increase kidney stone risk in most normocalciuric adults who form calcium oxalate stones. Journal of the American Dietetic Association. 1998; 98(3):303-8

61. Massey LK, Kynast-Gales SA. Diets with either beef or plant proteins reduce risk of calcium oxalate precipitation in patients with a history of calcium kidney stones. Journal of the American Dietetic Association. 2001; 101(3):326-31

62. Massey LK, Liebman M, Kynast-Gales SA. Ascorbate increases human oxaluria and kidney stone risk. Journal of Nutrition. 2005; 135(7):1673-7

63. Matsumoto ED, Heller HJ, Adams-Huet B, Brinkley LJ, Pak CY, Pearle MS. Effect of high and low calcium diets on stone forming risk during liberal oxalate intake. Journal of Urology. 2006; 176(1):132-6

64. Mattle D, Hess B. Preventive treatment of nephrolithiasis with alkali citrate--a critical review. Urological Research. 2005; 33(2):73-9

65. McHarg T, Rodgers A, Charlton K. Influence of cranberry juice on the urinary risk factors for calcium oxalate kidney stone formation. BJU International. 2003; 92(7):765-8

66. Mechlin C, Kalorin C, Asplin J, White M. Splenda® improves tolerance of oral potassium citrate supplementation for prevention of stone formation: results of a randomized double-blind trial. Journal of Endourology. 2011; 25(9):1541-5

67. Miao TJ. An evaluation of effect of magnetized water in the treatment of urinary calculus by double-blind test. Chinese Journal of Urology. 1984; 5(3):135-6

68. Moyad MA, Combs MA, Crowley DC, Baisley JE, Sharma P, Vrablic AS et al. Vitamin C with metabolites reduce oxalate levels compared to ascorbic acid: a preliminary and novel clinical urologic finding. Urologic Nursing. 2009; 29(2):95-102

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

70. Nomura K, Ito H, Masai M, Akakura K, Shimazaki J. Reduction of urinary stone recurrence by dietary counseling after SWL. Journal of Endourology. 1995; 9(4):305-12

71. Noori N, Honarkar E, Goldfarb DS, Kalantar-Zadeh K, Taheri M, Shakhssalim N et al. Urinary lithogenic risk profile in recurrent stone formers with hyperoxaluria: a randomized controlled trial comparing DASH (Dietary Approaches to Stop Hypertension)-style and low-oxalate diets. American Journal of Kidney Diseases. 2014; 63(3):456-63

72. Nouvenne A, Meschi T, Guerra A, Allegri F, Prati B, Fiaccadori E et al. Diet to reduce mild hyperoxaluria in patients with idiopathic calcium oxalate stone formation: a pilot study. Urology. 2009; 73(4):725-30, 730.e1

73. Nouvenne A, Meschi T, Prati B, Guerra A, Allegri F, Vezzoli G et al. Effects of a low-salt diet on idiopathic hypercalciuria in calcium-oxalate stone formers: a 3-mo randomized controlled trial. American Journal of Clinical Nutrition. 2010; 91(3):565-70

74. Nutrition Science Team. Government Dietary Recommendations: government recommendations for energy and nutrients for males and females aged 1 – 18 years and 19+ years. London. Public Health England, 2016. Available from: https://www.gov.uk/government/publications/the-eatwell-guide

75. Odvina CV. Comparative value of orange juice versus lemonade in reducing stone-forming risk. Clinical Journal of the American Society of Nephrology. 2006; 1(6):1269-74

76. Osorio AV, Alon US. The relationship between urinary calcium, sodium, and potassium excretion and the role of potassium in treating idiopathic hypercalciuria. Pediatrics. 1997; 100(4):675-81

77. Osther PJ. Effect of acute acid loading on acid-base and calcium metabolism. Scandinavian Journal of Urology and Nephrology. 2006; 40(1):35-44

78. Parivar F, Low RK, Stoller ML. The influence of diet on urinary stone disease. Journal of Urology. 1996; 155(2):432-40

79. Phillips R, Hanchanale VS, Myatt A, Somani B, Nabi G, Biyani CS. Citrate salts for preventing and treating calcium containing kidney stones in adults. Cochrane Database of Systematic Reviews 2015, Issue 10. Art. No.: CD010057. DOI: 10.1002/14651858.CD010057.pub2.

80. Pinheiro VB, Baxmann AC, Tiselius HG, Heilberg IP. The effect of sodium bicarbonate upon urinary citrate excretion in calcium stone formers. Urology. 2013; 82(1):33-7

81. Prasetyo T, Birowo P, Rasyid N. The influence of increased fluid intake in the prevention of urinary stone formation: a systematic review. Acta Medica Indonesiana. 2013; 45(4):253-8

82. Prieto RM, Fiol M, Perello J, Estruch R, Ros E, Sanchis P et al. Effects of Mediterranean diets with low and high proportions of phytate-rich foods on the urinary phytate excretion. European Journal of Nutrition. 2010; 49(6):321-26

83. Public Health England, Welsh Government, Food Standards Scotland, Food Standards Agency Northern Ireland. Eatwell guide: colour PDF. London. Public Health England, 2016. Available from: https://www.gov.uk/government/publications/the-eatwell-guide

