National Institute for Health and Care Excellence

Final

Renal and ureteric stones: assessment and management

Medical expulsive therapy

NICE guideline NG118

Intervention evidence review (D)

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Final

This evidence review was developed by the National Guideline Centre

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1.1 Review question: Is medical expulsive therapy clinically and cost-effective in managing people with ureteric stones?

1.2 Introduction

Most acute stone episodes are initially treated with a period of observation as spontaneous passage of a stone often occurs. The passage of the stone is influenced by the size and site of the stone , the smaller stones <5mm having the greatest chance of stone passage along with stones in the distal ureter as this site is closest to the bladder. The majority of stones are expelled in 4-6 weeks but during this period the patient will often experience deterioration in quality of life, as they have concerns about episodes of severe pain and admission to hospital as well as the economic implications of not being able to work. There would therefore be considerable benefit to patients and the health system if this potential time to stone passage in suitable patients could be reduced by medical expulsive therapy which is the medication used to enhance the passage of stones or stone fragments . A similar benefit to promoting stone passage may also be present if medical expulsive therapy is used following active stone treatment, SWL and ureteroscopy to remove residual fragments. It has been shown that both alpha blockers and calcium channel blockers may have a role in medical expulsive therapy though there are no clear guidelines on their use in initial conservative management or following definitive stone treatment .

1.3 PICO table

For full details see the review protocol in appendix A.

Table 1: PICO characteristics of review question

Population	People with ureteric stones
Intervention(s)	• Alpha blockers (Tamsulosin, Alfuzosin, Doxazosin, Silodosin, Naftopidil, Terazosin) • Calcium channel blocker (Nifedipine)
Comparison(s)	Compared to: • Each other • Placebo • No treatment • Steroids
Outcomes	Critical outcomes: • Time to stone passage • Stone passage • Use of healthcare services/Hospitalisation • Quality of life • Adverse events (hypotension, dizzy spells, falls, floppy iris, retrograde ejaculation, headaches, flushing) Important outcomes: • Pain intensity (visual analogue scale, verbal ratings, descriptive scales, time to pain relief, need to rescue medication) • Analgesic use

Study design	• Randomised controlled trials (RCTs), systematic reviews of RCTs • If no RCTs are available, non-randomised comparative studies (prospective and retrospective observational studies) will be included

1.4 Clinical evidence

1.4.1 Included studies

A search was conducted for randomised trials comparing the effectiveness of alpha blockers or calcium channel blockers versus each other, placebo, no treatment or steroids alone or as an adjunctive therapy to surgery for people with ureteric stones. Seventy-one studies (72 papers) were included in the review;[1, 3, 5-9, 14-17, 20-22, 24, 28-31, 42, 43, 49, 57, 58, 60, 62, 63, 65, 68-70, 76, 86, 92, 93, 95, 103, 114, 116, 125, 130, 137, 138, 140, 143, 147, 150, 152-154, 165, 170, 171, 174, 176, 179, 186, 187, 194, 196, 197, 199, 206, 208, 213, 215, 216, 218, 219, 222, 224] these are summarised in Table 2 below. Evidence from these studies is summarised in the clinical evidence summary below (Table 7-23).

In adults with distal ureteric stones <10mm, 7 studies compared alpha blockers versus calcium channel blockers, 32 studies compared alpha blockers versus no treatment, 13 studies compared alpha blockers versus placebo, 3 studies compared calcium channel blockers versus no treatment and 1 study compared calcium channel blockers versus placebo.

In adults with mid ureteric stones <10mm, 1 study compared alpha blockers versus calcium channel blockers, 1 study compared alpha blockers versus no treatment and 2 studies compared alpha blockers versus placebo. No evidence was identified comparing calcium blockers versus no treatment or placebo for mid ureteric stones.

In adults with proximal ureteric stones <10mm, 1 study compared alpha blockers versus calcium channel blockers, 3 studies compared alpha blockers versus no treatment and 2 studies compared alpha blockers versus placebo. No evidence was identified comparing calcium blockers versus no treatment or placebo for proximal ureteric stones.

Three studies compared alpha blockers versus no treatment, and 2 studies compared alpha blockers versus placebo in children with distal ureteric stones <10mm. No evidence was identified comparing alpha blockers versus calcium channel blockers, calcium blockers versus no treatment or calcium channel blockers versus placebo in children. No evidence was identified for mid or proximal ureteric stones in children.

No evidence was identified for medical expulsive therapy alone (not as an adjunct to surgery) for ureteric stones >10mm in adults or children.

In adults with distal ureteric stones, 6 studies compared alpha blockers as adjunctive therapy to surgery versus surgery only for stones <10mm, 1 study compared alpha blockers as adjunctive therapy to surgery versus surgery only for stones 10-20mm and 1 study compared alpha blockers as adjunctive therapy to surgery versus placebo and surgery for stones <10mm. No evidence was identified comparing alpha blockers versus calcium channel blockers as adjunctive therapy to surgery, or calcium channel blockers as adjunctive therapy to surgery versus placebo or surgery only.

In adults with mid ureteric stones 10-20mm, 1 study compared alpha blockers as adjunctive therapy to surgery versus surgery only. No evidence was identified for alpha blockers versus calcium channel blockers as adjunctive therapy to surgery, alpha blockers versus placebo as an adjunctive therapy to surgery, or calcium channel blockers as adjunctive therapy to surgery versus placebo or surgery only. No evidence was identified for mid ureteric stones <10mm.

In adults with proximal ureteric stones, 6 studies compared alpha blockers as adjunctive therapy to surgery versus surgery only for stones <10mm, 4 studies compared alpha blockers as adjunctive therapy to surgery versus surgery only for stones 10-20mm, and 1 study compared alpha blockers as adjunctive therapy to surgery versus placebo and surgery for stones <10mm. No evidence was identified comparing alpha blockers versus calcium channel blockers as adjunctive therapy to surgery or calcium channel blockers as adjunctive therapy to surgery versus placebo or surgery only.

No evidence was identified for medical expulsive therapy as an adjunctive therapy to surgery for ureteric stones in children.

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 Heterogeneity

For the comparison of alpha blockers versus Calcium channel blockers for distal ureteric stones <10mm in adults, there was substantial heterogeneity between the studies when they were meta-analysed for the outcome of stone passage. For the comparison of alpha blockers versus no treatment (pain management only) for distal ureteric stones <10mm in adults, there was substantial heterogeneity between the studies when they were meta-analysed for the outcomes of time to stone passage, stone passage, pain intensity (number of pain episodes) and analgesic use (number of times and diclofenac dose). For the comparison alpha blockers versus placebo for distal ureteric stones <10mm in adults, there was substantial heterogeneity between the studies when they were meta-analysed for the outcomes of stone passage and analgesic use (number of people using analgesics and diclofenac dose). For the comparison alpha blockers versus no treatment (pain management only) for distal ureteric stones <10mm in children, there was substantial heterogeneity between the studies when they were meta-analysed for the outcome of time to stone passage. For the comparison alpha blockers versus placebo for distal ureteric stones <10mm in children, there was substantial heterogeneity between the studies when they were meta-analysed for the outcome of time to stone passage and pain intensity (daily pain episodes). For the comparison alpha blockers as adjunctive therapy to shock wave lithotripsy versus shock wave lithotripsy only for proximal ureteric stones <10mm in adults, there was substantial heterogeneity between the studies when they were meta-analysed for the outcomes pain intensity (VAS), time to stone passage and analgesic use (number of people using analgesia). Where pre-specified subgroup analyses (see Appendix A:) were either unable to be performed, or did not explain the heterogeneity, a random effects meta-analysis was applied to these outcomes, and the evidence was downgraded for inconsistency in GRADE.

1.4.4 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
Abdelaziz 2017[3]	Intervention (n=51): Tamsulosin 0.4mg daily before URS for 1 week. Concurrent medication/care: URS and NSAIDs Comparison (n=47): ureterorenoscopy. Concurrent medication/care: NSAIDs	n=98 People with a single, radio opaque, lower ureteral stone, 5-10mm in maximum diameter Mean (SD) age: 36.27 (6.7) Male to female ratio 64:34 Saudi Arabia	Stone passage (2 weeks) Use of healthcare services/hospitalisation (2 weeks): defined as length of stay, days	
Abdel-Meguid 2010[1]	Intervention (n=75): Tamsulosin 0.4mg oral tablets once daily. Duration up to 4 weeks. Concurrent medication/care: hydration and analgesia (diclofenac 100mg) as needed, patients with non-symptomatic urinary tract infections given antibiotics Comparison (n=75): Placebo. Duration up to 4 weeks. Concurrent medication/care: hydration and analgesia (diclofenac 100mg) as needed, patients with non-symptomatic urinary tract infections given antibiotics	n=150 People with newly diagnosed single, unilateral, distal ureteral 4-10mm stones >18 years Male to female ratio 103:47 Saudi Arabia	Stone passage (4 weeks) Pain intensity (4 weeks): defined as number of pain episodes	
Agarwal 2009[5]	Intervention (n=20): Tamsulosin 0.4mg daily starting just before the session of SWL. SWL performed a maximum of 4 sessions for any significant ureteric fragment, ureteroscopy offered if stone did not show adequate	n=40 People with a single upper ureteric stone <15mm electing SWL	Time to stone passage (5 weeks) Stone passage (5 weeks)	Included 14 patients with stones <10mm, 20 with 10mm stones and 10 with stones >10mm. Included in

Study	Intervention and comparison	Population	Outcomes	Comments
	fragmentation after 2 sessions. Duration up to 3 months. Concurrent medication/care: over-the-counter NSAIDs, antispasmodics or Tramadol on demand Comparison (n=20): SWL performed a maximum of 4 sessions for any significant ureteric fragment, ureteroscopy offered if stone did not show adequate fragmentation after 2 sessions. Duration up to 5 weeks. Concurrent medication/care: over-the-counter NSAIDs, antispasmodics or Tramadol on demand	Mean (SD) age: alpha blocker group 32.4 (8.7); SWL only group 35.5 (15.4) Male to female ratio 31:9 India	Pain intensity (5 weeks): defined as visual analogue scale (0-10)	the <10mm stones analysis and downgraded for indirectness.
Agrawal 2009[6]	Intervention (n=34): Tamsulosin 0.4mg once daily. Duration up to 4 weeks. Concurrent medication/care: instructions to drink at least 3L fluids daily, diclofenac injection (75mg) intramuscularly on demand Intervention (n=34): Alfuzosin 10mg once daily. Duration up to 4 weeks. Concurrent medication/care: instructions to drink at least 3L fluids daily, diclofenac injection (75mg) intramuscularly on demand Comparison (n=34): Placebo. Duration up to 4 weeks. Concurrent medication/care: instructions to drink at least 3L fluids daily, diclofenac injection (75mg) intramuscularly on demand	n=102 People with a stone <10mm located in the distal part of the ureter 15-60 years Male to female ratio 78:24 India	Stone passage (4 weeks) Adverse events (4 weeks): hypotension, retrograde ejaculation	
Ahmad 2015[7]	Intervention (n=50): Tamsulosin 0.4mg daily. Duration up to 4 weeks. Concurrent medication/care: Diclofenac Sodium 50mg 8 hourly on required basis	n=100	Stone passage (4 weeks) Use of healthcare services/hospitalisation (4	

Study	Intervention and comparison	Population	Outcomes	Comments
	Comparison (n=50): Placebo 1 capsule daily. Duration up to 4 weeks. Concurrent medication/care: Diclofenac Sodium 50mg 8 hourly on required basis.	People with a stone size 8mm or smaller in distal third of the ureter >18 years Gender not reported Pakistan	weeks): defined as hospitalisation Adverse events (4 weeks) Analgesic use (4 weeks)	
Ahmed 2010[8]	Intervention (n=29): Tamsulosin 0.4mg once daily. Duration up to 30 days. Concurrent medication/care: diclofenac injection (75mg) intramuscularly as needed (up to twice a day) Intervention (n=30): Alfuzosin 10mg once daily. Duration up to 30 days. Concurrent medication/care: diclofenac injection (75mg) intramuscularly as needed (up to twice a day) Comparison (n=28): no intervention. Duration up to 30 days. Concurrent medication/care: diclofenac injection (75mg) intramuscularly as needed (up to twice a day)	n=87 People with acute renal colic and a distal ureteral stone ≤10 mm ≥18 years Male to female ratio 56:31 Saudi Arabia	Stone passage (30 days) Time to stone passage Use of healthcare services/hospitalisation (30 days): hospital readmission Adverse events (30 days): retrograde ejaculation Pain intensity (30 days): number of pain attacks	
Ahmed 2017[9]	Intervention (n=91): Tamsulosin 0.4mg daily before ureteroscopy. Duration 1 week. Concurrent medication/care: not reported Comparison (n=92): Ureteroscopy. Duration procedure time. Concurrent medication/care: not reported.	n=183 People with proximal ureteral stones ≥10mm scheduled for URS lithotripsy ≥18 years	Stone passage (4 weeks) Use of healthcare services/hospitalisation; (8 weeks): defined as initial procedure hospitalisation time	

Study	Intervention and comparison	Population	Outcomes	Comments
		Male to female ratio 98:67 Saudi Arabia		
Al-Ansari 2010[14]	Intervention (n=50): Tamsulosin 0.4mg once daily. Duration up to 4 weeks. Concurrent medication/care: Diclofenac 75mg injection on demand and advice to drink a minimum of 2 L of water daily Comparison (n=50): Placebo. Duration up to 4 weeks. Concurrent medication/care: Diclofenac 75mg injection on demand and advice to drink a minimum of 2 L of water daily	n=100 People with ureteral stones 10mm or smaller located below the common iliac vessels as assessed on non-contrast computed tomography >18 years Male to female ratio 67:33 Qatar	Time to stone passage (4 weeks) Stone passage (4 weeks) Adverse events (4 weeks) Pain intensity (4 weeks) Analgesic use (4 weeks)	
Aldaqadossi 2015[15]	Intervention (n=33): Tamsulosin 0.4mg for patients >5 years and 0.2mg for younger patients. Duration up to 4 weeks. Concurrent medication/care: Ibuprofen 4-10mg/kg orally every 6-8 hours as needed; in the case of intractable pain, Ketorolac 0.5-1mg/kg intramuscularly Comparison (n=34): Ibuprofen 4-10mg/kg every 6-8 hours as needed; in the case of intractable pain Ketorolac 0.5-1mg/kg intramuscularly. Duration 4 weeks. Concurrent medication/care: NA	n=67 Children presenting with a distal ureteric stone of <1cm below the common iliac vessels as assessed by enhanced CT Mean (SD) age: tamsulosin group: 7.7 years (3.02); pain management only (NSAIDs) group 7.25 years (2.7) Male to female ratio 36:27 Egypt	Time to stone passage (4 weeks) Stone passage (4 weeks) Adverse events (4 weeks) Pain intensity (4 weeks) Analgesic use (4 weeks)	

Study	Intervention and comparison	Population	Outcomes	Comments
Aldemir 2011[16]	Intervention (n=31): Tamsulosin 0.4mg once daily. Duration up to 10 days. Concurrent medication/care: Diclofenac as needed and advice to drink at least 2 L of water daily Comparison (n=29): Diclofenac 100mg once daily. Duration up to 10 days. Concurrent medication/care: advice to drink at least 2 L of water daily	n=60 People with stones located in the distal ureter with a size of <10mm in largest diameter >17 years Male to female ratio 58:32 Turkey	Stone passage (10 days) Adverse events (10 days) Pain intensity (10 days) Analgesic use (10 days)	
Alizadeh 2014[17]	Intervention (n=50): Tamsulosin 0.4mg daily. Duration up to 4 weeks. Concurrent medication/care: Indomethacin 100mg as needed and advice to drink 2 L of water daily Comparison (n=46): Indomethacin 100mg as needed. Duration up to 4 weeks. Concurrent medication/care: advice to drink 2 L of water daily	n=96 People with renal colic (3-6mm ureteral stone of distal ureteral or UVj) 18-60 years of age Male to female ratio 61:35 Iran	Time to stone passage (4 weeks) Stone passage (4 weeks) Adverse events (4 weeks) Analgesic use (4 weeks)	
Arrabal-Martin 2010[20]	Intervention (n=35): Tamsulosin 0.4mg daily. Duration 3 weeks. Concurrent medication/care: Ibuprofen 600mg every 12 hours, 2 L of water daily and Tramadol in case of pain Comparison (n=35): Ibuprofen 600mg every 12 hours. Duration 3 weeks. Concurrent medication/care: 2 L of water daily and Tramadol in case of pain	n=70 Age not reported Gender not reported People with ureteral lithiasis below the S3 and S4 levels and a calculus size of 4-10mm	Stone passage (30 days) Adverse events (30 days) Analgesic use (30 days)	

Study	Intervention and comparison	Population	Outcomes	Comments
		Spain		
Ates 2012[21]	Intervention (n=35): Doxazosin controlled release 4mg daily within 24 hours before SWL, if stone was not fragmented into pieces ≥6mm a second session was performed 3 days after the first procedure. Duration up to 14 days. Concurrent medication/care: oral Diclofenac on demand and advice to drink at least 2L of fluid daily Comparison (n=44): SWL, if stone was not fragmented into pieces ≥6mm a second session was performed 3 days after the first procedure. Duration procedure time. Concurrent medication/care: oral Diclofenac on demand and advice to drink at least 2 L of fluid daily	n=79 People with radio-opaque upper ureteral stones Mean (SD) age: doxazosin + SWL group: 38.35 (11.41); SWL group: 30.95 (9.68) Male to female ratio 58:21 Turkey	Time to stone passage (14 days) Stone passage (14 days) Use of healthcare services/hospitalisation (14 days) Pain intensity (time-point unclear) Analgesic use (14 days)	Included stones < and >10mm but mean diameter <10mm in both groups. Included in <10mm analysis and downgraded for indirectness.
Autorino 2005[22] De Sio 2006[49]	Intervention (n=32): Tamsulosin 0.4mg daily. Duration up to 2 weeks. Concurrent medication/care: Diclofenac 100mg daily, Aescin 80mg daily, advice to drink 2 L of water daily, Omeprazole 20mg daily for the treatment period and Levofloxacin 250mg daily for the first week Comparison (n=32): Diclofenac 100mg daily and Aescin 80mg daily. Duration up to 2 weeks. Concurrent medication/care: advice to drink 2 L of water daily, Omeprazole 20mg daily for the treatment period and Levofloxacin 250mg daily for the first week	n=64 People with unilateral distal ureteral calculi Mean (SD not reported) age: tamsulosin group: 45; NSAID group: 43 Male to female ratio 62:34 Italy	Time to stone passage (2 weeks) Stone passage (4 weeks) Use of healthcare services/hospitalisation (2 weeks) Adverse events (2 weeks) Analgesic use (2 weeks)	
Aydogdu 2009[24]	Intervention (n=19): Doxazosin 0.03mg/kg once daily administered at bedtime. Duration up to 3 weeks. Concurrent medication/care:	n=39	Time to stone passage (3 weeks)	

Study	Intervention and comparison	Population	Outcomes	Comments
	Ibuprofen 20mg/kg daily divided in 2 equal doses for pain episodes Comparison (n=20): Ibuprofen 20mg/kg daily divided in 2 equal doses for pain episodes. Duration up to 3 weeks. Concurrent medication/care: none	People with radiopaque lower ureteral stones 2-10mm in diameter Age 2-14 years Male to female ratio 21:18 Turkey	Stone passage (3 weeks) Adverse events (3 weeks)	
Bajwa 2013[28]	Intervention (n=30): Tamsulosin 0.4mg once daily. Duration up to 4 weeks. Concurrent medication/care: not reported Comparison (n=30): Diclofenac 50mg 12 hourly. Duration up to 4 weeks. Concurrent medication/care: not reported	n=60 People with lower ureteric stone <1cm, who were symptom free Mean (SD) age: 33.15 (8.97) Male to female ratio 37:23 Pakistan	Time to stone passage (4 weeks) Stone passage (4 weeks)	Unclear whether intervention group also received Diclofenac
Balci 2014[29]	Intervention (n=25): Tamsulosin 0.4mg daily. Duration up to 4 weeks. Concurrent medication/care: Diclofenac 50mg when required and advice to drink 2-2.5 L of water daily Comparison (n=25): Nifedipine 30mg daily. Duration up to 4 weeks. Concurrent medication/care: Diclofenac 50mg when required and advice to drink 2-2.5 L of water daily	n=75 People with stones of 5-10mm diameter in the lower third of the ureter (below the common iliac vessels) Mean (SD) age: 36.8 (11.3) Male to female ratio 53:22 Turkey	Stone passage (4 weeks) Adverse events (4 weeks) Analgesic use (4 weeks)	

Study	Intervention and comparison	Population	Outcomes	Comments
	Comparison (n=25): Diclofenac 50mg when required. Duration up to 4 weeks. Concurrent medication/care: advice to drink 2-2.5 L of water daily			
Basri 2013[30]	Intervention (n=59): Tamsulosin 0.4mg daily immediately after shock wave lithotripsy. Duration up to 4 weeks. Concurrent medication/care: Diclofenac 75mg injected intramuscularly on demand, gastro protective therapy 40mg Pantoprazole once daily and instruction to drink a minimum of 2L of water daily Comparison (n=64): Shock wave lithotripsy. Duration unclear. Concurrent medication/care: Diclofenac 75mg injected intramuscularly on demand, gastro protective therapy 40mg Pantoprazole daily and instruction to a minimum of 2L of water daily	n=123 People with solitary ureteral stone 6-15mm located in the upper, mid or lower ureter Mean (SD) age: tamsulosin + SWL group: 44.66 (13.25); SWL group: 42.19 (13.17) Male to female ratio 98:25 Turkey	Time to stone passage (4weeks) Pain intensity (4 weeks)	Results for distal, mid and proximal ureteric stones analysed separately. Included stones < and >10mm but mean stone size was >10mm. Included in 10-20mm stone analysis and downgraded for indirectness.
Bayraktar 2017[31]	Intervention (n=60): Tamsulosin 0.4 mg daily. Duration up to 4 weeks. Concurrent medication/care: recommended daily intake of liquids to urinate at least 1.5-2L, and 75mg diclofenac was injected when needed Comparison (n=64): Diclofenac 75mg injected when needed. Duration up to 4 weeks. Concurrent medication/care: recommended daily intake of liquids to urinate at least 1.5-2L	n=124 People with radiopaque distal ureter stones 5-10mm Age >18 years Males only Turkey	Time to stone passage (4 weeks) Stone passage (4 weeks) Analgesic use (4 weeks): defined as number of daily analgesic injections	
Chau 2011[42]	Intervention (n=33): Alfuzosin slow release 10mg daily. Duration 4 weeks. Concurrent medication/care: Dologesic (Paracetamol + Dextropropoxyphene) four tablets daily on demand for 2 weeks and Diclofenac slow	n=67 People with acute ureteric stone 5-10mm	Stone passage (5 weeks) Adverse events (5 weeks)	

Study	Intervention and comparison	Population	Outcomes	Comments
	release 100mg daily on demand for 2 weeks in case of suboptimal pain control by Dologesic Comparison (n=34): Dologesic (Paracetamol + Dextropropoxyphene) four tablets daily on demand for 2 weeks and Diclofenac slow release 100mg daily on demand for 2 weeks in case of suboptimal pain control by Dologesic. Duration 2 weeks. Concurrent medication/care: not reported	Mean (SD) age: 47.7 (12.3) Male to female ratio 41:26 China		
Cho 2013[43]	Intervention (n=41): ESWL then Alfuzosin 10mg daily, if the ureter stone remained and was larger than 5mm at the next follow up visit then additional ESWL was performed. Duration up to 42 days. Concurrent medication/care: Loxoprofen 68.1mg as needed and recommendation to drink at least 2L hydration daily Comparison (n=43): ESWL, if the ureter stone remained and was larger than 5mm at the next follow up visit then additional ESWL was performed. Duration up to 42 days. Concurrent medication/care: Loxoprofen 68.1mg as needed and recommendation to drink at least 2L hydration daily	n=84 People with radio-opaque ureter stones; 5-10mm in diameter Mean (SD) age: alfuzosin + SWL group: 47.4 (12.6); SWL 47.7 (12.1) Male to female ratio 60:24 South Korea	Time to stone passage (42 days) Stone passage (42 days) Adverse events (42 days) Pain intensity (time-point unclear) Analgesic use (42 days)	Included distal and proximal stones, >80% were proximal stones. Included in proximal analysis and downgraded for indirectness.
El Said 2015[57]	Intervention (n=28): Alfuzosin sustained release 5mg twice daily after meals. Duration up to 4 weeks. Concurrent medication/care: oral hydration with ≥2 L of water daily, Diclofenac 75mg intramuscularly on demand and education from the clinical pharmacist about potential adverse events, methods of reporting adverse events, self-reporting of pain on the visual analogue scale, importance	n=54 People presenting with radio-opaque stones ≤10mm and located in the distal third of the ureter >18 years	Stone passage (4 weeks) Use of healthcare services/hospitalisation (4 weeks) Adverse events (4 weeks)	

Study	Intervention and comparison	Population	Outcomes	Comments
	of adherence to medications and daily water intake Comparison (n=26): Oral hydration with ≥2 L of water daily and Diclofenac 75mg intramuscularly on demand. Duration up to 4 weeks. Concurrent medication/care: education by the clinical pharmacist on potential adverse events, methods of reporting adverse events, self-reporting of pain on the visual analogue scale, importance of adherence to medications and daily water intake	Male to female ratio 34:20 Egypt		
Elgalaly 2017[58]	Intervention (n=20): Silodosin 4mg at bedtime. Duration up to 4 weeks. Concurrent medication/care: ibuprofen 20mg/kg/day was divided into two doses for pain episodes, fluids were encouraged Comparison (n=20): Placebo taken at bedtime. Duration up to 4 weeks. Concurrent medication/care: ibuprofen 20mg/kg/day was divided into two doses for pain episodes, fluids were encouraged	n=40 Children with unilateral radiopaque distal ureteric stones <10mm < 18 years Male to female ratio 27:13 Egypt	Time to stone passage (4 weeks) (days) Stone passage (4 weeks): defined as visual confirmation of stone passage Pain intensity (4 weeks): defined as number of pain episodes	
Elkoushy 2012[60]	Intervention (n=63): SWL repeated every 3 weeks until the patient became stone free, Tamsulosin 0.4mg daily starting immediately after SWL. Duration up to 3 months. Concurrent medication/care: Diclofenac 50mg tablets or 75mg intramuscular injection on demand Comparison (n=63): SWL repeated every 3 weeks until the patient became stone free,	n=126 People with single radio-opaque renal or upper ureteral stones <2cm in largest diameter Mean (SD) age: tamsulosin + SWL group: 52.8 (8.2); SWL + placebo group: 49.4 (11.3)	Time to stone passage (3 months) Stone passage (3 months)	Reports results for renal and proximal ureteric stones separately. Data extracted for ureteric stones only. Included stones < and >10mm but mean stone diameter was

Study	Intervention and comparison	Population	Outcomes	Comments
	placebo daily starting immediately after SWL. Duration up to 3 months. Concurrent medication/care: Diclofenac 50mg tablets or 75mg intramuscular injection on demand	Male to female ratio 72:54 Egypt		<10mm. Included in <10mm analysis and downgraded for indirectness.
Erturhan 2007[63]	Intervention (n=30): Tamsulosin 0.4mg daily. Duration up to 3 weeks. Concurrent medication/care: prophylactic antibiotic therapy (Ceforoxime axetil 250mg daily) and 2.5 L hydration daily, injectable Diclofenac (max 200mg/day) recommended for routine use during pain episodes Comparison (n=30): Injectable Diclofenac (max 200mg/day) recommended for routine use during pain episodes. Duration up to 3 weeks. Concurrent medication/care: prophylactic antibiotic therapy (Cefuroxime axetil 250mg daily) and 2.5 L hydration daily	n=60 People with distal ureteral stones <10mm and allowing urinary flow Mean (range) age: 31.5 (19-51) Male to female ratio 64:56 Turkey	Stone passage (4 weeks) Use of healthcare services/hospitalisation (4 weeks) Adverse events (4 weeks)	
Erturhan 2013[62]	Intervention (n=24): Doxazosin 0.03mg/kg daily. Duration up to 3 weeks. Concurrent medication/care: Ibuprofen 20mg/kg daily divided in to 2 equal doses or a maximum 40mg/kg daily divided in to 4 equal doses in the case of intractable pain Comparison (n=21): Ibuprofen 20mg/kg daily divided in to 2 equal doses or a maximum of 40mg/kg daily divided in to 4 equal doses in the case of intractable pain. Duration up to 3 weeks. Concurrent medication/care: NA	n=45 People with a single radiopaque lower ureteral stone Mean (SD) age: 6.65 (3.78) Male to female ratio 24:26 Turkey	Stone passage (3 weeks)	
Eryildirim 2016[65]	Intervention (n=40): SWL and Tamsulosin 0.4mg daily. Duration up to 4 weeks. Concurrent medication/care: Diclofenac 75mg if needed	n=80	Stone passage (4 weeks)	

Study	Intervention and comparison	Population	Outcomes	Comments
	Comparison (n=40): SWL. Duration up to 4 weeks. Concurrent medication/care: Diclofenac 75mg if needed	People with 5-10mm single radio-opaque upper ureteral stones Mean (SD) age: 39.41 (12.99) Male to female ratio 36:18 Turkey	Use of healthcare services/hospitalisation (4 weeks) Quality of life (4 weeks) Pain intensity (4 weeks) Analgesic use (4 weeks)	
Ferre 2009[68]	Intervention (n=39): Tamsulosin 0.4mg daily. Duration 10 days. Concurrent medication/care: Ibuprofen 800mg 3 times a day and Oxycodone 5010mg every 4-6 hours as needed for pain Comparison (n=41): Ibuprofen 800mg 3 times a day and Oxycodone 5-10mg every 4-6 hours as needed for pain. Duration up to 14 days. Concurrent medication/care: NA	n=80 People with CT confirmed diagnosis of a single calculus in the distal third of the ureter (distal to the internal iliac vessels) inconsistent with phleboliths as determined by a board-certified radiologist ≥18 years of age Male to female ratio 56:21 USA	Stone passage (14 days) Use of healthcare service/hospitalisation s (14 days) Adverse events (14 days) Pain intensity (14 days) Analgesic use (14 days)	
Furyk 2016[69]	Intervention (n=198): Tamsulosin 0.4mg daily. Duration up to 4 weeks. Concurrent medication/care: analgesia at the discretion of the treating physician - recommended regimens were Indomethacin 25-50mg 3 times daily and Oxycodone 5-10mg 3 times daily as required for breakthrough	n=393 People with symptoms suggestive of ureteric colic; calculus demonstrated in the distal ureter (distal to the sacroiliac joint)	Stone passage (4 weeks) Use of healthcare services/hospitalisation (4 weeks)	

Study	Intervention and comparison	Population	Outcomes	Comments
	Comparison (n=195): Placebo. Duration up to 4 weeks. Concurrent medication/care: analgesia at the discretion of the treating physician - recommended regimens were Indomethacin 25-50mg 3 times daily and Oxycodone 5-10mg 3 times daily as required for breakthrough	>18 years Male to female ratio 320:73 Australia	Pain intensity (1, 2, 3 and 4 weeks)	
Gandhi 2013[70]	Intervention (n=64): Nifedipine 30mg slow-release daily. Duration up to 4 weeks. Concurrent medication/care: oral prednisolone 30mg daily for a maximum of 10 days, Diclofenac 75mg intramuscularly on demand and ≥2 L of water daily Comparison (n=64): Tamsulosin 0.4mg. Duration up to 4 weeks. Concurrent medication/care: oral prednisolone 30mg daily for a maximum of 10 days, Diclofenac 75mg intramuscularly on demand and ≥2 L of water daily	n=128 People with a solitary stone in the distal ureter at the juxtavesical tract or vesico-ureteric junction of 5-15mm Mean (SD) age nifedipine group: 30.4 (11.36); tamsulosin group; 34 (12.83) Male to female ration nifedipine group 1.48:1; tamsulosin group 1.28:1 Nepal	Stone passage (4 weeks) Adverse events (4 weeks) Analgesic use (4 weeks)	Included stones < and >10mm but mean stone diameter was <10mm in both groups. Included in <10mm stones analysis and downgraded for indirectness.
Gravas 2007[76]	Intervention (n=30): ESWL then Tamsulosin 0.4mg daily. Duration up to 4 weeks. Concurrent medication/care: hydration of at least 2 L daily and Diclofenac 50mg on demand Comparison (n=31): ESWL. Duration up to 4 weeks. Concurrent medication/care: hydration of at least 2 L daily and Diclofenac 50mg on demand	n=61 People with a single radiopaque distal ureteral stone (below the sacral-iliac joint), ≥6mm in diameter undergoing ESWL for the first time	Stone passage (4 weeks) Adverse events (4 weeks)	Included stones < and >10mm but mean stone diameter was <10mm in both groups. Included in <10mm stones analysis and downgraded for indirectness.