84. Rodgers AL. The influence of South African mineral water on reduction of risk of calcium oxalate kidney stone formation. South African Medical Journal. 1998; 88(4):448-51

85. Rotily M, Léonetti F, Iovanna C, Berthezene P, Dupuy P, Vazi A et al. Effects of low animal protein or high-fiber diets on urine composition in calcium nephrolithiasis. Kidney International. 2000; 57(3):1115-23

86. Sakhaee K, Poindexter JR, Griffith CS, Pak CY. Stone forming risk of calcium citrate supplementation in healthy postmenopausal women. Journal of Urology. 2004; 172(3):958-61

87. Sarica K, Erturhan S, Yurtseven C, Yagci F. Effect of potassium citrate therapy on stone recurrence and regrowth after extracorporeal shockwave lithotripsy in children. Journal of Endourology. 2006; 20(11):875-9

88. Shuster J, Jenkins A, Logan C, Barnett T, Riehle R, Zackson D et al. Soft drink consumption and urinary stone recurrence: a randomized prevention trial. Journal of Clinical Epidemiology. 1992; 45(8):911-6

89. Silverio F, D'Angelo AR. [Prevention of renal calculosis: efficacy of Fiuggi water cure. Research Group on Renal Calculosis]. Archivio Italiano di Urologia, Andrologia. 1994; 66(5):253-8

90. Silverio F, Ricciuti GP, D'Angelo AR, Fraioli A, Simeoni G. Stone recurrence after lithotripsy in patients with recurrent idiopathic calcium urolithiasis: efficacy of treatment with Fiuggi water. European Urology. 2000; 37(2):145-8

91. Soygür T, Akbay A, Küpeli S. Effect of potassium citrate therapy on stone recurrence and residual fragments after shockwave lithotripsy in lower caliceal calcium oxalate urolithiasis: a randomized controlled trial. Journal of Endourology. 2002; 16(3):149-52

92. Tosukhowong P, Yachantha C, Sasivongsbhakdi T, Ratchanon S, Chaisawasdi S, Boonla C et al. Citraturic, alkalinizing and antioxidative effects of limeade-based regimen in nephrolithiasis patients. Urological Research. 2008; 36(3-4):149-55

93. Tracy CR, Best S, Bagrodia A, Poindexter JR, Adams-Huet B, Sakhaee K et al. Animal protein and the risk of kidney stones: a comparative metabolic study of animal protein sources. Journal of Urology. 2014; 192(1):137-41

94. Turney BW, Appleby PN, Reynard JM, Noble JG, Key TJ, Allen NE. Diet and risk of kidney stones in the Oxford cohort of the European Prospective Investigation into Cancer and Nutrition (EPIC). European Journal of Epidemiology. 2014; 29(5):363-9

95. Valli PP, Cesaroni M, Mearini L, Rociola W, Cervelli B, Porena M. [Hyperhydration with low mineral Rocchetta water after extracorporeal lithotripsy]. Archivio Italiano di Urologia, Andrologia. 2000; 72(1):29-31

96. Vescini F, Buffa A, La Manna G, Ciavatti A, Rizzoli E, Bottura A et al. Long-term potassium citrate therapy and bone mineral density in idiopathic calcium stone formers. Journal of Endocrinological Investigation. 2005; 28(3):218-22

97. Wabner CL, Pak CY. Effect of orange juice consumption on urinary stone risk factors. Journal of Urology. 1993; 149(6):1405-8

98. Wallace RB, Wactawski-Wende J, O'Sullivan MJ, Larson JC, Cochrane B, Gass M et al. Urinary tract stone occurrence in the Women's Health Initiative (WHI) randomized clinical trial of calcium and vitamin D supplements. American Journal of Clinical Nutrition. 2011; 94(1):270-7

99. Whalley NA, Meyers AM, Martins M, Margolius LP. Long-term effects of potassium citrate therapy on the formation of new stones in groups of recurrent stone formers with hypocitraturia. British Journal of Urology. 1996; 78(1):10-4

100. Worster AS, Bhanich SW. Fluids and diuretics for acute ureteric colic. Cochrane Database of Systematic Reviews 2012, Issue 2. Art. No.: CD004926. DOI: 10.1002/14651858.CD004926.pub3.

101. Xu C, Zhang C, Wang XL, Liu TZ, Zeng XT, Li S et al. Self-fluid management in prevention of kidney stones: a PRISMA-Compliant systematic review and dose-response meta-analysis of observational studies. Medicine. 2015; 94(27):e1042

102. Yatzidis H. Successful sodium thiosulphate treatment for recurrent calcium urolithiasis. Clinical Nephrology. 1985; 23(2):63-7

103. Zerwekh JE, Odvina CV, Wuermser LA, Pak CY. Reduction of renal stone risk by potassium-magnesium citrate during 5 weeks of bed rest. Journal of Urology. 2007; 177(6):2179-84