Study	Intervention and comparison	Population	Outcomes	Comments
		Mean (range) age: tamsulosin + SWL group 48.8 (27-73); SWL group: 49.2 (30-72) Male to female ratio 38:23 Greece		
Hermanns 2009[86]	Intervention (n=50): Tamsulosin 0.4mg daily. Duration up to 3 weeks. Concurrent medication/care: after initial analgesia for acute pain management, no regular analgesic medication was maintained. Oral Diclofenac (up to 3 X 50mg) as first line and oral Metamizole (up to 4 X 1g) as second line on-demand analgesics were prescribed Comparison (n=50): Placebo. Duration up to 3 weeks. Concurrent medication/care: after initial analgesia for acute pain management, no regular analgesic medication was maintained. Oral Diclofenac (up to 3 X 50mg) as first-line and oral Metamizole (up to 4 X 1g) as second-line on demand analgesics were prescribed	n=100 People with acute renal colic with a single ureteral stone ≤7mm below the common iliac vessels as assessed by CT ≥18 years Male to female ratio 75:15 Switzerland	Time to stone passage (3 weeks) Stone passage (3 weeks) Use of healthcare services/hospitalisation (3 weeks) Adverse events (3 weeks)	
Islam 2012[93]	Intervention (n=33): Tamsulosin 0.4mg daily. Duration up to 4 weeks. Concurrent medication/care: prophylactic antibiotic therapy (Ciprofloxacin 500mg twice daily), 2.5 L hydration daily and Diclofenac recommended for routine use during pain episodes Comparison (n=33): Nifedipine 20mg (slow release) daily. Duration up to 4 weeks. Concurrent medication/care: prophylactic	n=98 People with distal ureteral stones (juxtavesical tract and ureterovesical junction) ≤1cm in size Mean (SD not reported) age: tamsulosin group: 46.6;	Stone passage (4 weeks) Use of healthcare services/hospitalisation (4 weeks) Adverse events (4 weeks)	

Study	Intervention and comparison	Population	Outcomes	Comments
	antibiotic therapy (Ciprofloxacin 500mg twice daily), 2.5 L hydration daily and Diclofenac recommended for routine use during pain episodes Comparison (n=32): No treatment. Duration up to 4 weeks. Concurrent medication/care: prophylactic antibiotic therapy (Ciprofloxacin 500mg twice daily), 2.5 L hydration daily and Diclofenac recommended for routine use during pain episodes	nifedipine group 47.4; no treatment group: 42.8 Male to female ratio 58:33 Bangladesh		
Ibrahim 2013[92]	Intervention (n=50): Tamsulosin 0.4mg daily. Duration up to 4 weeks. Concurrent medication/care: diclofenac potassium 50mg given orally and/or diclofenac sodium 75mg given intramuscularly. Duration up to 4 weeks. Intervention (n=50): Alfuzosin 10mg daily. Duration up to 4 weeks. Concurrent medication/care: diclofenac potassium 50mg given orally and/or diclofenac sodium 75mg given intramuscularly. Duration up to 4 weeks. Comparison (n=50): Diclofenac potassium 50mg given orally and/or diclofenac sodium 75mg given intramuscularly. Duration up to 4 weeks.	n=150 People with symptomatic ureteric stone or <10mm >18 years Male to female ratio 91: 21 Iraq	Stone passage (4 weeks): not defined	Included proximal, mid and distal ureteral stones and results were reported separately
Itoh 2011[95]	Intervention (n=89): Silodosin 8mg daily. Duration up to 8 weeks. Concurrent medication/care: instruction to drink 2 L of water daily	n=187 People with symptomatic unilateral ureteral calculi <10mm in diameter	Time to stone passage (8 weeks) Stone passage (8 weeks)	Included proximal, mid and distal ureteral stones and results were reported separately

Study	Intervention and comparison	Population	Outcomes	Comments
	Comparison (n=92): No treatment. Duration up to 8 weeks. Concurrent medication/care: instruction to drink 2 L of water daily	Mean (SD) age: silodosin group: 57.2 (12.7); no treatment group: 56.5 (10.1) Male participants only Japan	Analgesic use (8 weeks): number of times of analgesic use	
Ketabchi 2014[103]	Intervention (n=52): Tamsulosin 0.4mg daily starting one day before URS. Duration up to 2 weeks. Concurrent medication/care: recommendation to drink 2 L of water daily, those with moderate to severe pain (>5 VAS) consumed Pethidine 25mg intravenously after the procedure in the recovery room and Indomethacin 500mg suppository daily Comparison (n=50): Placebo daily starting one day before URS. Duration up to 2 weeks. Concurrent medication/care: recommendation to drink 2 L of water daily, those with moderate to severe pain (>5 VAS) consumed Pethidine 25mg intravenously after the procedure in the recovery room and Indomethacin 500mg suppository daily	n=102 People with a single radio opaque lower ureteral stone with 5-10mm diameter Mean (SD) age: tamsulosin + URS group: 24 (6.5); placebo + URS group: 27 (8.8) Male to female ratio 77:25 Iran	Stone passage (2 weeks) Pain intensity (2 weeks) Analgesic use (2 weeks)	
Kupeli 2004[114]	Intervention (n=15): Tamsulosin 0.4mg daily. Duration 15 days. Concurrent medication/care: conventional treatment - oral hydration and oral Diclofenac 100mg daily Comparison (n=15): Oral Diclofenac 100mg daily. Duration 15 days. Concurrent medication/care: oral hydration Comparison (n=24): Tamsulosin 0.4mg daily beginning after shock wave lithotripsy.	n=78 People with lower ureteral stones within the distal 5cm of the ureter that ranged between 3 and 15mm in size Mean (range) age: 42.9 (21-67)	Stone passage (15 days) Adverse events (15 days)	Stone size <5mm given Tamsulosin or conventional treatment, stone size 6-15mm given SWL + conventional treatment or SWL + Tamsulosin + conventional treatment

Study	Intervention and comparison	Population	Outcomes	Comments
	Duration 15 days. Concurrent medication/care: conventional treatment – oral hydration and oral Diclofenac100mg daily Comparison (n=24): Shock wave lithotripsy. Concurrent medication/care: conventional treatment – oral hydration and oral Diclofenac 100mg daily	Male to female ratio 56:22 Turkey		Adjunctive therapy groups included 3 patients with stones >10mm. Included in the <10mm stones analysis and downgraded for indirectness.
Lee 2014[116]	Intervention (n=54): Tamsulosin 0.2mg daily. Duration up to 4 weeks. Concurrent medication/care: instruction to drink 2 L of water daily and oral painkiller (Ultracet® combination of Tramadol and Acetaminophen) on demand Comparison (n=54): No treatment. Duration up to 4 weeks. Concurrent medication/care: instruction to drink 2 L of water daily and oral painkiller (Ultracet® combination of Tramadol and Acetaminophen) on demand	n=108 People presenting with renal colic, with single, unilateral radiopaque, proximal ureteral calculi ≤6mm in diameter ≥18 years Male to female ratio 68:40 South Korea	Time to stone passage (4 weeks) Stone passage (4 weeks) Quality of life (4 weeks): EuroQoL Analgesic use (4 weeks): requirement of oral analgesics	
Lojanapiwat 2008[125]	Intervention (n=50): Tamsulosin 0.2mg or 0.4mg daily. Duration up to 4 weeks. Concurrent medication/care: Diclofenac 50mg twice daily for 10 days and Diclofenac 75mg infection if renal colic developed during treatment Comparison (n=25): Diclofenac 50mg twice daily. Duration 10 days. Concurrent medication/care: Diclofenac 75mg injection if renal colic developed	n=75 People with distal ureteric stones of 4-10mm; measured by plain KUB; gave informed consent; interviewed prior to taking part Mean (SD) age: tamsulosin 0.2mg group: 48 (15.74); tamsulosin 0.4mg group: 46.71 (12.2); pain management only (NSAID): 46.52 (13.63)	Time to stone passage (4 weeks) Stone passage (4 weeks) Adverse events (4 weeks): hypotension; retrograde ejaculation Analgesic use (4 weeks): number of people using analgesia	

Study	Intervention and comparison	Population	Outcomes	Comments
		Male to female ratio 55:20 Thailand		
Lv 2014[130]	Intervention (n=35): Naftopidil 50mg daily. Duration up to 2 weeks. Concurrent medication/care: instruction to drink at least 2 L of fluids daily Comparison (n=35): Naftopidil 50mg daily and Celecoxib 400mg immediately then 200mg every 12 hours. Duration up to 2 weeks. Concurrent medication/care: instruction to drink at least 2 L of fluids daily Comparison (n=33): Celecoxib 400mg immediately then 200mg every 12 hours. Duration up to 2 weeks. Concurrent medication/care: instruction to drink at least 2 L of fluids daily	n=105 People with a distal ureteral stone 4-9mm Mean (SD) age: naftopidil group: 31.4 (2.94); naftopidil + celecoxib group: 33.2 (5.28); celecoxib group: 33.75 (5.24) Male to female ratio 59:44 China	Time to stone passage (2 weeks) Stone passage (2 weeks) Adverse events (2 weeks): headache; retrograde ejaculation Pain intensity (2 weeks): defined as number of pain episodes; visual analogue scale	
Mokhless 2012[138]	Intervention (n=33): Tamsulosin 0.4mg for age ≥4 years and 0.2 mg for age <4 years. Duration up to 4 weeks. Concurrent medication/care: standard analgesia (ibuprofen) Comparison (n=28): Placebo. Duration up to 4 weeks. Concurrent medication/care: standard analgesia (ibuprofen)	n=61 Children with radiopaque lower ureteral stones of 12mm or smaller Mean (SD) age: 8.1 (6.8) Male to female ratio 36:25 Egypt	Time to stone passage (4 weeks) Stone passage (4 weeks) Adverse events (4 weeks): hypotension, headache Pain intensity (4 weeks): defined as number of pain episodes	

Study	Intervention and comparison	Population	Outcomes	Comments
			Analgesia use (4 weeks): need for analgesia	
Mohseni 2006[137]	Intervention (n=32): Indomethacin. Duration up to 4 weeks. Concurrent medication/care: intravenous Pethidine in cases of incomplete pain control Comparison (n=32): Terazosin 10mg daily. Duration up to 4 weeks. Concurrent medication/care: Indomethacin and intravenous Pethidine in cases of incomplete pain control	n=64 People with a lower ureteral stone Mean (SD) age: terazosin group: 44.2 (12.9); indomethacin group: 39.3 (14.2) Male to female ratio 44:20 Iran	Time to stone passage (4 weeks) Stone passage (4 weeks) Adverse events (4 weeks): hypotension Analgesic use (4 weeks): pain analgesia dose	
Moursy 2010[140]	Intervention (n=44): Tamsulosin 0.4mg daily. Duration up to 4 weeks. Concurrent medication/care: Indomethacin 100mg suppository on demand and encouragement to drink a minimum 2.5 L of water daily Comparison (n=44): Pain management only. Duration up to 4 weeks. Concurrent medication/care: Indomethacin 100mg suppository on demand and encouragement to drink a minimum 2.5 L of water daily	n=88 People with unilateral steinstrasse after SWL >18 years Mean (SD) age: tamsulosin group: 35.6 (9.95); pain management only group: 33.9 (9.71) Egypt	Time to stone passage (4 weeks) Stone passage (4 weeks) Use of healthcare services/hospitalisation (4 weeks) Adverse events (4 weeks) Analgesic use (4 weeks)	
Mshemish 2012[141]	Intervention (n=35): Tamsulosin 0.4mg daily. Duration up to 45 days. Concurrent medication/care: high fluid intake and pain	People with acute renal colic and a single ureteral stone	Time to stone passage (45 days)	

Study	Intervention and comparison	Population	Outcomes	Comments
	management (15mg meloxicam intramuscular injection, with a second dose if needed; then 7.5mg meloxicam tablets every 12 hours for 1 week and then 15mg meloxicam injection as needed, up to twice daily) Intervention (n=35): Doxazosin 4mg daily. Duration up to 45 days. Concurrent medication/care: high fluid intake and pain management (15mg meloxicam intramuscular injection, with a second dose if needed; then 7.5mg meloxicam tablets every 12 hours for 1 week and then 15mg meloxicam injection as needed, up to twice daily) and high fluid intake Comparison (n=35): Pain management only (15mg meloxicam intramuscular injection, with a second dose if needed; then 7.5mg meloxicam tablets every 12 hours for 1 week and then 15mg meloxicam injection as needed, up to twice daily). Duration up to 45 days. Concurrent medication/care: high fluid intake	≤10mm below the common iliac vessels ≥ 18 years Male to female ratio 68:32 Iraq	Stone passage (45 days) Use of healthcare services/hospitalisation (45 days): hospitalisation, emergency department visits Adverse events (45 days): hypotension, retrograde ejaculation Pain intensity (45 days): defined as number of pain episodes	
Mustafa 2016[143]	Intervention (n=64): Tamsulosin 0.4mg daily. Duration up to 4 weeks. Concurrent medication/care: conventional treatment - hydration with minimum 2 L of water daily, physical exertion and analgesics (Diclofenac 50mg suppository with H2 blocker) if required Comparison (n=64): No treatment. Duration up to 4 weeks. Concurrent medication/care:	n=128 People with unilateral, juxtavesical ureteral stone; normal functioning kidney; absence of clinical and laboratory signs of urinary tract infection; stone size up to 8mm	Stone passage (4 weeks) Pain intensity (4 weeks): defined as number of pain episodes	

Study	Intervention and comparison	Population	Outcomes	Comments
	hydration with minimum 2 L of water daily, physical exertion and analgesics (Diclofenac 50mg suppository with H2 blocker) if required	>18 years Gender not reported Bangladesh		
Ochoa-Gomez 2011[147]	Intervention (n=32): Tamsulosin 0.4mg daily. Duration up to 4 weeks. Concurrent medication/care: instruction to drink at least 2 L of water daily Comparison (n=33): Placebo. Duration up to 4 weeks. Concurrent medication/care: instruction to drink at least 2 L of water daily	n=65 People with reno-ureteral stones 5-10mm determined by plain abdominal film and kidney ultrasound >18 years Male to female ratio 36:29 Mexico	Time to stone passage (4 weeks) Stone passage (4 weeks) Adverse events (4 weeks): dizziness, retrograde ejaculation	
Park 2013[150]	Intervention (n=48): Tamsulosin 0.2mg once daily,starting just before ESWL. Duration up to 3 weeks. Concurrent medication/care: Aceclofenac 100mg on demand and asked to drink 1.5-2L of water daily Comparison (n=48): ESWL. Duration up to 3 weeks. Concurrent medication/care: Aceclofenac 100mg on demand and asked to drink 1.5-2L of water daily	n=96 People with symptomatic, unilateral, single, proximal ureteral stone 6-20mm in longest axis 18-70 years Male to female ratio 57:31 South Korea	Stone passage (3 weeks) Adverse events (3 weeks)	
Pedro 2008[152]	Intervention (n=34): Alfuzosin daily. Duration up to 4 weeks. Concurrent medication/care: not reported	n=69	Time to stone passage (4 weeks)	

Study	Intervention and comparison	Population	Outcomes	Comments
	Placebo (n=35). Duration up to 4 weeks. Concurrent medication/care: not reported	People with a distal ureteral calculus Mean (SD) age: alfuzosin group: 36.69 (13.06); placebo group: 42.03 (12.85) Male to female ratio 55:14 USA	Stone passage (4 weeks) Adverse events (4 weeks) Analgesic use (4 weeks)	
Pickard 2015[153, 154]	Intervention (n=391): Tamsulosin 0.4mg daily. Duration up to 4 weeks. Concurrent medication/care: standard care - analgesics, antiemetics, advice on adequate fluid intake and resumption of normal activity Comparison (n=387): Nifedipine 30mg daily. Duration up to 4 weeks. Concurrent medication/care: standard care - analgesics, antiemetics and advice on adequate fluid intake and resumption of normal activity Comparison (n=389): Placebo. Duration up to 4 weeks. Concurrent medication/care: standard care - analgesics, antiemetics and advice on adequate fluid intake and resumption of normal activity	n=1167 People presenting acutely with ureteric colic, with a stone ≤ 10 mm confirmed by non-contrast CT KUB, within any segment of the ureter ≥ 18 years to ≤ 65 years Male to female ratio 931:219 UK	Time to stone passage (4 weeks) Stone passage (4 weeks) Hospitalisation (4 weeks) Use of healthcare services (4 weeks): doctor/nurse/ outpatient visits; excess admission days Adverse events (4 weeks): discontinuation due to adverse events Quality of life (12 weeks): SF36; EQ5D Pain intensity (4 and 12 weeks): VAS; EQ5D	Included proximal, mid and distal ureteric stones. Results reported separately.

Study	Intervention and comparison	Population	Outcomes	Comments
			Analgesic use (4 and 12 weeks): pain medication use; number of days of medication use	
Rahim 2012[165]	Intervention (n=45): Terazosin 2mg daily. Duration up to 4 weeks. Concurrent medication/care: Diclofenac 50mg twice daily Comparison (n=45): Diclofenac 50mg twice daily. Duration up to 4 weeks. Concurrent medication/care: NA	n=90 People with 4-7mm stones in the distal segment of the ureter confirmed on ultrasound 16-63 years Male to female ratio 63:27 Pakistan	Time to stone passage (4 weeks) Stone passage (4 weeks)	
Resim 2005[170]	Intervention (n=30): Tamsulosin 0.4mg daily. Duration up to 6 weeks. Concurrent medication/care: conservative treatment - hydration and Tenoxicam 20mg daily Comparison (n=30): Conservative treatment - hydration and Tenoxicam 20mg daily. Duration up to 6 weeks. Concurrent medication/care: NA	n=60 People with lower ureteral calculi Mean (SD) age: tamsulosin group: 35.3 (10.9); pain management only (NSAID): 33.5 (9.7) Male to female ratio 45:15 Turkey	Stone passage (6 weeks) Adverse events (6 weeks): headache, dizziness, abnormal ejaculation, hypotension	Included stones < and >10mm but mean stone diameter in both groups was <10mm. Included in <10mm analysis and downgraded for indirectness.
Resim 2005[171]	Intervention (n=32): Tamsulosin 0.4mg daily. Duration up to 6 weeks. Concurrent medication/care: hydration and Tenoxicam 20mg daily	n=67 People with steinstrasse in the lower ureter (juxtavesical or	Stone passage (6 weeks) Adverse events (6 weeks)	

Study	Intervention and comparison	Population	Outcomes	Comments
	Comparison (n=35): Pain management only. Duration up to 6 weeks. Concurrent medication/care: hydration and Tenoxicam 20mg daily	intramural portion) after undergoing ESWL ≥ 18 years Male to female ratio 43:24 Turkey		
Sameer 2014[174]	Intervention (n=35): Nifedipine 30mg daily. Duration up to 4 weeks. Concurrent medication/care: Diclofenac 50mg every 12 hours for 1 week, Diclofenac 75mg injection as needed and Tramadol 100mg injection for persistent pain Intervention (n=35): Alfuzosin 10mg daily. Duration up to 4 weeks. Concurrent medication/care: Diclofenac 50mg every 12 hours for 1 week, Diclofenac 75mg injection as needed and Tramadol 100mg injection for persistent pain Comparison (n=35): Diclofenac 50mg every 12 hours for 1 week. Duration up to 4 weeks. Concurrent medication/care: Diclofenac 75mg injection as needed and Tramadol 100mg injection for persistent pain	n=105 People with single, unilateral ureteral stone of ≤10mm; distal defined as the segment from the lower border of the sacroiliac joint to the vesico-ureteric junction ≥8 years Male to female ratio: 68:37 India	Time to stone passage (4 weeks) Stone passage (4 weeks) Use of healthcare services/hospitalisation (4 weeks): re-admission Pain intensity (4 weeks): defined as number of pain episodes	
Sayed 2008[176]	Intervention (n=45): Tamsulosin 0.4mg daily. Duration up to 4 weeks. Concurrent medication/care: hydration (at least 2 L of water daily) and Diclofenac 100mg injection on demand	n=90 People with radiopaque stones 5-10mm in diameter in the distal ureter >18 years	Time to stone passage (4 weeks) Stone passage (4 weeks) Adverse events (4 weeks): unspecified	

Study	Intervention and comparison	Population	Outcomes	Comments
	Comparison (n=45): No treatment. Duration up to 4 weeks. Concurrent medication/care: hydration (at least 2 L of water daily) and Diclofenac 100mg injection on demand	Male to female ratio 69:21 Egypt	Pain intensity (4 weeks): defined as number of pain episodes Analgesic use (4 weeks): number of times analgesic was used	
Sen 2017[179]	Intervention (n=25): Doxasozin 4mg. Duration up to 3 weeks. Concurrent medication/care: diclofenac 100mg and daily 1500-2000 cc hydration Intervention (n=22): Doxasozin 8mg. Duration up to 3 weeks. Concurrent medication/care: diclofenac 100mg and daily 1500-2000 cc hydration Comparison (n=19): Diclofenac 100mg up to 3 weeks. Concurrent medication/care: daily 1500-2000 cc hydration	n=66 People with radio-opaque distal ureteral stones ≤10mm Mean (SD) age: doxazosin group: 33.7 (10.4); pain management only (NSAID): 33 (11.3) Male to female ratio 46:20 Turkey	Time to stone passage (3 weeks) Stone passage (3 weeks) Pain intensity (3 weeks): defined as number of pain episodes Adverse events (3 weeks): hypotension	
Singh 2011[187]	Intervention (n=59): Tamsulosin 0.4mg daily beginning just before the session of SWL, SWL repeated every 3 weeks for incomplete fragmented calculus. Duration up to 3 months. Concurrent medication/care: advice to drink 2.5L of fluid daily and Diclofenac on demand Comparison (n=58): SWL repeated every 3 weeks for incomplete fragmented calculus up to 3 sessions. Duration up to 3 months. Concurrent medication/care: advice to drink 2.5L of fluid daily and Diclofenac on demand	n=120 People with symptomatic, unilateral and solitary upper (between the peli-ureteral junction and sacroiliac joint) ureteral calculi 6-15mm in major axis 18-70 years Gender not reported	Time to stone passage (3 months) Stone passage (3 months) Pain intensity (3 months)	Results for stones 6-10mm and 11-15mm analysed separately for primary outcome (stone passage). Included in the <10mm stones analysis and downgraded for indirectness for other outcomes.

Study	Intervention and comparison	Population	Outcomes	Comments
		India		
Singh 2011[186]	Intervention (n=60): Tamsulosin 0.4mg daily from the day of ESWL just before the session. Duration up to 4 weeks. Concurrent medication/care: advice to drink 2.5L of fluid daily, antibiotics and Diclofenac on demand Comparison (n=59): ESWL and placebo. Duration up to 4 weeks. Concurrent medication/care: advice to drink 2.5L of fluid daily, antibiotics and Diclofenac on demand	n=120 People with symptomatic unilateral solitary lower ureteric calculus 4-12mm in major axis >18 years Male to female ratio 84:35 India	Time to stone passage (4 weeks) Stone passage (4 weeks) Analgesic use (4 weeks)	Included stones < and >10mm but the majority were <10mm. Included in the <10mm stones analysis and downgraded for indirectness.
Su 2016[194]	Intervention (n=76): Tamsulosin 0.4mg daily. Duration up to 2 weeks. Concurrent medication/care: Ketorolac 10mg three times daily, Buprenorphine 0.2mg on demand and encouragement to drink a minimum of 2 L of water daily Intervention (n=79): Silodosin 8mg daily. Duration up to 2 weeks. Concurrent medication/care: Ketorolac 10mg three times daily, Buprenorphine 0.2mg on demand and encouragement to drink a minimum of 2 L of water daily Comparison (n=82): Placebo. Duration up to 2 weeks. Concurrent medication/care: Ketorolac 10mg three times daily, Buprenorphine 0.2mg on demand and encouragement to drink a minimum of 2 L of water daily	n=272 People with radiopaque distal ureteral stones <10mm Mean (SD) age: tamsulosin group: 50.74 (10.08); silodosin group: 51.58 (8.27); placebo group: 52.16 (9.2) Male to female ratio 122:82 Taiwan	Time to stone passage (2 weeks) Stone passage (2 weeks) Adverse events (2 weeks) Analgesic use (2 weeks)	

Study	Intervention and comparison	Population	Outcomes	Comments
Sun 2009[196]	Intervention (n=30): Naftopidil 50mg daily. Duration up to 2 weeks. Concurrent medication/care: instruction to drink a minimum of 2 L of water daily and Indomethacin suppository to control acute episodes of ureteral colic if present Comparison (n=30): Watchful waiting. Duration up to 2 weeks. Concurrent medication/care: instruction to drink a minimum of 2 L of water daily and Indomethacin suppository used to control acute episodes of ureteral colic if present	n=60 People with unilateral distal (below the lower border of the sacroiliac joint) ureteral stones 18-65 years Male to female ratio 50:10 China	Stone passage (2 weeks) Use of healthcare services/hospitalisation (2 weeks) Adverse events (2 weeks): dizziness Pain intensity (2 weeks): defined as episodes of renal colic	
Sur 2015[197]	Intervention (n=115): Silodosin 8mg. Duration up to 4 weeks. Concurrent medication/care: Oxycodone 5mg to provide analgesia for renal colic and us concomitant pre-enrolment medications that would not confound study results Comparison (n=117): Placebo. Duration up to 4 weeks. Concurrent medication/care: Oxycodone 5mg to provide analgesia for renal colic and use of other concomitant pre-enrolment medications that would not confound study results	n=239 People with unilateral calculus ≥4mm and ≤10mm in any location of the ureter ≥18 years Male to female ratio 152:87 USA	Stone passage (4 weeks): visualisation of the stone or imaging Adverse events (4 weeks): retrograde ejaculation, dizziness, headache	
Thapa 2014[199]	Intervention (n=35): Tamsulosin 0.4mg daily. Duration up to 3 weeks. Concurrent medication/care: advice to have high fluid intake more than 3 L daily and Diclofenac 50mg 3 times daily for 5 days, then on demand	n=70 People with symptomatic, unilateral, solitary lower ureteral stones (located below sacroiliac joint) of 5-10mm >15 years	Stone passage (3 weeks)	

Study	Intervention and comparison	Population	Outcomes	Comments
	Comparison (n=35): Diclofenac 50mg 3 times daily for 5 days, then on demand. Duration up to 3 weeks. Concurrent medication/care: advice to have high fluid intake more than 3 L daily	Male to female ratio 41:29 Nepal		
Wang 2008[206]	Intervention (n=32): Tamsulosin 0.4mg daily. Duration up to 2 weeks. Concurrent medication/care: Ketorolac 10mg 3 times daily, sublingual Buprenorphine 0.2mg as needed and a minimum of 2 L of water daily Intervention (n=32): Terazosin 2mg daily. Duration up to 2 weeks. Concurrent medication/care: Ketorolac 10mg 3 times daily, sublingual Buprenorphine 0.2mg on demand and a minimum of 2 L of water daily Comparison (n=31): Ketorolac 10mg 3 times daily. Duration up to 2 weeks. Concurrent medication/care: sublingual Buprenorphine 0.2mg as needed and a minimum of 2 L of water daily	n=95 People with radiopaque lower ureteral stones Mean (SD) age: tamsulosin group: 50.4 (9.7); terazosin group: 51.4 (8.6); pain management only (NSAID) group: 50.9 (9.6) Male to female ratio 66:29 China	Time to stone passage (2 weeks) Stone passage (2 weeks) Adverse events (2 weeks): unspecified Pain intensity (2 weeks): defined as number of colic episodes Analgesic use (2 weeks): average pain relief consumption (mg)	
Wang 2014[213]	Intervention (n=48): Tamsulosin 0.4mg daily after URS. Duration up to 6 weeks. Concurrent medication/care: 2-3L hydration and Diclofenac 75mg on demand Comparison (n=46): URS only. Duration up to 6 weeks. Concurrent medication/care: 2-3L hydration and Diclofenac 75mg on demand	n=94 People with symptomatic stone; 10-15mm in size; located in the proximal ureter (between the ureteropelvic junction and sacroiliac joint); associated with moderate hydroureteronephrosis Age not reported	Time to stone passage (6 weeks) Stone passage (6 weeks) Adverse events (6 weeks) Pain intensity (6 weeks)	

Study	Intervention and comparison	Population	Outcomes	Comments
		Gender not reported China		
Wang 2016[208]	Intervention (n=71): Silodosin 8mg daily. Duration up to 2 weeks. Concurrent medication/care: Ketorolac three times daily, sublingual Buprenorphine 0.2mg on demand and encouragement to drink a minimum of 2 L of water daily Comparison (n=70): Placebo. Duration up to 2 weeks. Concurrent medication/care: Ketorolac 10mg three times daily, sublingual Buprenorphine 0.2mg on demand and encouragement to drink a minimum of 2 L of water daily	n=141 People with radiopaque distal stones <10mm 28-72 years Male to female ratio 83:40 Taiwan	Time to stone passage (2 weeks) Stone passage (2 weeks): no residual fragments Adverse events(2 weeks): unspecified Pain intensity (2 weeks): defined as number of renal colic episodes Analgesic use (2 weeks): average pain relief consumption (mg)	
Ye 2011[215]	Intervention (n=1596): Tamsulosin 0.4mg daily. Duration up to 4 weeks. Concurrent medication/care: encouragement to maintain a water intake of 2-2.5 L daily, Levofloxacin 0.2g twice daily and Diclofenac 50mg suppository on demand Comparison (n=1593): Nifedipine 10mg 3 times daily. Duration up to 4 weeks. Concurrent medication/care: encouragement to maintain a water intake of 2-2.5 L daily, Levofloxacin 0.2g twice daily and Diclofenac 50mg suppository on demand	n=3189 People with emergency admission for renal colic; radiopaque or radiolucent single distal ureteric stone (juxtavesical or intramural portion) of 4-7mm 18-50 years Male to female ratio 1987:1202	Stone passage (4 weeks): stone free on non-contrast CT Adverse events (4 weeks): not specified Analgesic use (4 weeks): number of participants using pain relief therapy	

Study	Intervention and comparison	Population	Outcomes	Comments
		China		
Ye 2018[216]	Intervention (n=1695): Tamsulosin 0.4mg (two capsules of 0.2mg). Duration until spontaneous stone passage, up to 28 days. Concurrent medication/care: 2L water per day. 50mg sodium diclofenac suppository on demand Comparison (n=1695): Placebo. Duration until spontaneous stone passage, up to 28 days. Concurrent medication/care: 2L water per day. 50mg sodium diclofenac suppository on demand	n=3390 People with a stone in the distal ureter with a dimension of 4-7mm 18-60 years Male to female ratio 2135:1161 China	Time to stone passage (28 days) Stone passage (28 days) Adverse events (28 days): retrograde ejaculation, dizziness, headache Pain intensity (28 days): defined as rate of pain relief therapy Analgesic use (28 days): average dose of diclofenac	
Yilmaz 2005[218]	Intervention (n=28): Tamsulosin 0.4mg daily. Duration up to 4 weeks. Concurrent medication/care: symptomatic therapy with Diclofenac 75mg injections on demand and consumption of a minimum of 2 L of water daily Intervention (n=28): Terazosin 5mg daily. Duration up to 4 weeks. Concurrent medication/care: symptomatic therapy with Diclofenac 75mg injections on demand and consumption of a minimum of 2 L of water daily Intervention (n=29): Doxazosin 4mg daily. Duration up to 4 weeks. Concurrent	n=114 People with radiopaque stones ≤10mm located in the distal tract of the ureter (juxtavesical tract and ureterovesical junction) 18-65 years old Male to female ratio 46:68 Turkey	Time to stone passage (4 weeks) Stone passage (4 weeks) Adverse events (4 weeks): unspecified Pain intensity (4 weeks): defined as number of pain episodes Analgesic use (4 weeks): analgesic dose required	

Study	Intervention and comparison	Population	Outcomes	Comments
	medication/care: symptomatic therapy with Diclofenac 75mg injections on demand and consumption of a minimum of 2 L of water daily Comparison (n=28): Symptomatic therapy with Diclofenac 75mg injections on demand. Duration up to 4 weeks. Concurrent medication/care: consumption of a minimum of 2 L of water daily			
Yuksel 2015[219]	Intervention (n=35): Silodosin 4mg daily. Duration up to 3 weeks. Concurrent medication/care: Diclofenac 75mg daily as necessary, advice to remain active and drink at least 2 L of water daily Comparison (n=35): Diclofenac 75mg daily as necessary. Duration up to 3 weeks. Concurrent medication/care: advice to remain active and drink at least 2 L of water daily	n=70 People with a distal ureteral stone 4-10mm 18-65 years old Male to female ratio 39:31 Turkey	Time to stone passage (3 weeks) Stone passage (3 weeks) Pain intensity (3 weeks): defined as renal colic episodes Analgesic use (3 weeks): analgesic dosage	
Zhang 2009[222]	Intervention (n=102): Tamsulosin 0.4mg daily. Duration up to 4 weeks. Concurrent medication/care: 2.5 L hydration daily, Levofloxacin 0.1g twice daily for the first 7 days and Diclofenac 75mg injection daily if needed Comparison (n=97): Nifedipine 30mg 3 times daily. Duration up to 4 weeks. Concurrent medication/care: 2.5 L hydration daily, Levofloxacin 0.1g twice daily for the first 7 days and Diclofenac 75mg injection daily if needed	n=199 People with distal ureteral stones Mean (SD) age: tamsulosin group: 34.6 (11.4); nifedipine group: 36.3 (9.7) Male to female ratio 131:58 China	Stone passage (4 weeks): absence of any stone on x-ray	

Study	Intervention and comparison	Population	Outcomes	Comments
Zhou 2011[224]	Intervention (n=43): Naftopidil 10mg daily. Duration up to 2 weeks. Concurrent medication/care: instruction to drink at least 2 L of fluids daily and an Indomethacin suppository recommended for use during pain episodes Comparison (n=45): Tamsulosin 0.4mg daily. Duration up to 2 weeks. Concurrent medication/care: instruction to drink at least 2 L of fluids daily and Indomethacin suppository recommended for routine use during pain episodes Comparison (n=43): Watchful waiting. Duration up to 2 weeks. Concurrent medication/care: instruction to drink at least 2 L of fluids daily and Indomethacin suppository recommended for routine use during pain episodes	n=131 People with distal ureteral stones ≤9mm to >4mm Mean (SD) age: naftopidil group: 33.73 (8.84); tamsulosin group: 34.42 (8.64); watch and wait group: 34.79 (9.63) Male to female ratio 79:52 China	Time to stone passage (2 weeks) Stone passage (2 weeks) Pain intensity (2 weeks): defined as number of pain episodes	

See appendix D for full evidence tables.