Appendices

Appendix A: Review protocols

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)	• 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	• 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	Critical outcomes: • 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 Important outcomes: • 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	Strata: • Adults (≥16 years) • Children and young people (<16 years) • People with specific metabolic abnormalities Subgroups: • 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)	• Pairwise meta-analyses performed using Cochrane Review Manager (RevMan5). • GRADEpro used to assess the quality of evidence for each outcome • Endnote for bibliography, citations, sifting and reference management • Data extractions performed using EviBase, a platform designed and maintained by the National Guideline Centre (NGC)
Information sources – databases and dates	Clinical search databases to be used: Medline, Embase, Cochrane Library Date: all years Health economics search databases to be used: Medline, Embase, NHSEED, HTA Date: Medline, Embase from 2014 NHSEED, HTA – all years Language: Restrict to English only Supplementary search techniques: backward citation searching Key papers: Not known
Identify if an update	Not applicable
Author contacts	https://www.nice.org.uk/guidance/indevelopment/gid-ng10033
Highlight if amendment to previous protocol	For details please see section 4.5 of Developing NICE guidelines: the manual.
Search strategy – for one database	For details please see appendix B
Data collection process – forms / duplicate	A standardised evidence table format will be used, and published as appendix D of the evidence report.
Data items – define all variables to be collected	For details please see evidence tables in Appendix D (clinical evidence tables) or H (health economic evidence tables).
Methods for assessing bias at outcome / study level	Standard study checklists were used to critically appraise individual studies. For details please see section 6.2 of Developing NICE guidelines: the manual 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/

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

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	• Populations, interventions and comparators must be as specified in the individual review protocol above. • Studies must be of a relevant economic study design (cost-utility analysis, cost-effectiveness analysis, cost-benefit analysis, cost-consequences analysis, comparative cost analysis). • Studies must not be a letter, editorial or commentary, or a review of economic evaluations. (Recent reviews will be ordered although not reviewed. The bibliographies will be checked for relevant studies, which will then be ordered.) • Unpublished reports will not be considered unless submitted as part of a call for evidence. • Studies must be in English.
Search strategy	An economic study search will be undertaken using population-specific terms and an economic study filter – see Appendix G *[in the Full guideline]*.
Review strategy	Studies not meeting any of the search criteria above will be excluded. Studies published before 2002, abstract-only studies and studies from non-OECD countries or the USA will also be excluded.

Each remaining study will be assessed for applicability and methodological limitations using the NICE economic evaluation checklist which can be found in Appendix G of the 2014 NICE guidelines manual.[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.	(nephrolitiasis or nephrolith or nephroliths or urolithias?s or ureterolithias?s).ti,ab.
3.	((renal or kidney* or urinary or ureter* or urethra*) adj3 (stone* or calculi or calculus or calculosis or lithiasis or c?olic*)).ti,ab.
4.	stone disease*.ti,ab.
5.	((calculi or calculus or calcium oxalate or cystine) adj3 (crystal* or stone* or lithiasis)).ti,ab.
6.	or/1-5
7.	letter/
8.	editorial/
9.	news/
10.	exp historical article/
11.	Anecdotes as Topic/
12.	comment/
13.	case report/
14.	(letter or comment*).ti.
15.	or/7-14

16.	randomized controlled trial/ or random*.ti,ab.
17.	15 not 16
18.	animals/ not humans/
19.	exp Animals, Laboratory/
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

Embase (Ovid) search terms

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

Cochrane Library (Wiley) search terms

#1.	MeSH descriptor: [Urolithiasis] explode all trees
#2.	(nephrolitiasis 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