1.4.5 Quality assessment of clinical studies included in the evidence review

1.4.5.1 Distal ureteric stones, <10mm, adults

Table 3: Clinical evidence summary: Alpha blockers versus placebo for distal ureteric stones <10mm in adults

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Placebo (<10mm)	Risk difference with Alpha blockers (95% CI)
Time to stone passage	3788 (6 studies)	⊕⊖⊖⊖ VERY LOW2,3,8 due to risk of bias, imprecision, inconsistency		The mean time to stone passage in the control groups was 12.71	The mean time to stone passage in the intervention groups was 3.5 lower (2.66 to 3.93 lower)
Time to stone passage mean number of hours for spontaneous stone passage	80 (1 study) 3 weeks	⊕⊖⊖⊖ VERY LOW2,3 due to risk of bias, imprecision	HR 0.99 (0.55 to 1.78)	Moderate	
				0 per 1000	Not estimable7
Stone passage number of people spontaneously passing stones during follow up	5154 (13 studies) 1-4 weeks	⊕⊕⊖⊖ LOW1,2 due to inconsistency, imprecision	RR 1.19 (1.09 to 1.29)	Moderate	
				609 per 1000	116 more per 1000 (from 55 more to 177 more)
Hospitalisation number of people hospitalised during follow up	580 (3 studies) 3-4 weeks	⊕⊕⊖⊖ LOW2 due to imprecision	RR 0.99 (0.59 to 1.64)	Moderate	
				44 per 1000	0 fewer per 1000 (from 18 fewer to 28 more)
Hospitalisation (excess admission days)	493 (1 study) 4 weeks	⊕⊕⊕⊕ HIGH		The mean hospitalization (excess admission days) in the control groups was 0.18 days	The mean hospitalization (excess admission days) in the intervention groups was 0.03 lower (0.17 lower to 0.11 higher)
Use of healthcare services (re-presentation to ED)	393 (1 study) 4 weeks	⊕⊕⊖⊖ LOW2 due to imprecision	RR 0.87 (0.56 to 1.36)	Moderate	
				180 per 1000	23 fewer per 1000 (from 79 fewer to 65 more)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Placebo (<10mm)	Risk difference with Alpha blockers (95% CI)
number of people who re-presented to ED during follow up					
Use of healthcare services - Doctor visits	439 (1 study) 4 weeks	⊕⊕⊕⊕ HIGH		The mean use of healthcare services - doctor visits in the control groups was 0.09 visits	The mean use of healthcare services - doctor visits in the intervention groups was 0.07 higher (0.04 lower to 0.18 higher)
Use of healthcare services - Nurse visits	439 (1 study) 4 weeks	⊕⊕⊕⊕ HIGH		The mean use of healthcare services - nurse visits in the control groups was 0.02 visits	The mean use of healthcare services - nurse visits in the intervention groups was 0.01 lower (0.04 lower to 0.02 higher)
Use of healthcare services - Outpatient visits	535 (1 study) 4 weeks	⊕⊕⊕⊖ MODERATE3 due to risk of bias		The mean use of healthcare services - outpatient visits in the control groups was 0.67 visits	The mean use of healthcare services - outpatient visits in the intervention groups was 0.01 lower (0.12 lower to 0.1 higher)
Quality of life (SF36; 12 weeks) - SF36 physical component Scale from: 0 to 100.	210 (1 study) 12 weeks	⊕⊕⊖⊖ LOW2,3 due to risk of bias, imprecision		The mean quality of life (sf36; 12 weeks) - sf36 physical component in the control groups was 52.24	The mean quality of life (sf36; 12 weeks) - sf36 physical component in the intervention groups was 1.15 lower (3.75 lower to 1.45 higher)
Quality of life (SF36; 12 weeks) - SF36 mental component Scale from: 0 to 100.	210 (1 study) 12 weeks	⊕⊕⊖⊖ LOW2,3 due to risk of bias, imprecision		The mean quality of life (sf36; 12 weeks) - sf36 mental component in the control groups was 51.39	The mean quality of life (sf36; 12 weeks) - sf36 mental component in the intervention groups was 1.79 lower (4.7 lower to 1.12 higher)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Placebo (<10mm)	Risk difference with Alpha blockers (95% CI)
Quality of life (EQ5D; 12 weeks) Scale from: 0 to 1.	217 (1 study) 12 weeks	⊕⊕⊕⊖ MODERATE3 due to risk of bias		The mean quality of life (eq5d; 12 weeks) in the control groups was 0.9	The mean quality of life (eq5d; 12 weeks) in the intervention groups was 0.04 lower (0.1 lower to 0.02 higher)
Adverse events (discontinuation due to AE)	302 (1 study)	⊕⊖⊖⊖ VERY LOW2,3 due to risk of bias, imprecision	RR 1.71 (0.77 to 3.79)	Moderate 59 per 1000	42 more per 1000 (from 14 fewer to 165 more)
Adverse events (unspecified) number of people experiencing adverse events during follow up	363 (3 studies) 2-4 weeks	⊕⊖⊖⊖ VERY LOW3 due to risk of bias	RR 5.65 (1.5 to 21.29)	Moderate 0 per 1000	70 more per 1000 (from 29 more to 112 more)5
Adverse events (retrograde ejaculation) number of people experiencing retrograde ejaculation during follow up	3728 (6 studies) 3-4 weeks	⊕⊕⊖⊖ LOW2,3 due to risk of bias, imprecision	Peto OR 1.73 (1.23 to 2.43)	Moderate 0 per 1000	20 more per 1000 (from 8 more to 32 more)5
Adverse events (dizziness) number of people experiencing dizziness during follow up	3957 (7 studies) 1-4 weeks	⊕⊖⊖⊖ VERY LOW2,3 due to risk of bias, imprecision	RR 1.28 (0.92 to 1.79)	Moderate 22 per 1000	6 more per 1000 (from 2 fewer to 17 more)
Adverse events (headache) number of people	3733 (4 studies) 4 weeks	⊕⊕⊖⊖ LOW2 due to imprecision	RR 1.06 (0.72 to 1.56)	Moderate 29 per 1000	2 more per 1000 (from 8 fewer to 16 more)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Placebo (<10mm)	Risk difference with Alpha blockers (95% CI)
experiencing headache during follow up					
Adverse events (hypotension) number of people experiencing hypotension during follow up	198 (2 studies) 4 weeks	⊕⊖⊖⊖ VERY LOW2,3 due to risk of bias, imprecision	Peto OR 6.82 (0.13 to 344.93)	Moderate	
				0 per 1000	9 more per 1000 (from 18 fewer to 35 more)5
Pain intensity (VAS score) Scale from: 0 to 10.	279 (1 study) 4 weeks	⊕⊕⊕⊕ HIGH		The mean pain intensity (vas score) in the control groups was 1.11	The mean pain intensity (vas score) in the intervention groups was 0.1 lower (0.49 lower to 0.29 higher)
Pain intensity (EQ5D No pain/discomfort) at 12 weeks	219 (1 study)	⊕⊕⊕⊖ MODERATE3 due to risk of bias	RR 0.96 (0.82 to 1.11)	Moderate	
				774 per 1000	31 fewer per 1000 (from 139 fewer to 85 more)
Pain intensity (EQ5D Moderate pain/discomfort) at 12 weeks	219 (1 study)	⊕⊖⊖⊖ VERY LOW2,3 due to risk of bias, imprecision	RR 0.97 (0.59 to 1.62)	Moderate	
				217 per 1000	7 fewer per 1000 (from 89 fewer to 135 more)
Pain intensity (EQ5D Extreme pain/discomfort) at 12 weeks	219 (1 study)	⊕⊖⊖⊖ VERY LOW2,3 due to risk of bias, imprecision	RR 5.53 (0.66 to 46.55)	Moderate	
				9 per 1000	41 more per 1000 (from 3 fewer to 410 more)
				Moderate	

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Placebo (<10mm)	Risk difference with Alpha blockers (95% CI)
Pain intensity (pain episodes) number of people experiencing episodes of renal colic	150 (1 study) 4 weeks	⊕⊕⊕⊖ MODERATE3 due to risk of bias	RR 0.34 (0.23 to 0.51)	773 per 1000	510 fewer per 1000 (from 379 fewer to 595 fewer)
Pain intensity (pain episodes) mean number of pain episodes	219 (2 studies) 2-4 weeks	⊕⊕⊖⊖ LOW2,3 due to risk of bias, imprecision		The mean pain intensity (pain episodes) in the control groups was 2.53	The mean pain intensity (pain episodes) in the intervention groups was 0.51 lower (0.86 to 0.15 lower)
Pain intensity (pain score >0) at 1 week verbal numeric pain scale	367 (1 study) 1 weeks	⊕⊕⊕⊕ HIGH	RR 0.98 (0.88 to 1.09)	Moderate	
				786 per 1000	16 fewer per 1000 (from 94 fewer to 71 more)
Pain intensity (pain score >0) at 2 weeks verbal numeric pain scale	353 (1 study) 2 weeks	⊕⊕⊖⊖ LOW2 due to imprecision	RR 1.04 (0.77 to 1.4)	Moderate	
				328 per 1000	13 more per 1000 (from 75 fewer to 131 more)
Pain intensity (pain score >0) at 3 weeks verbal numeric pain scale	343 (1 study) 3 weeks	⊕⊕⊖⊖ LOW2 due to imprecision	RR 0.94 (0.62 to 1.42)	Moderate	
				214 per 1000	13 fewer per 1000 (from 81 fewer to 90 more)
Pain intensity (pain score >0) at 4 weeks verbal numeric pain scale	347 (1 study) 4 weeks	⊕⊕⊖⊖ LOW2 due to imprecision	RR 0.93 (0.57 to 1.53)	Moderate	
				161 per 1000	11 fewer per 1000 (from 69 fewer to 85 more)
Analgesic use (number of people using analgesics)	3693 (3 studies)	⊕⊖⊖⊖ VERY LOW2,3,6 due to risk of bias, inconsistency, imprecision	RR 0.45 (0.13 to 1.54)	Moderate	
				396 per 1000	218 fewer per 1000 (from 345 fewer to 214 more)
Analgesic use (number of times) mean number of times	165 (2 studies) 4-12 weeks	⊕⊕⊕⊖ MODERATE3 due to risk of bias		The mean analgesic use (number of times) in the control groups was	The mean analgesic use (number of times) in the intervention groups was

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Placebo (<10mm)	Risk difference with Alpha blockers (95% CI)
analgesics were used during follow up				5.61	0.9lower (1.35 to 0.45 lower)
Analgesic use (days)	153 (1 study)	⊕⊕⊕⊕ HIGH		The mean analgesic use (days) in the control groups was 10.78	The mean analgesic use (days) in the intervention groups was 0.41 higher (2.36 lower to 3.18 higher)
Analgesic use (Buprenorphine dose) mean dose (mg) of Buprenorphine used during follow up	267 (2 studies)	⊕⊕⊖⊖ LOW3 due to risk of bias		The mean analgesic use (buprenorphine dose) in the control groups was 0.47	The mean analgesic use (buprenorphine dose) in the intervention groups was 0.06 lower (0.12 lower to 0 higher)
Analgesic use (Ketorolac dose) mean dose (mg) of Ketorolac used during follow up	315 (2 studies) 2 weeks	⊕⊕⊖⊖ LOW3 due to risk of bias		The mean analgesic use (ketorolac dose) in the control groups was 337.87	The mean analgesic use (ketorolac dose) in the intervention groups was 97.44 lower (124.25 to 70.62 lower)
Analgesic use (Diclofenac dose) mean dose (mg) of Diclofenac used during follow up	3392 (2 studies) 4 weeks	⊕⊕⊕⊖ LOW6 due to inconsistency		The mean analgesic use (mean dose of drug) - diclofenac dose in the control groups was 181.5	The mean analgesic use (mean dose of drug) - diclofenac dose in the intervention groups was 149.03 lower (152.37 to 145.68 lower)

1 Downgraded by 1 or 2 increments because heterogeneity, I2= 71%, 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

3 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

4 Downgraded by 1 or 2 increments because the majority of the evidence included an indirect population (downgrade by one increment) or a very indirect population (downgrade by two increments)

5 Risk difference calculated in Review Manager

6 Downgraded by 1 or 2 increments because heterogeneity, I2= 97%, p= > 0.1, unexplained by subgroup analysis

7 Could not be calculated

8 Downgraded by 1 or 2 increments because heterogeneity, I2= 54%, p= > 0.1, unexplained by subgroup analysis

Table 4: Clinical evidence summary: Alpha blockers versus no treatment (pain management only) for distal ureteric stones <10mm in adults

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with no treatment (pain management only) (<10mm)	Risk difference with Alpha blockers (95% CI)
Time to stone passage (days) (mean number of days for spontaneous stone passage)	1642 (18 studies) 2-8 weeks	⊕⊖⊖⊖ VERY LOW1,4 due to risk of bias, inconsistency		The mean time to stone passage (days) in the control groups was 12.8 days	The mean time to stone passage (days) in the intervention groups was 4.28 lower (5.36 to 3.2 lower)
Stone passage number of people spontaneously passing stones during follow up	2530 (32 studies) 10 days - 8 weeks	⊕⊖⊖⊖ VERY LOW1,6 due to risk of bias, inconsistency	RR 1.64 (1.49 to 1.81)	Moderate	
				506 per 1000	324 more per 1000 (from 248 more to 410 more)
Hospitalisation number of people admitted to hospital during follow up	587 (8 studies) 2-4 weeks	⊕⊕⊖⊖ LOW1 due to risk of bias	RR 0.3 (0.18 to 0.49)	Moderate	
				102 per 1000	71 fewer per 1000 (from 52 fewer to 84 fewer)
Use of healthcare services (return to ED/primary care visit) number of people returning to ED or having an unscheduled primary care visit	177 (2 studies) 2 weeks	⊕⊖⊖⊖ VERY LOW1,3 due to risk of bias, imprecision	RR 0.77 (0.29 to 2.01)	Moderate	
				103 per 1000	24 fewer per 1000 (from 73 fewer to 104 more)
Adverse events (unspecified) number of people experiencing adverse events during follow up	716 (9 studies) 10 days - 4 weeks	⊕⊕⊖⊖ LOW1 due to risk of bias	Peto OR 5.89 (1.57 to 22.13)	Moderate	
				0 per 1000	25 more per 1000 (from 8 more to 41 more)5
Adverse events (dizziness) number of people experiencing dizziness during follow up	514 (7 studies) 2-6 weeks	⊕⊖⊖⊖ VERY LOW1,3 due to risk of bias, imprecision	RR 1.34 (0.74 to 2.4)	Moderate	
				0 per 1000	37 more per 1000 (from 6 fewer to 79 more)5
Adverse events (hypotension) number of people experiencing hypotension during follow up	608 (8 studies)	⊕⊕⊖⊖ LOW1 due to risk of bias	Peto OR 5.72 (1.65 to 19.87)	Moderate	
				0 per 1000	30 more per 1000 (from 11 more to 49 more)5

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with no treatment (pain management only) (<10mm)	Risk difference with Alpha blockers (95% CI)
Adverse events (retrograde ejaculation) number of people experiencing retrograde ejaculation during follow up	346 (5 studies) 2-8 weeks	⊕⊖⊖⊖ VERY LOW1,3 due to risk of bias, imprecision	Peto OR 2.05 (0.32 to 13.06)	Moderate 8 per 1000	8 more per 1000 (from 6 fewer to 89 more)5
Adverse events (headache) number of people experiencing headache during follow up	163 (2 studies) 2-6 weeks	⊕⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, indirectness, imprecision	RR 1.48 (0.47 to 4.69)	Moderate 67 per 1000	32 more per 1000 (from 36 fewer to 47 more)
Pain intensity number of people experiencing pain during follow up	240 (3 studies) 10 days-4 weeks	⊕⊖⊖⊖ VERY LOW1,3 due to risk of bias, imprecision	RR 0.77 (0.64 to 0.94)	Moderate 793 per 1000	182 fewer per 1000 (from 48 fewer to 285 fewer)
Pain intensity (colicky pain episodes) mean number of colicky pain episodes	72 (1 study) 2 weeks	⊕⊖⊖⊖ VERY LOW1,3 due to risk of bias, imprecision		The mean pain intensity (colicky pain episodes) in the control groups was 7.9	The mean pain intensity (colicky pain episodes) in the intervention groups was 0.05 lower (4.81 lower to 4.71 higher)
Pain intensity (pain episodes) mean number of pain episodes during follow up	1077 (11 studies)2-4 weeks	⊕⊖⊖⊖ VERY LOW1,3,7 due to risk of bias, inconsistency, imprecision		The mean pain intensity (pain episodes) in the control groups was 2.2	The mean pain intensity (pain episodes) in the intervention groups was 0.68 lower (0.93 to 0.44 lower)
Pain intensity (VAS score) at 3 days visual analogue scale	103 (1 study) 3 days	⊕⊕⊖⊖ LOW1 due to risk of bias		The mean pain intensity (VAS score) in the control groups was 3.06	The mean pain intensity (VAS score) in the intervention groups was 1.37 higher (0.84 to 1.90 higher)
Pain intensity (VAS score) at 7 days visual analogue scale	103 (1 study) 7 days	⊕⊕⊖⊖ LOW1 due to risk of bias		The mean pain intensity (VAS score) in the control groups was	The mean pain intensity (VAS score) in the intervention groups was