B.2 Health Economics literature search strategy

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

Table 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

Medline (Ovid) search terms

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

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

Embase (Ovid) search terms

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

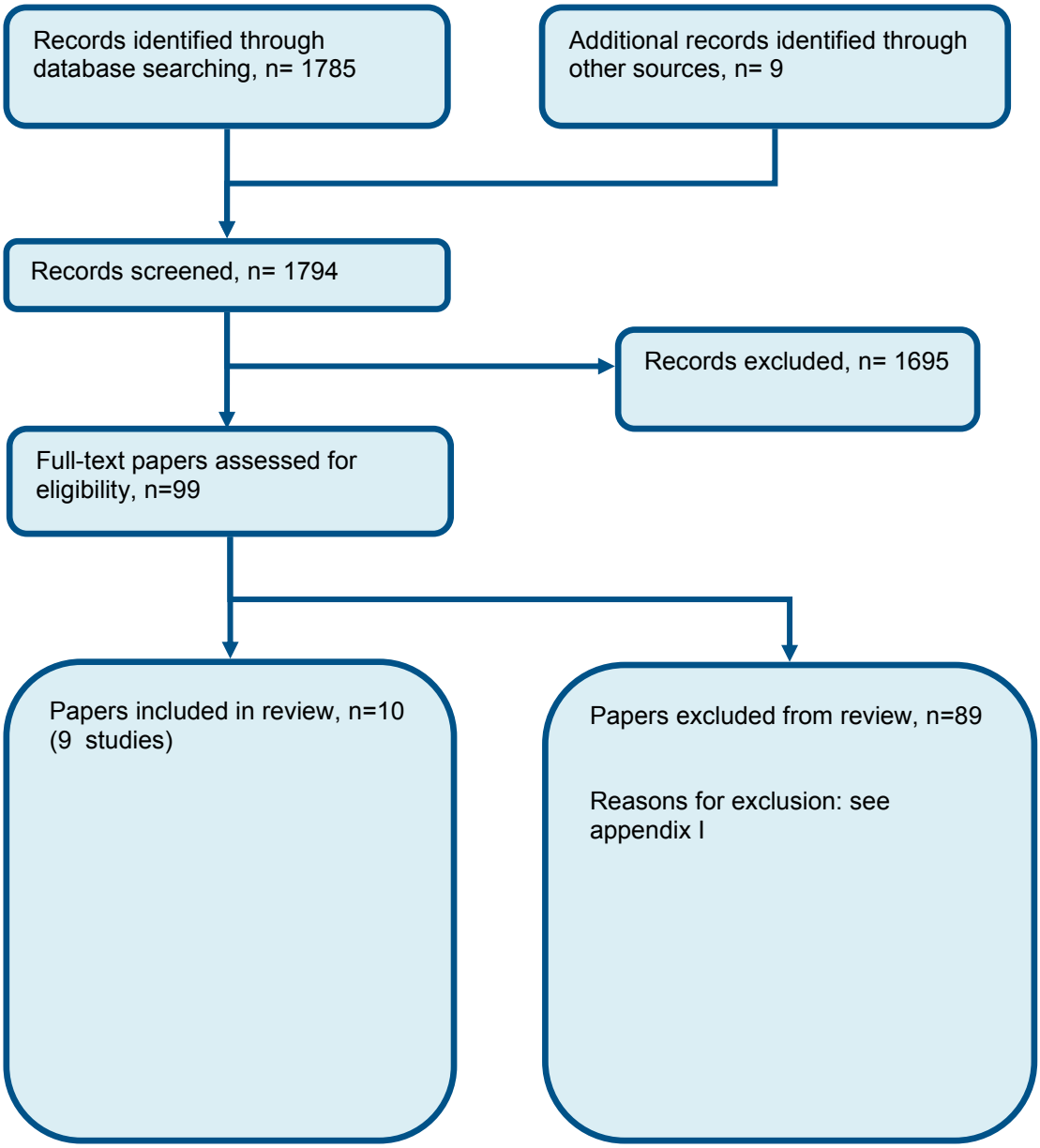
36.	(financ* or fee or fees).ti,ab.
37.	(value adj2 (money or monetary)).ti,ab.
38.	or/25-37
39.	24 and 38

NHS EED and HTA (CRD) search terms

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

Appendix C: Clinical evidence selection

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



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, hyperparathyrodism, 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 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: 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: 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:	
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 1996[11]**
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

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:

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 hypercalcuria (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)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: CALCIUM - LOW versus CALCIUM - NORMAL-HIGH 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	
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	(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 (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 (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
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 diary products and lower in saturated fat, total fat, and cholesterol; it contained more whole grains and fewer refined grains, sweets, and res 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	(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 of800–1000 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,6.3mgMg/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 (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

	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

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: LOW SODIUM DIET versus NO INTERVENTION

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

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

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

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

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

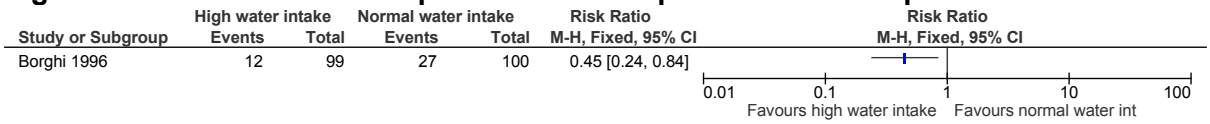
Study	**Silverio 2000[90]**
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=384)
Countries and setting	Conducted in Italy; Setting:
Line of therapy	1st line
Duration of study	Intervention time: Mean: 19 months (range: 14-34 months)
Method of assessment of 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

Appendix E: Forest plots

E.1 High water intake versus normal water intake

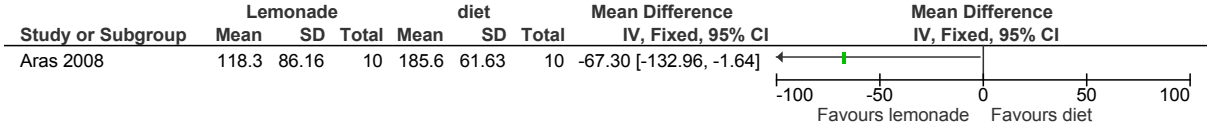
Figure 2: stone recurrence in patients with idiopathic calcium nephrolithiasis



Follow up: 5 years

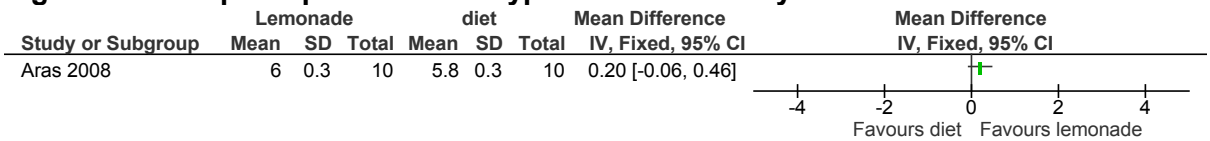
E.2 Lemonade (fresh lemon juice in water) versus diet

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



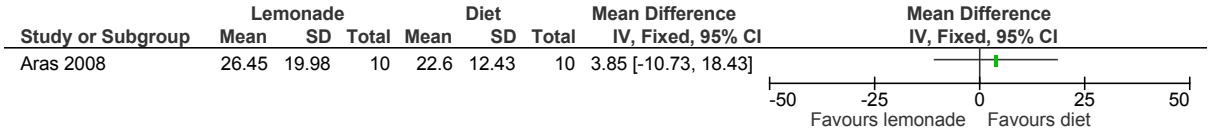
Follow up: 3 months

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



Follow up: 3 months

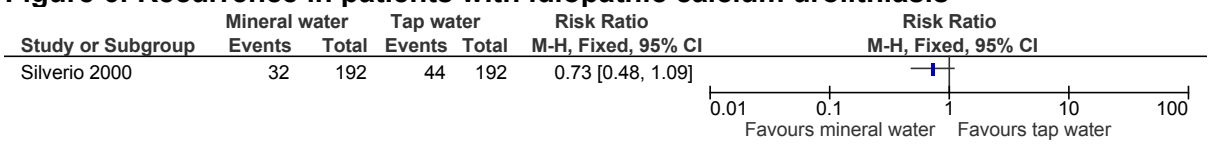
Figure 5: Urine oxalate in patients with hypocitraturic urinary calcium stones



Follow up: 3 months

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

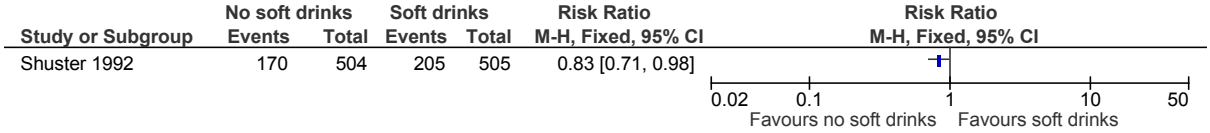
Figure 6: Recurrence in patients with idiopathic calcium urolithiasis



Follow up: 19 months

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

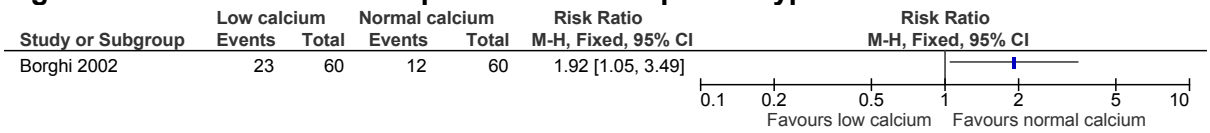
Figure 7: Recurrence in patients with urinary stone (all stone subtypes were included)



Follow up: 3 years

E.5 Low calcium diet versus normal calcium diet

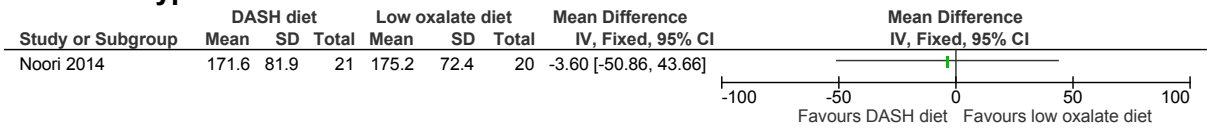
Figure 8: Stone recurrence in patients with idiopathic hypercalcuria