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with no treatment (pain management only) (<10mm)	Risk difference with Alpha blockers (95% CI)
				1.57	1.63 higher (1.2 to 2.06 higher)
Analgesic use number of people using analgesics	301 (4 studies) 10 days-4 weeks	⊕⊕⊖⊖ LOW1 due to risk of bias	RR 0.42 (0.29 to 0.62)	Moderate	
				485 per 1000	281 fewer per 1000 (from 184 fewer to 344 fewer)
Analgesic use (number of times) mean number of times analgesics were used during follow up	421 (4 studies)	⊕⊖⊖⊖ VERY LOW1,3,9 due to risk of bias, inconsistency, imprecision		The mean analgesic use (number of times) in the control groups was 1.995	The mean analgesic use (number of times) in the intervention groups was 1.18 lower (2.49 lower to 0.13 higher)
Analgesic use (Diclofenac dose) mean Diclofenac dose (mg) during follow up	234 (3 studies) 3-4 weeks	⊕⊖⊖⊖ VERY LOW1,8 due to risk of bias, inconsistency		The mean analgesic use (diclofenac dose) in the control groups was 582.19	The mean analgesic use (diclofenac dose) in the intervention groups was 169.99 lower (314.6 to 25.37 lower)
Analgesic use (days) mean number of days analgesics were used	77 (1 study) 2 weeks	⊕⊖⊖⊖ VERY LOW1,3 due to risk of bias, imprecision		The mean analgesic use (days) in the control groups was 4.3	The mean analgesic use (days) in the intervention groups was 4.94 lower (12.04 lower to 2.16 higher)
Analgesic use (Pethidine dose) mean dose (mg) of Pethidine used during follow up	64 (1 study) 4 weeks	⊕⊕⊖⊖ LOW1 due to risk of bias		The mean analgesic use (pethidine dose) in the control groups was 62.1	The mean analgesic use (pethidine dose) in the intervention groups was 27.7 lower (33.41 to 21.99 lower)
Analgesic use (Ketorolac dose) mean dose (mg) of Ketorolac used during follow up	95 (1 study) 2 weeks	⊕⊕⊖⊖ LOW1 due to risk of bias		The mean analgesic use (ketorolac dose) in the control groups was 347	The mean analgesic use (ketorolac dose) in the intervention groups was 103.5 lower (149.92 to 57.08 lower)
Analgesic use (Buprenorphine dose) mean dose (mg) of Buprenorphine during follow up	65 (1 study) 2 weeks	⊕⊕⊖⊖ LOW1 due to risk of bias		The mean analgesic use (buprenorphine dose) in the control groups was 0.39	The mean analgesic use (buprenorphine dose) in the intervention groups was

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with no treatment (pain management only) (<10mm)	Risk difference with Alpha blockers (95% CI)
					0.01 lower (0.16 lower to 0.14 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 or 2 increments because the majority of the evidence included an indirect population or the majority of the evidence had indirect outcomes
3 Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs
4 Downgraded by 1 or 2 increments because heterogeneity, I2= 91%, p= > 0.1, unexplained by subgroup analysis
5 Risk difference calculated in Review Manager
6 Downgraded by 1 or 2 increments because heterogeneity, I2= 55%, p= > 0.1, unexplained by subgroup analysis
7 Downgraded by 1 or 2 increments because heterogeneity, I2= 75%, p= > 0.1, unexplained by subgroup analysis
8 Downgraded by 1 or 2 increments because heterogeneity, I2= 92%, p= > 0.1, unexplained by subgroup analysis
9 Downgraded by 1 or 2 increments because heterogeneity, I2= 93%, p= > 0.1, unexplained by subgroup analysis

Table 5: Clinical evidence summary: Calcium channel blockers versus placebo for distal ureteric stones <10mm in adults

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with placebo (<10mm)	Risk difference with Calcium channel blockers (95% CI)
Time to stone passage	113 (1 study)	⊕⊕⊕⊕ HIGH		The mean time to stone passage in the control groups was 14.68	The mean time to stone passage in the intervention groups was 0 higher (5.28 lower to 5.28 higher)
Stone passage number of people spontaneously passing stones during follow up	493 (1 study) 28-45 days	⊕⊕⊕⊕ HIGH	RR 1.06 (0.98 to 1.14)	Moderate	
				821 per 1000	49 more per 1000 (from 16 fewer to 115 more)
Use of healthcare services - Doctor visits	441 (1 study) 4 weeks	⊕⊕⊕⊕ HIGH		The mean use of healthcare services - doctor visits in the control	The mean use of healthcare services - doctor visits in the intervention groups was

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with placebo (<10mm)	Risk difference with Calcium channel blockers (95% CI)
				groups was 0.098 visits	0.08 higher (0.04 lower to 0.2 higher)
Use of healthcare services - Nurse visits	441 (1 study) 4 weeks	⊕⊕⊕⊕ HIGH		The mean use of healthcare services - nurse visits in the control groups was 0.02 visits	The mean use of healthcare services - nurse visits in the intervention groups was 0.01 lower (0.04 lower to 0.02 higher)
Use of healthcare services - Outpatient visits	535 (1 study) 4 weeks	⊕⊕⊕⊕ HIGH		The mean use of healthcare services - outpatient visits in the control groups was 0.67 visits	The mean use of healthcare services - outpatient visits in the intervention groups was 0.05 lower (0.17 lower to 0.07 higher)
Hospitalisation (excess admission days)	493 (1 study) 4 weeks	⊕⊕⊕⊕ HIGH		The mean hospitalisation (excess admission days) in the control groups was 0.18 days	The mean hospitalisation (excess admission days) in the intervention groups was 0.01 lower (0.17 lower to 0.15 higher)
Quality of life (12 weeks) - SF36 physical component Scale from: 0 to 100.	226 (1 study) 12 weeks	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean quality of life (12 weeks) - sf36 physical component in the control groups was 52.24	The mean quality of life (12 weeks) - sf36 physical component in the intervention groups was 0.11 lower (2.38 lower to 2.16 higher)
Quality of life (12 weeks) - SF36 mental component Scale from: 0 to 100.	226 (1 study) 12 weeks	⊕⊕⊖⊖ LOW1,2 due to risk of bias, imprecision		The mean quality of life (12 weeks) - sf36 mental component in the control groups was 51.39	The mean quality of life (12 weeks) - sf36 mental component in the intervention groups was 0.49 lower (3.09 lower to 2.11 higher)
Quality of life (EQ5D) at 12 weeks Scale from: 0 to 1.	237 (1 study) 12 weeks	⊕⊕⊕⊖ MODERATE1 due to risk of bias		The mean quality of life (eq5d) at 12 weeks in the control groups was 0.9	The mean quality of life (eq5d) at 12 weeks in the intervention groups was 0.02 lower (0.08 lower to 0.03 higher)
				Moderate	

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with placebo (<10mm)	Risk difference with Calcium channel blockers (95% CI)
Adverse events (discontinuation due to adverse events)	315 (1 study)	⊕⊕⊕⊖ MODERATE1 due to risk of bias	RR 3.04 (1.49 to 6.22)	59 per 1000	120 more per 1000 (from 29 more to 308 more)
Pain intensity (VAS scale) at 4 weeks Scale from: 0 to 10.	297 (1 study) 4 weeks	⊕⊕⊕⊕ HIGH		The mean pain intensity (vas scale) in the control groups was 1.11	The mean pain intensity (vas scale) in the intervention groups was 0.05 lower (0.52 lower to 0.42 higher)
Pain intensity (EQ5D no pain/discomfort) at 12 weeks	238 (1 study) 12 weeks	⊕⊕⊕⊖ MODERATE1 due to risk of bias	RR 0.97 (0.84 to 1.11)	Moderate	
				774 per 1000	23 fewer per 1000 (from 124 fewer to 85 more)
Pain intensity (EQ5D moderate pain/discomfort) at 12 weeks	238 (1 study) 12 weeks	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision	RR 1.05 (0.65 to 1.68)	Moderate	
				217 per 1000	11 more per 1000 (from 76 fewer to 148 more)
Pain intensity (EQ5D extreme pain/discomfort) at 12 weeks	238 (1 study) 12 weeks	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision	RR 2.8 (0.3 to 26.58)	Moderate	
				9 per 1000	16 more per 1000 (from 6 fewer to 230 more)
Analgesic use	314 (1 study)	⊕⊕⊖⊖ LOW1,2 due to risk of bias, imprecision	RR 0.94 (0.76 to 1.16)	Moderate	
				536 per 1000	32 fewer per 1000 (from 129 fewer to 86 more)
Analgesic use (days)	157 (1 study)	⊕⊕⊕⊕ HIGH		The mean analgesic use (days) in the control groups was 10.78	The mean analgesic use (days) in the intervention groups was 1.22 lower (3.9 lower to 1.46 higher)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with placebo (<10mm)	Risk difference with Calcium channel blockers (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 6: Clinical evidence summary: Calcium channel blockers versus no treatment (pain management only) for distal ureteric stones <10mm in adults

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with no treatment (pain management only) (<10mm)	Risk difference with Calcium channel blockers (95% CI)
Time to stone passage mean number of days for spontaneous stone passage	70 (1 study) 4 weeks	⊕⊕⊕⊖ MODERATE1 due to risk of bias		The mean time to stone passage in the control groups was 12.29	The mean time to stone passage in the intervention groups was 0.29 lower (4.13 lower to 3.55 higher)
Stone passage number of people spontaneously passing stones during follow up	179 (3 studies) 4 weeks	⊕⊕⊕⊖ MODERATE1 due to risk of bias	RR 1.95 (1.4 to 2.71)	Moderate 360 per 1000	342 more per 1000 (from 144 more to 616 more)
Hospitalisation number of people admitted to hospital during follow up	129 (2 studies) 4 weeks	⊕⊕⊕⊖ MODERATE1 due to risk of bias	RR 0.41 (0.24 to 0.69)	Moderate 386 per 1000	228 fewer per 1000 (from 120 fewer to 293 fewer)
Adverse events (hypotension) number of people experiencing hypotension during follow up	59 (1 study) 4 weeks	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision	Peto OR 6.71 (0.13 to 339.76)	Moderate 0 per 1000	32 more per 1000 (from 55 fewer to 120 more)3
Adverse events (dizziness) number of people experiencing dizziness during follow up	50 (1 study) 4 weeks	⊕⊕⊖⊖ LOW1 due to risk of bias	Not estimable 4	Moderate 0 per 1000	0 more per 1000 (from 7 fewer to 7 more)3
Pain intensity (pain episodes) mean number of pain episodes during follow up	70 (1 study) 4 weeks	⊕⊕⊖⊖ LOW1,2		The mean pain intensity (pain episodes) in the control groups was	The mean pain intensity (pain episodes) in the intervention groups was

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with no treatment (pain management only) (<10mm)	Risk difference with Calcium channel blockers (95% CI)
		due to risk of bias, imprecision		2.82	0.09 higher (0.41 lower to 0.59 higher)
Analgesic use (Diclofenac dose) mean Diclofenac dose (mg) during follow up	50 (1 study) 4 weeks	⊕⊕⊖⊖ LOW1 due to risk of bias		The mean analgesic use (diclofenac dose) in the control groups was 1408	The mean analgesic use (diclofenac dose) in the intervention groups was 806 lower (1103.31 to 508.69 lower)

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
3 Risk difference calculated in Review Manager
4 Could not be calculated as there were no events in the intervention or comparison group

Table 7: Clinical evidence summary: Alpha blockers versus Calcium channel blockers for distal ureteric stones <10mm in adults

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Calcium channel blockers (<10mm)	Risk difference with Alpha blockers (95% CI)
Time to stone passage	182 (2 studies)	⊕⊕⊕⊖ MODERATE1 due to risk of bias		The mean time to stone passage in the control groups was 13.34	The mean time to stone passage in the intervention groups was 0.16 higher (2.53 lower to 2.85 higher)
Stone passage number of people spontaneously passing stones during follow up	4189 (7 studies) 4 weeks	⊕⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, inconsistency, imprecision	RR 1.2 (1.05 to 1.39)	Moderate	
				680 per 1000	136 more per 1000 (from 34 more to 265 more)
Hospitalisation number of people requiring Hospitalisation during follow up	133 (2 studies) 4 weeks	⊕⊕⊖⊖ LOW1,3	RR 0.45 (0.18 to 1.17)	Moderate	
				157 per 1000	86 fewer per 1000 (from 129 fewer to 27 more)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Calcium channel blockers (<10mm)	Risk difference with Alpha blockers (95% CI)
		due to risk of bias, imprecision			
Hospitalisation (excess admission days)	494 (1 study) 4 weeks	⊕⊕⊕⊕ HIGH		The mean hospitalisation (excess admission days) in the control groups was 0.17 days	The mean hospitalisation (excess admission days) in the intervention groups was 0.02 lower (0.15 lower to 0.11 higher)
Use of healthcare services - Doctor visits	450 (1 study) 4 weeks	⊕⊕⊕⊕ HIGH		The mean use of healthcare services - doctor visits in the control groups was 0.17 visits	The mean use of healthcare services - doctor visits in the intervention groups was 0.01 lower (0.13 lower to 0.11 higher)
Use of healthcare services - Nurse visits	450 (1 study) 4 weeks	⊕⊕⊕⊕ HIGH		The mean use of healthcare services - nurse visits in the control groups was 0.01 visits	The mean use of healthcare services - nurse visits in the intervention groups was 0 higher (0.02 lower to 0.02 higher)
Use of healthcare services - Outpatient visits	535 (1 study) 4 weeks	⊕⊕⊕⊖ MODERATE1 due to risk of bias		The mean use of healthcare services - outpatient visits in the control groups was 0.62 visits	The mean use of healthcare services - outpatient visits in the intervention groups was 0.04 higher (0.07 lower to 0.15 higher)
Quality of life (12 weeks) - SF36 physical component Scale from: 0 to 100.	216 (1 study) 12 weeks	⊕⊖⊖⊖ VERY LOW1,3 due to risk of bias, imprecision		The mean quality of life (12 weeks) - sf36 physical component in the control groups was 52.13	The mean quality of life (12 weeks) - sf36 physical component in the intervention groups was 0.15 lower (2.68 lower to 2.38 higher)
Quality of life (12 weeks) - SF36 mental component Scale from: 0 to 100.	216 (1 study) 12 weeks	⊕⊕⊖⊖ LOW1,3		The mean quality of life (12 weeks) - sf36 mental component in	The mean quality of life (12 weeks) - sf36 mental component in the intervention groups was

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Calcium channel blockers (<10mm)	Risk difference with Alpha blockers (95% CI)
		due to risk of bias, imprecision		the control groups was 50.9	1.3 lower (4.26 lower to 1.66 higher)
Quality of life (EQ5D) Scale from: 0 to 1.	226 (1 study) 12 weeks	⊕⊕⊕⊖ MODERATE1 due to risk of bias		The mean quality of life (eq5d) in the control groups was 0.876	The mean quality of life (eq5d) in the intervention groups was 0.01 lower (0.08 lower to 0.05 higher)
Adverse events (discontinuation due to AE)	311 (1 study)	⊕⊕⊖⊖ LOW1,3 due to risk of bias, imprecision	RR 0.56 (0.31 to 1.01)	Moderate	
				179 per 1000	79 fewer per 1000 (from 124 fewer to 2 more)
Adverse events (headache) number of people experiencing headache during follow up	122 (1 study) 4 weeks	⊕⊖⊖⊖ VERY LOW1,3 due to risk of bias, imprecision	RR 1.16 (0.79 to 1.7)	Moderate	
				431 per 1000	69 more per 1000 (from 91 fewer to 302 more)
Adverse events (dizziness) number of people experiencing dizziness during follow up	172 (2 studies) 4 weeks	⊕⊖⊖⊖ VERY LOW1,4 due to risk of bias, indirectness	RR 4.86 (1.62 to 14.56)	Moderate	
				26 per 1000	100 more per 1000 (from 16 more to 353 more)
Adverse events (hypotension) number of people experiencing hypotension during follow up	63 (1 study) 4 weeks	⊕⊖⊖⊖ VERY LOW1,3 due to risk of bias, imprecision	Peto OR 0.13 (0 to 6.61)	Moderate	
				32 per 1000	28 fewer per 1000 (from 32 fewer to 147 more)
Adverse events (not specified) number of people experiencing adverse events during follow up	3189 (1 study) 4 weeks	⊕⊖⊖⊖ VERY LOW1,3 due to risk of bias, imprecision	RR 0.92 (0.69 to 1.21)	Moderate	
				62 per 1000	5 fewer per 1000 (from 19 fewer to 13 more)
				Moderate	