Follow up: 5 years

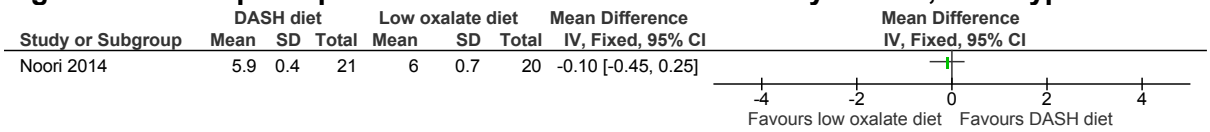
E.6 DASH diet versus low oxalate diet

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



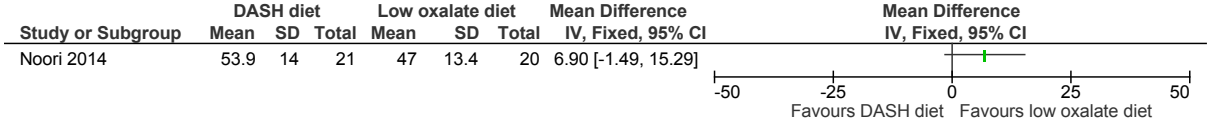
Follow up: 8 weeks

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



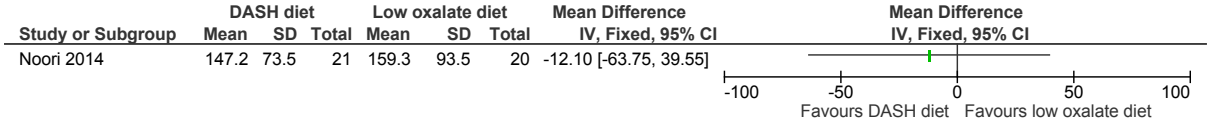
Follow up: 8 weeks

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



Follow up: 8 weeks

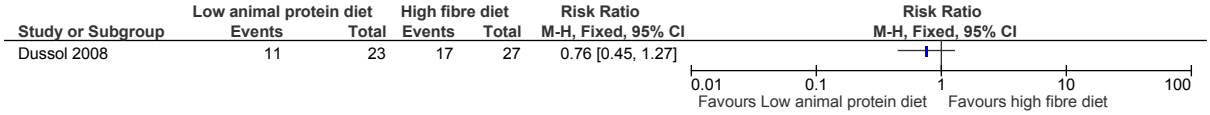
Figure 12: Urine sodium in patients with calcium oxalate kidney stones, with hyperoxaluria



Follow up: 8 weeks

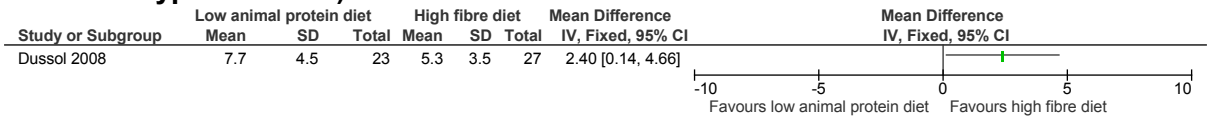
E.7 Low animal protein diet versus high fibre diet

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



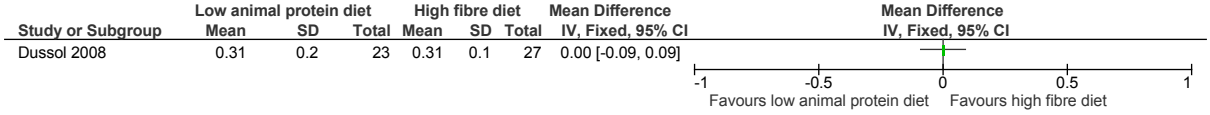
Follow up: 4 years

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



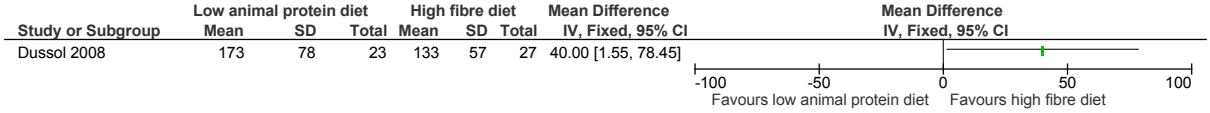
Follow up: 4 years

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



Follow up: 4 years

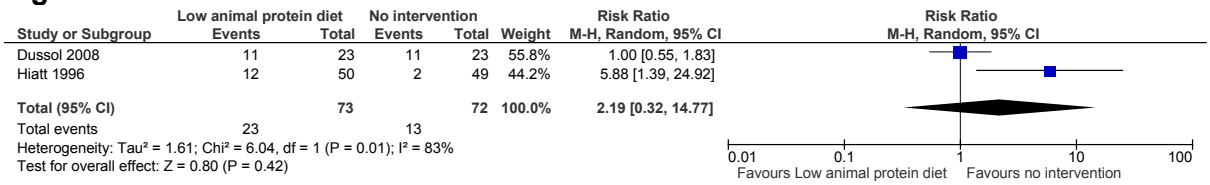
Figure 16: Urine sodium in patients with idiopathic calcium stones (38% had hypercalciuria)



Follow up: 4 years

E.8 Low animal protein diet versus no intervention

Figure 17: Recurrence

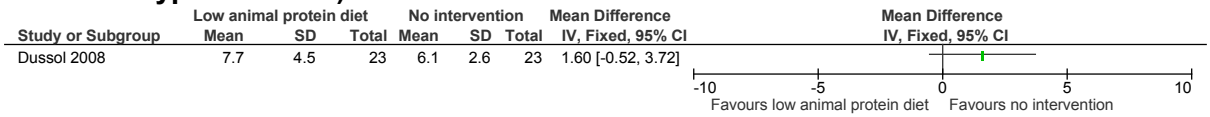


Follow up: 4 years

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

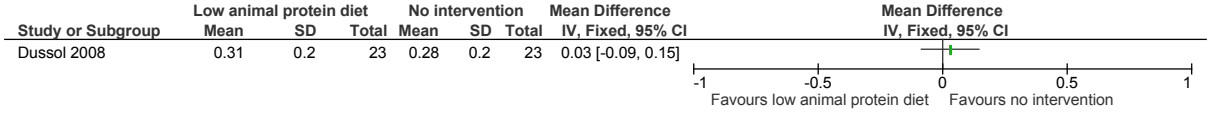
Hiatt 1996: Calcium oxalate kidney stone (≥65%calcium oxalate)