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Calcium channel blockers (<10mm)	Risk difference with Alpha blockers (95% CI)
Adverse events (flushing) number of people experiencing flushing during follow up	122 (1 study) 4 weeks	⊕⊖⊖⊖ VERY LOW1,3,4 due to risk of bias, indirectness, imprecision	Peto OR 0.12 (0.01 to 1.16)	52 per 1000	45 fewer per 1000 (from 51 fewer to 8 more)
Pain intensity (VAS score) at 4 weeks Scale from: 0 to 10.	292 (1 study) 4 weeks	⊕⊕⊕⊕ HIGH		The mean pain intensity (vas score) in the control groups was 1.06	The mean pain intensity (vas score) in the intervention groups was 0.05 lower (0.49 lower to 0.39 higher)
Pain intensity (EQ5D no pain/discomfort)	227 (1 study) 12 weeks	⊕⊕⊕⊖ MODERATE1 due to risk of bias	RR 0.99 (0.85 to 1.15)	Moderate	
				748 per 1000	7 fewer per 1000 (from 112 fewer to 112 more)
Pain intensity (EQ5D moderate pain/discomfort)	227 (1 study) 12 weeks	⊕⊖⊖⊖ VERY LOW1,3 due to risk of bias, imprecision	RR 0.93 (0.57 to 1.52)	Moderate	
				228 per 1000	16 fewer per 1000 (from 98 fewer to 119 more)
Pain intensity (EQ5D extreme pain/discomfort)	227 (1 study) 12 weeks	⊕⊖⊖⊖ VERY LOW1,3 due to risk of bias, imprecision	RR 1.97 (0.48 to 8.05)	Moderate	
				24 per 1000	23 more per 1000 (from 12 fewer to 169 more)
Pain intensity (pain episodes) mean number of pain episodes	70 (1 study) 4 weeks	⊕⊕⊕⊖ MODERATE1 due to risk of bias		The mean pain intensity (pain episodes) in the control groups was 2.91 episodes	The mean pain intensity (pain episodes) in the intervention groups was 1.11 lower (1.54 to 0.68 lower)
				Moderate	

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Calcium channel blockers (<10mm)	Risk difference with Alpha blockers (95% CI)
Analgesic use (number of people using analgesia)	3497 (2 studies)	⊕⊖⊖⊖ VERY LOW1,3,5 due to risk of bias, imprecision, inconsistency	RR 0.57 (0.16 to 2.01)	276 per 1000	119 fewer per 1000 (from 232 fewer to 279 more)
Analgesic use (days)	152 (1 study)	⊕⊕⊕⊖ MODERATE3 due to imprecision		The mean analgesic use (days) in the control groups was 9.56	The mean analgesic use (days) in the intervention groups was 1.63 higher (1.03 lower to 4.29 higher)
Analgesic use (mg) mean Diclofenac mg used during follow up	50 (1 study) 4 weeks	⊕⊖⊖⊖ VERY LOW1,3 due to risk of bias, imprecision		The mean analgesic use (mg) in the control groups was 602 mg	The mean analgesic use (mg) in the intervention groups was 58 lower (315.47 lower to 199.47 higher)
Analgesic use mean number of diclofenac injections	122 (1 study) 4-12 weeks	⊕⊕⊖⊖ LOW1 due to risk of bias,		The mean analgesic use in the control groups was 1.19	The mean analgesic use in the intervention groups was 0.77 lower (0.93 to 0.61 lower)

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 or 2 increments because heterogeneity, I2= 88%, p= > 0.1, unexplained by subgroup analysis
3 Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs
4 Downgraded by 1 or 2 increments because the majority of the evidence included an indirect population (downgrade by one increment) or a very indirect population (downgrade by two increments) or the majority of the evidence had indirect outcomes
5 Downgraded by 1 or 2 increments because heterogeneity, I2= 96%, p= > 0.1, unexplained by subgroup analysis

1.4.5.2 Mid ureteric stones <10mm in adults

Table 8: Clinical evidence summary: Alpha blockers versus placebo for mid ureteric stones <10mm in adults

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Placebo (<10mm)	Risk difference with Alpha blockers (95% CI)
Time to stone passage (days)	21 (1 study)	⊕⊕⊖⊖ LOW2 due to imprecision		The mean time to stone passage (days) in the control groups was 18.15 days	The mean time to stone passage (days) in the intervention groups was 7.73 higher (5.09 lower to 20.55 higher)
Stone passage number of people spontaneously passing stones during follow up	126 (2 studies) 4 weeks	⊕⊕⊕⊖ MODERATE2 due to imprecision	RR 0.86 (0.67 to 1.09)	Moderate	
				647 per 1000	91 fewer per 1000 (from 214 fewer to 58 more)
Hospitalisation (excess admissions days)	81 (1 study) 4 weeks	⊕⊕⊕⊖ MODERATE2 due to imprecision		The mean hospitalisation (excess admissions days) in the control groups was 0.05 days	The mean hospitalisation (excess admissions days) in the intervention groups was 0.21 higher (0.03 lower to 0.45 higher)
Use of healthcare services - Doctor visits	74 (1 study) 4 weeks	⊕⊕⊕⊖ MODERATE2 due to imprecision		The mean use of healthcare services - doctor visits in the control groups was 0.31 visits	The mean use of healthcare services - doctor visits in the intervention groups was 0.09 higher (0.26 lower to 0.44 higher)
Use of healthcare services - Nurse visits	74 (1 study) 4 weeks	⊕⊕⊖⊖ LOW2 due to imprecision		The mean use of healthcare services - nurse visits in the control groups was 0.05 visits	The mean use of healthcare services - nurse visits in the intervention groups was 0.17 higher (0.12 lower to 0.46 higher)
Use of healthcare services - Outpatient visits	85 (1 study) 4 weeks	⊕⊕⊕⊖ MODERATE2 due to imprecision		The mean use of healthcare services - outpatient visits in the control groups	The mean use of healthcare services - outpatient visits in the intervention groups was

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Placebo (<10mm)	Risk difference with Alpha blockers (95% CI)
				was 0.77 visits	0.05 higher (0.27 lower to 0.37 higher)
Quality of life (SF36; 12 weeks) - SF36 physical component Scale from: 0 to 100.	50 (1 study) 12 weeks	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean quality of life (sf36; 12 weeks) - sf36 physical component in the control groups was 51.53	The mean quality of life (sf36; 12 weeks) - sf36 physical component in the intervention groups was 0.64 lower (5.9 lower to 4.62 higher)
Quality of life (SF36; 12 weeks) - SF36 mental component Scale from: 0 to 100.	50 (1 study) 12 weeks	⊕⊕⊖⊖ LOW1,2 due to risk of bias, imprecision		The mean quality of life (sf36; 12 weeks) - sf36 mental component in the control groups was 52.27	The mean quality of life (sf36; 12 weeks) - sf36 mental component in the intervention groups was 4.86 lower (11.01 lower to 1.29 higher)
Quality of life (EQ5D; 12 weeks) Scale from: 0 to 1.	56 (1 study) 12 weeks	⊕⊕⊖⊖ LOW1,2 due to risk of bias, imprecision		The mean quality of life (eq5d; 12 weeks) in the control groups was 0.908	The mean quality of life (eq5d; 12 weeks) in the intervention groups was 0.09 lower (0.21 lower to 0.03 higher)
Adverse events (discontinuation due to AE)	63 (1 study)	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision	RR 0.65 (0.12 to 3.61)	Moderate	
				97 per 1000	34 fewer per 1000 (from 85 fewer to 253 more)
Pain intensity (VAS) Scale from: 0 to 10.	59 (1 study) 4 weeks	⊕⊕⊕⊖ MODERATE2 due to imprecision		The mean pain intensity (vas) in the control groups was 1.14	The mean pain intensity (vas) in the intervention groups was 0.44 higher (0.88 lower to 1.76 higher)
Pain intensity (EQ5D no pain/discomfort; 12 weeks)	56 (1 study) 12 weeks	⊕⊖⊖⊖ VERY LOW1,2	RR 0.89 (0.6 to 1.32)	Moderate	
				679 per 1000	75 fewer per 1000 (from 272 fewer to 217 more)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Placebo (<10mm)	Risk difference with Alpha blockers (95% CI)
		due to risk of bias, imprecision			
Pain intensity (EQ5D moderate pain/discomfort; 12 weeks)	56 (1 study) 12 weeks	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision	RR 1 (0.47 to 2.14)	Moderate	
				321 per 1000	0 fewer per 1000 (from 170 fewer to 366 more)
Pain intensity (EQ5D extreme pain/discomfort; 12 weeks)	53 (1 study) 12 weeks	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision	Peto OR 6.89 (0.42 to 113.67)	Moderate	
				0 per 1000	71 more per 1000 (from 44 fewer to 186 more)3
Analgesic use (pain medication use)	63 (1 study)	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision	RR 1.12 (0.78 to 1.61)	Moderate	
				613 per 1000	74 more per 1000 (from 135 fewer to 374 more)
Analgesic use (number of days of pain medication use)	41 (1 study)	⊕⊕⊖⊖ LOW2 due to imprecision		The mean analgesic use (number of days of pain medication use) in the control groups was 8.32 days	The mean analgesic use (number of days of pain medication use) in the intervention groups was 3.98 higher (0.55 lower to 8.51 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

3 Risk difference calculated with Review Manager

Table 9: Clinical evidence summary: Alpha blockers versus no treatment (pain management only) for mid ureteric stones <10mm in adults

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with No treatment (<10mm)	Risk difference with Alpha blockers (95% CI)
Time to stone passage mean number of days for spontaneous stone passage	16 (1 study) 8 weeks	⊕⊕⊖⊖ LOW1 due to risk of bias		The mean time to stone passage in the control groups was 21	The mean time to stone passage in the intervention groups was 12.33 lower (17.26 to 7.4 lower)
Stone passage number of people spontaneously passing stones during follow up	27 (2 studies) 4-8 weeks	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision	RR 4.09 (1.09 to 15.33)	Moderate	
				163 per 1000	504 more per 1000 (from 15 more to 1000 more)
Analgesic use mean number of times analgesics were used during follow up	16 (1 study) 8 weeks	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean analgesic use in the control groups was 1.3	The mean analgesic use in the intervention groups was 1.2 lower (2.67 lower to 0.27 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 10: Clinical evidence summary: Calcium channel blockers versus placebo for mid ureteric stones <10mm in adults

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Placebo	Risk difference with Calcium channel blockers (95% CI)
Time to stone passage (days)	24 (1 study)	⊕⊕⊕⊖ MODERATE2 due to imprecision		The mean time to stone passage (days) in the control groups was 18.15 days	The mean time to stone passage (days) in the intervention groups was 4.03 higher (2.16 lower to 10.22 higher)
Stone passage	84 (1 study) 4 weeks	⊕⊕⊖⊖ LOW1,2	RR 0.98 (0.79 to 1.2)	Moderate	
				818 per 1000	16 fewer per 1000 (from 172 fewer to 164 more)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Placebo	Risk difference with Calcium channel blockers (95% CI)
		due to risk of bias, imprecision			
Hospitalisation (excess admission days)	81 (1 study) 4 weeks	⊕⊕⊕⊖ MODERATE2 due to imprecision		The mean hospitalisation (excess admission days) in the control groups was 0.05 days	The mean hospitalisation (excess admission days) in the intervention groups was 0.08 lower (0.09 lower to 0.25 higher)
Use of healthcare services - Doctor visits	77 (1 study) 4 weeks	⊕⊕⊕⊖ MODERATE2 due to imprecision		The mean use of healthcare services - doctor visits in the control groups was 0.31 visits	The mean use of healthcare services - doctor visits in the intervention groups was 0.13 lower (0.41 lower to 0.15 higher)
Use of healthcare services - Nurse visits	77 (1 study) 4 weeks	⊕⊕⊕⊖ MODERATE2 due to imprecision		The mean use of healthcare services - nurse visits in the control groups was 0.05 visits	The mean use of healthcare services - nurse visits in the intervention groups was 0.02 lower (0.11 lower to 0.07 higher)
Use of healthcare services - Outpatient visits	81 (1 study) 4 weeks	⊕⊕⊕⊕ HIGH		The mean use of healthcare services - outpatient visits in the control groups was 0.77 visits	The mean use of healthcare services - outpatient visits in the intervention groups was 0.74 lower (0.92 to 0.56 lower)
Quality of life (SF36; 12 weeks) - SF36 physical component Scale from: 0 to 100.	48 (1 study) 12 weeks	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean quality of life (sf36; 12 weeks) - sf36 physical component in the control groups was 51.53	The mean quality of life (sf36; 12 weeks) - sf36 physical component in the intervention groups was 2.74 lower (8.96 lower to 3.48 higher)
Quality of life (SF36; 12 weeks) - SF36 mental	48 (1 study) 12 weeks	⊕⊖⊖⊖ VERY LOW1,2		The mean quality of life (sf36; 12 weeks) - sf36 mental component in the	The mean quality of life (sf36; 12 weeks) - sf36 mental component in the intervention groups was

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Placebo	Risk difference with Calcium channel blockers (95% CI)
component Scale from: 0 to 100.		due to risk of bias, imprecision		control groups was 52.27	2.17 lower (7.57 lower to 3.23 higher)
Quality of life (EQ5D; 12 weeks) Scale from: 0 to 1.	52 (1 study)	⊕⊕⊖⊖ LOW1,2 due to risk of bias, imprecision		The mean quality of life (eq5d; 12 weeks) in the control groups was 0.908	The mean quality of life (eq5d; 12 weeks) in the intervention groups was 0.12 lower (0.26 lower to 0.02 higher)
Adverse events (discontinuation due to AE)	59 (1 study)	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision	RR 1.11 (0.24 to 5.04)	Moderate	
				97 per 1000	11 more per 1000 (from 74 fewer to 392 more)
Pain intensity (VAS) Scale from: 0 to 10.	55 (1 study) 4 weeks	⊕⊕⊕⊖ MODERATE2 due to imprecision		The mean pain intensity (vas) in the control groups was 1.14	The mean pain intensity (vas) in the intervention groups was 0.71 higher (0.75 lower to 2.17 higher)
Pain intensity (EQ5D no pain/discomfort)	53 (1 study) 12 weeks	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision	RR 0.83 (0.54 to 1.27)	Moderate	
				679 per 1000	115 fewer per 1000 (from 312 fewer to 183 more)
Pain intensity (EQ5D moderate pain/discomfort)	53 (1 study) 12 weeks	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision	RR 1.12 (0.53 to 2.37)	Moderate	
				321 per 1000	39 more per 1000 (from 151 fewer to 440 more)
Pain intensity (EQ5D extreme pain/discomfort)	53 (1 study) 12 weeks	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision	Peto OR 8.68 (0.53 to 143.3)	Moderate	
				0 per 1000	80 more per 1000 (from 43 fewer to 203 more)3

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Placebo	Risk difference with Calcium channel blockers (95% CI)
Analgesia use (pain medication use)	59 (1 study)	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision	RR 1.05 (0.71 to 1.55)	Moderate	
				613 per 1000	31 more per 1000 (from 178 fewer to 337 more)
Analgesia use (number of days of pain medication use)	36 (1 study) 4 weeks	⊕⊕⊕⊖ MODERATE2 due to imprecision		The mean analgesia use (number of days of pain medication use) in the control groups was 8.32 days	The mean analgesia use (number of days of pain medication use) in the intervention groups was 1.86 higher (2.87 lower to 6.59 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. 3 Risk difference calculated in Review Manager					

Table 11: Clinical evidence summary: Alpha blockers versus Calcium channel blockers for mid ureteric stones <10mm in adults