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



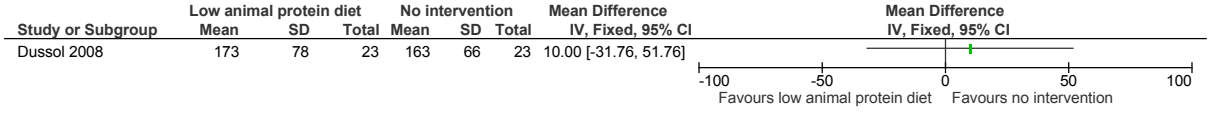
Follow up: 4 years

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



Follow up: 4 years

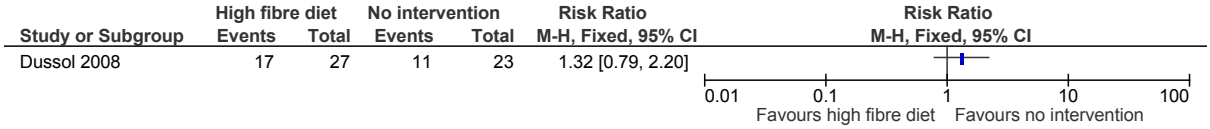
Figure 20: Urine sodium in patients with idiopathic calcium stones (38% had hypercalciuria)



Follow up: 4 years

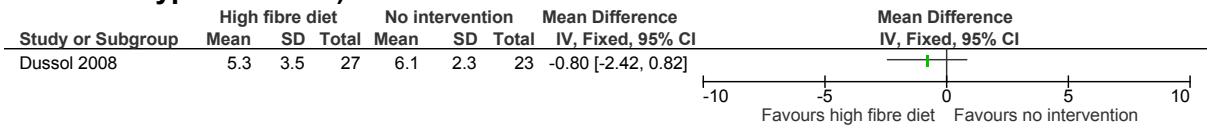
E.9 High fibre diet versus no intervention

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



Follow up: 4 years

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



Follow up: 4 years

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

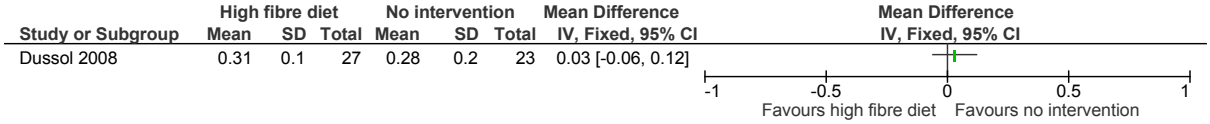
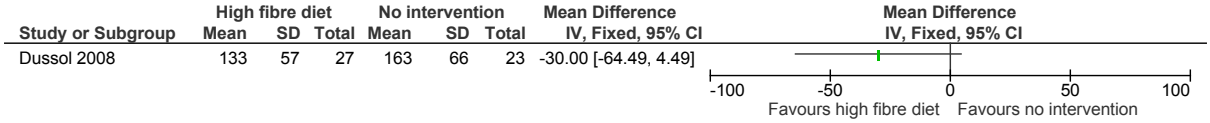


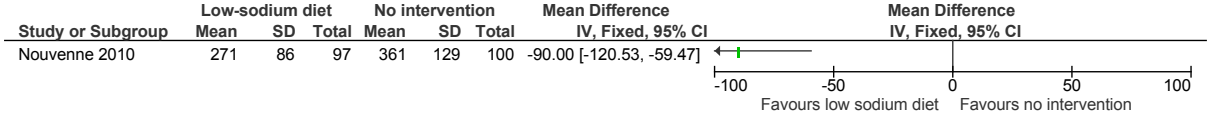
Figure 24: Urine sodium in patients with idiopathic calcium stones (38% had hypercalciuria)



Follow up: 4 years

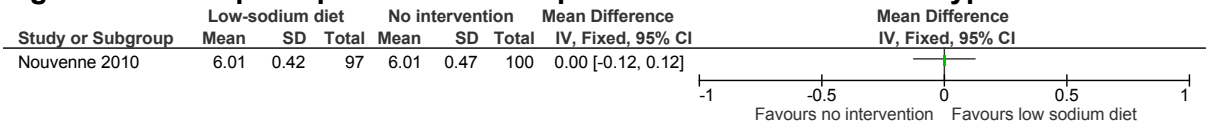
E.10 Low salt diet versus no intervention

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



Follow up: 3 months

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



Follow up: 3 months

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

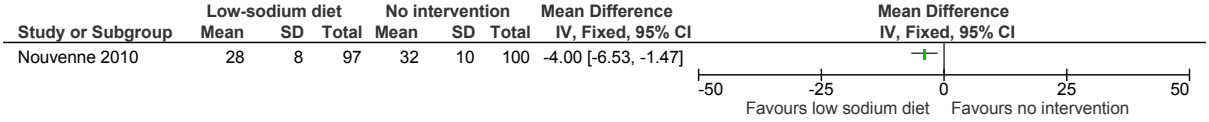
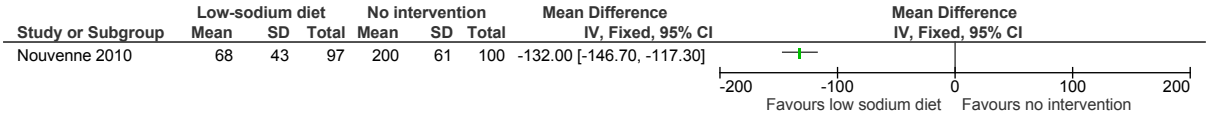


Figure 28: Urine sodium in patients with idiopathic calcium stones and hypercalcinuria



Follow up: 3 months

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)	⊕⊕OO 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)	⊕OOO 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)	⊕⊕OO 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)	⊕⊕OO 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)	⊕⊕OO 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)												

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)	⊕⊕OO 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] 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)	⊕⊕OO 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)	⊕OOO 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)	⊕⊕OO 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)	⊕⊕OO 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)	⊕⊕OO 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)	⊕⊕OO 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)	⊕⊕⊕O 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)	⊕⊕⊕O 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)	⊕⊕OO 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)	⊕OOO 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)	⊕⊕OO 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)	⊕⊕⊕O 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)	⊕⊕⊕O 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)	⊕⊕⊕O 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)	⊕⊕⊕O 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)	⊕⊕⊕O 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)	⊕⊕⊕O 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

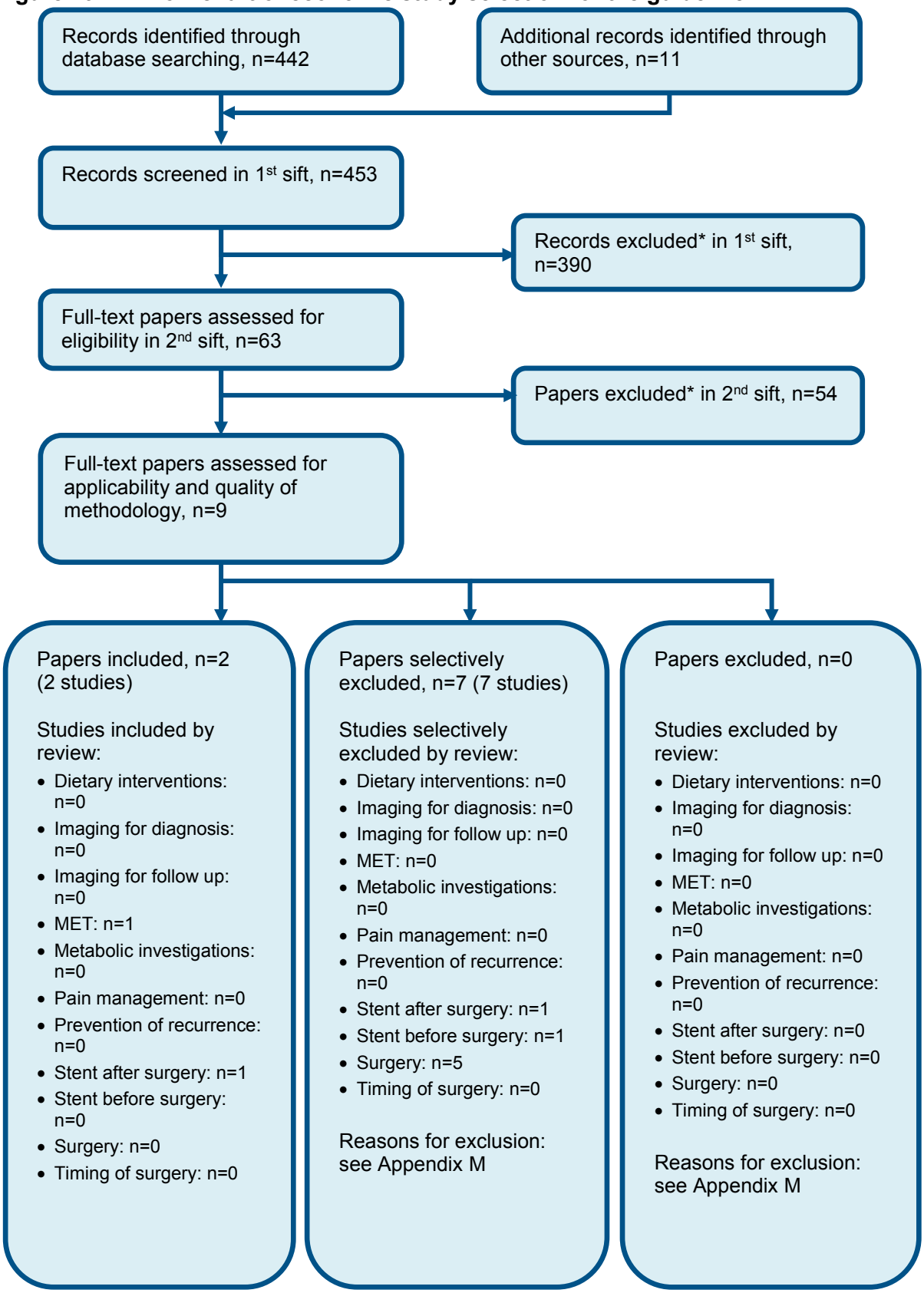
Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Low salt diet**	**No intervention**	**Relative (95% CI)**	**Absolute**		
Urine sodium (follow-up mean 3 months; Better 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)	⊕⊕⊕O 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)	⊕⊕⊕O 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

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

Appendix G: Health economic evidence 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 hystory 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)
Odvina 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)

I.2 Excluded health economic studies

None