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Calcium channel blockers (<10mm)	Risk difference with Alpha blockers (95% CI)
Time to stone passage (days)	19 (1 study)	⊕⊕⊖⊖ LOW2 due to imprecision		The mean time to stone passage (days) in the control groups was 22.18	The mean time to stone passage (days) in the intervention groups was 3.7 higher (9.33 lower to 16.73 higher)
Stone passage number of people spontaneously passing stones during follow up	81 (1 study) 4 weeks	⊕⊕⊕⊖ MODERATE2 due to imprecision	RR 0.88 (0.69 to 1.14)	Moderate	
				800 per 1000	96 fewer per 1000 (from 248 fewer to 112 more)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Calcium channel blockers (<10mm)	Risk difference with Alpha blockers (95% CI)
Hospitalisation (excess admissions days)	80 (1 study) 4 weeks	⊕⊕⊕⊖ MODERATE2 due to imprecision		The mean hospitalisation (excess admissions days) in the control groups was 0.13 days	The mean hospitalisation (excess admissions days) in the intervention groups was 0.13 higher (0.15 lower to 0.41 higher)
Use of healthcare services - Doctor visits	73 (1 study) 4 weeks	⊕⊕⊖⊖ LOW1,2 due to risk of bias, imprecision		The mean use of healthcare services - doctor visits in the control groups was 0.18 visits	The mean use of healthcare services - doctor visits in the intervention groups was 0.22 higher (0.15 lower to 0.59 higher)
Use of healthcare services - Nurse visits	73 (1 study) 4 weeks	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean use of healthcare services - nurse visits in the control groups was 0.03 visits	The mean use of healthcare services - nurse visits in the intervention groups was 0.19 higher (0.09 lower to 0.47 higher)
Use of healthcare services - Outpatient visits	78 (1 study) 4 weeks	⊕⊕⊕⊕ HIGH		The mean use of healthcare services - outpatient visits in the control groups was 0.03 visits	The mean use of healthcare services - outpatient visits in the intervention groups was 0.79 higher (0.52 to 1.06 higher)
Quality of life (SF36; 12 weeks) - SF36 physical component Scale from: 0 to 100.	50 (1 study) 12 weeks	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean quality of life (sf36; 12 weeks) - sf36 physical component in the control groups was 48.79	The mean quality of life (sf36; 12 weeks) - sf36 physical component in the intervention groups was 2.1 higher (4.17 lower to 8.37 higher)
Quality of life (SF36; 12 weeks) - SF36 mental component Scale from: 0 to 100.	50 (1 study) 12 weeks	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean quality of life (sf36; 12 weeks) - sf36 mental component in the control groups was 50.1	The mean quality of life (sf36; 12 weeks) - sf36 mental component in the intervention groups was 2.69 lower (9.47 lower to 4.09 higher)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Calcium channel blockers (<10mm)	Risk difference with Alpha blockers (95% CI)
Quality of life (EQ5D; 12 weeks) Scale from: 0 to 1.	52 (1 study) 12 weeks	⨁⨁⊖⊖ LOW1,2 due to risk of bias, imprecision		The mean quality of life (eq5d; 12 weeks) in the control groups was 0.789	The mean quality of life (eq5d; 12 weeks) in the intervention groups was 0.03 higher (0.14 lower to 0.2 higher)
Adverse events (discontinuation due to AE)	60 (1 study)	⨁⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision	RR 0.58 (0.1 to 3.24)	Moderate	
				107 per 1000	45 fewer per 1000 (from 96 fewer to 240 more)
Pain intensity (VAS) Scale from: 0 to 10.	58 (1 study) 4 weeks	⨁⨁⨁⊖ MODERATE2 due to imprecision		The mean pain intensity (vas) in the control groups was 1.85	The mean pain intensity (vas) in the intervention groups was 0.27 lower (1.83 lower to 1.29 higher)
Pain intensity (EQ5D no pain/discomfort; 12 weeks)	53 (1 study) 12 weeks	⨁⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision	RR 1.08 (0.69 to 1.71)	Moderate	
				560 per 1000	45 more per 1000 (from 174 fewer to 398 more)
Pain intensity (EQ5D moderate pain/discomfort; 12 weeks)	53 (1 study) 12 weeks	⨁⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision	RR 0.89 (0.42 to 1.89)	Moderate	
				360 per 1000	40 fewer per 1000 (from 209 fewer to 320 more)
Pain intensity (EQ5D extreme pain/discomfort; 12 weeks)	53 (1 study) 12 weeks	⨁⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision	RR 0.89 (0.14 to 5.88)	Moderate	
				80 per 1000	9 fewer per 1000 (from 69 fewer to 390 more)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Calcium channel blockers (<10mm)	Risk difference with Alpha blockers (95% CI)
Analgesic use (pain medication use)	60 (1 study) 4 weeks	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision	RR 1.07 (0.74 to 1.54)	Moderate	
				643 per 1000	45 more per 1000 (from 167 fewer to 347 more)
Analgesic use (number of days of pain medication use)	39 (1 study)	⊕⊕⊕⊖ MODERATE2 due to imprecision		The mean analgesic use (number of days of pain medication use) in the control groups was 10.18	The mean analgesic use (number of days of pain medication use) in the intervention groups was 2.12 higher (3.24 lower to 7.48 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

1.4.5.3 Proximal ureteric stones <10mm in adults

Table 12: Clinical evidence summary: Alpha blockers versus placebo for proximal ureteric stones <10mm in adults

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Placebo	Risk difference with Alpha blockers (95% CI)
Time to stone passage (days)	23 (1 study)	⊕⊕⊕⊖ MODERATE2 due to imprecision		The mean time to stone passage (days) in the control groups was 20.73 days	The mean time to stone passage (days) in the intervention groups was 4.31 lower (13.88 lower to 5.26 higher)
				Moderate	

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Placebo	Risk difference with Alpha blockers (95% CI)
Stone passage number of people spontaneously passing stones during follow up	257 (2 studies) 4 weeks	⊕⊕⊕⊖ MODERATE2 due to imprecision	RR 0.96 (0.79 to 1.15)	568 per 1000	23 fewer per 1000 (from 119 fewer to 85 more)
Hospitalisation (excess admission days)	176 (1 study) 4 weeks	⊕⊕⊕⊕ HIGH		The mean hospitalisation (excess admission days) in the control groups was 0.52 days	The mean hospitalisation (excess admission days) in the intervention groups was 0.35 lower (0.73 lower to 0.03 higher)
Use of healthcare services - Doctor visits	141 (1 study) 4 weeks	⊕⊕⊕⊖ MODERATE1 due to risk of bias		The mean use of healthcare services - doctor visits in the control groups was 0.2 visits	The mean use of healthcare services - doctor visits in the intervention groups was 0.04 higher (0.16 lower to 0.24 higher)
Use of healthcare services - Nurse visits	141 (1 study) 4 weeks	⊕⊕⊕⊖ MODERATE1 due to risk of bias		The mean use of healthcare services - nurse visits in the control groups was 0.24 visits	The mean use of healthcare services - nurse visits in the intervention groups was 0.21 lower (0.65 lower to 0.23 higher)
Use of healthcare services - Outpatients visits	176 (1 study) 4 weeks	⊕⊕⊕⊕ HIGH		The mean use of healthcare services - outpatients visits in the control groups was 0.01 visits	The mean use of healthcare services - outpatients visits in the intervention groups was 0.82 higher (0.65 to 0.99 higher)
Quality of life (SF36; 12 weeks) - SF36 physical component Scale from: 0 to 100.	84 (1 study) 12 weeks	⊕⊕⊖⊖ LOW1,2 due to risk of bias, imprecision		The mean quality of life (sf36; 12 weeks) - sf36 physical component in the control groups was 49.73	The mean quality of life (sf36; 12 weeks) - sf36 physical component in the intervention groups was 2 higher (1.98 lower to 5.98 higher)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Placebo	Risk difference with Alpha blockers (95% CI)
Quality of life (SF36; 12 weeks) - SF36 mental component Scale from: 0 to 100.	84 (1 study) 12 weeks	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean quality of life (sf36; 12 weeks) - sf36 mental component in the control groups was 50.18	The mean quality of life (sf36; 12 weeks) - sf36 mental component in the intervention groups was 0.4 lower (5.43 lower to 4.63 higher)
Quality of life (EQ5D; 12 weeks) Scale from: 0 to 1.	84 (1 study) 12 weeks	⊕⊕⊕⊖ MODERATE1 due to risk of bias		The mean quality of life (eq5d; 12 weeks) in the control groups was 0.884	The mean quality of life (eq5d; 12 weeks) in the intervention groups was 0.01 lower (0.11 lower to 0.08 higher)
Adverse events (discontinuation due to AE)	113 (1 study)	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision	RR 1.9 (0.53 to 6.78)	Moderate	
				64 per 1000	58 more per 1000 (from 30 fewer to 370 more)
Pain (VAS) Scale from: 0 to 10.	111 (1 study) 4 weeks	⊕⊕⊕⊖ MODERATE2 due to imprecision		The mean pain (vas) in the control groups was 1.37	The mean pain (vas) in the intervention groups was 0.52 lower (1.28 lower to 0.24 higher)
Pain intensity (EQ5D no pain/discomfort)	85 (1 study) 12 weeks	⊕⊕⊖⊖ LOW1,2 due to risk of bias, imprecision	RR 0.85 (0.64 to 1.14)	Moderate	
				735 per 1000	110 fewer per 1000 (from 265 fewer to 103 more)
Pain intensity (EQ5D moderate pain/discomfort)	85 (1 study) 12 weeks	⊕⊕⊖⊖ LOW1,2 due to risk of	RR 1.81 (0.85 to 3.83)	Moderate	
				206 per 1000	167 more per 1000 (from 31 fewer to 583 more)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Placebo	Risk difference with Alpha blockers (95% CI)
		bias, imprecision			
Pain intensity (EQ5D extreme pain/discomfort)	85 (1 study) 12 weeks	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision	Peto OR 0.08 (0 to 1.37)	Moderate	
				59 per 1000	54 fewer per 1000 (from 59 fewer to 20 more)
Analgesic use (pain medication use)	113 (1 study)	⊕⊕⊖⊖ LOW1,2 due to risk of bias, imprecision	RR 0.85 (0.67 to 1.09)	Moderate	
				745 per 1000	112 fewer per 1000 (from 246 fewer to 67 more)
Analgesic use (number of days of pain medication use)	74 (1 study) 4 weeks	⊕⊕⊕⊖ MODERATE2 due to imprecision		The mean analgesic use (number of days of pain medication use) in the control groups was 10.97 days	The mean analgesic use (number of days of pain medication use) in the intervention groups was 1.01 higher (2.74 lower to 4.76 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 13: Clinical evidence summary: Alpha blockers versus no treatment (pain management only) for proximal ureteric stones <10mm in adults

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with No treatment (pain management only)	Risk difference with Alpha blockers (95% CI)
Time to stone passage mean number of days for spontaneous stone passage	133 (2 studies) 4-8 weeks	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean time to stone passage in the control groups was 19.17	The mean time to stone passage in the intervention groups was 5.29 lower (8.43 to 2.16 lower)
Stone passage number of people spontaneously passing stones during follow up	213 (4 studies) 4-8 weeks	⊕⊕⊖⊖ LOW1,2 due to risk of bias, imprecision	RR 1.57 (1.2 to 2.03)	Moderate	
				357 per 1000	203 more per 1000 (from 71 more to 368 more)
Quality of life (EuroQoL) mean score on EuroQol	79 (1 study) 4 weeks	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean quality of life (EuroQoL) in the control groups was 5.5	The mean quality of life (EuroQoL) in the intervention groups was 0.1 lower (0.42 lower to 0.22 higher)
Analgesic use mean number of times analgesics were used	133 (2 studies) 4-8 weeks	⊕⊕⊖⊖ LOW1 due to risk of bias		The mean analgesic use in the control groups was 3.25	The mean analgesic use in the intervention groups was 0.55 lower (2.06 lower to 0.97 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 14: Clinical evidence summary: Calcium channel blockers versus placebo for proximal ureteric stones <10mm in adults

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Placebo	Risk difference with Calcium channel blockers (95% CI)
Time to stone passage (days)	21 (1 study)	⊕⊕⊕⊖ MODERATE2 due to imprecision		The mean time to stone passage (days) in the control	The mean time to stone passage (days) in the intervention groups was

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Placebo	Risk difference with Calcium channel blockers (95% CI)
				groups was 20.73 days	3.33 lower (11.81 lower to 5.15 higher)
Stone passage	181 (1 study) 4 weeks	⊕⊕⊕⊖ MODERATE2 due to imprecision	RR 0.86 (0.71 to 1.06)	Moderate	
				730 per 1000	102 fewer per 1000 (from 212 fewer to 44 more)
Hospitalisation (excess admission days)	179 (1 study) 4 weeks	⊕⊕⊕⊕ HIGH		The mean hospitalisation (excess admission days) in the control groups was 0.52 days	The mean hospitalisation (excess admission days) in the intervention groups was 0.08 higher (0.55 lower to 0.39 higher)
Use of healthcare services - Doctor visits	138 (1 study) 4 weeks	⊕⊕⊕⊖ MODERATE1 due to risk of bias		The mean use of healthcare services - doctor visits in the control groups was 0.2 visits	The mean use of healthcare services - doctor visits in the intervention groups was 0.01 lower (0.2 lower to 0.18 higher)
Use of healthcare services - Nurse visits	138 (1 study) 4 weeks	⊕⊕⊕⊖ MODERATE1 due to risk of bias		The mean use of healthcare services - nurse visits in the control groups was 0.24 visits	The mean use of healthcare services - nurse visits in the intervention groups was 0.2 lower (0.65 lower to 0.25 higher)
Use of healthcare services - Outpatients visits	181 (1 study) 4 weeks	⊕⊕⊕⊕ HIGH		The mean use of healthcare services - outpatients visits in the control groups was 0.01 visits	The mean use of healthcare services - outpatients visits in the intervention groups was 0.62 higher (0.48 to 0.76 higher)
Quality of life (SF36; 12 weeks) - SF36 physical component Scale from: 0 to 100.	70 (1 study) 12 weeks	⊕⊕⊖⊖ LOW1,2 due to risk of bias, imprecision		The mean quality of life (sf36; 12 weeks) - sf36 physical component in the control groups was 49.73	The mean quality of life (sf36; 12 weeks) - sf36 physical component in the intervention groups was 1.16 higher (3.1 lower to 5.42 higher)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Placebo	Risk difference with Calcium channel blockers (95% CI)
Quality of life (SF36; 12 weeks) - SF36 mental component Scale from: 0 to 100.	70 (1 study) 12 weeks	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean quality of life (sf36; 12 weeks) - sf36 mental component in the control groups was 50.18	The mean quality of life (sf36; 12 weeks) - sf36 mental component in the intervention groups was 0.93 lower (6.1 lower to 4.24 higher)
Quality of life (EQ5D; 12 weeks) Scale from: 0 to 1.	73 (1 study)	⊕⊕⊕⊖ MODERATE1 due to risk of bias		The mean quality of life (eq5d; 12 weeks) in the control groups was 0.884	The mean quality of life (eq5d; 12 weeks) in the intervention groups was 0 higher (0.09 lower to 0.11 higher)
Adverse events (discontinuation due to AE)	98 (1 study)	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision	RR 2.46 (0.69 to 8.72)	Moderate	
				64 per 1000	93 more per 1000 (from 20 fewer to 494 more)
Pain intensity (VAS) Scale from: 0 to 10.	95 (1 study) 4 weeks	⊕⊕⊕⊖ MODERATE2 due to imprecision		The mean pain intensity (vas) in the control groups was 1.37	The mean pain intensity (vas) in the intervention groups was 0.49 higher (0.49 lower to 1.47 higher)
Pain intensity (EQ5D no pain/discomfort)	74 (1 study) 12 weeks	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision	RR 1.02 (0.78 to 1.34)	Moderate	
				735 per 1000	15 more per 1000 (from 162 fewer to 250 more)
Pain intensity (EQ5D moderate pain/discomfort)	74 (1 study)	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision	RR 1.09 (0.46 to 2.62)	Moderate	
				206 per 1000	19 more per 1000 (from 111 fewer to 334 more)
				Moderate	

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Placebo	Risk difference with Calcium channel blockers (95% CI)
Pain intensity (EQ5D extreme pain/discomfort)	74 (1 study) 12 weeks	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision	RR 0.43 (0.04 to 4.49)	59 per 1000	34 fewer per 1000 (from 57 fewer to 206 more)
Analgesic use (pain medication use)	97 (1 study)	⊕⊕⊖⊖ LOW1,2 due to risk of bias, imprecision	RR 0.91 (0.71 to 1.18)	Moderate	
				745 per 1000	67 fewer per 1000 (from 216 fewer to 134 more)
Analgesic use (number of days of pain medication use)	67 (1 study) 4 weeks	⊕⊕⊕⊖ MODERATE2 due to imprecision		The mean analgesic use (number of days of pain medication use) in the control groups was 10.97 days	The mean analgesic use (number of days of pain medication use) in the intervention groups was 2.59 higher (1.77 lower to 6.95 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 15: Clinical evidence summary: Alpha blockers versus Calcium channel blockers for proximal ureteric stones <10mm in adults

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Calcium channel blockers	Risk difference with Alpha blockers (95% CI)
Time to stone passage (days)	22 (1 study)	⊕⊕⊖⊖ LOW2 due to imprecision		The mean time to stone passage (days) in the control groups was 17.4 days	The mean time to stone passage (days) in the intervention groups was 0.98 lower (9.78 lower to 7.82 higher)
				Moderate	

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Calcium channel blockers	Risk difference with Alpha blockers (95% CI)
Stone passage number of people spontaneously passing stones during follow up	180 (1 study) 4 weeks	⊕⊕⊕⊖ MODERATE2 due to imprecision	RR 1.12 (0.91 to 1.37)	630 per 1000	76 more per 1000 (from 57 fewer to 233 more)
Hospitalisation (excess admission days)	179 (1 study) 4 weeks	⊕⊕⊕⊕ HIGH		The mean hospitalisation (excess admission days) in the control groups was 0.44 days	The mean hospitalisation (excess admission days) in the intervention groups was 0.27 lower (0.62 lower to 0.08 higher)
Use of healthcare services - Doctor visits	137 (1 study) 4 weeks	⊕⊕⊕⊖ MODERATE1 due to risk of bias		The mean use of healthcare services - doctor visits in the control groups was 0.19 visits	The mean use of healthcare services - doctor visits in the intervention groups was 0.05 higher (0.16 lower to 0.26 higher)
Use of healthcare services - Nurse visits	137 (1 study) 4 weeks	⊕⊕⊕⊖ MODERATE1 due to risk of bias		The mean use of healthcare services - nurse visits in the control groups was 0.04 visits	The mean use of healthcare services - nurse visits in the intervention groups was 0.01 lower (0.09 lower to 0.07 higher)
Use of healthcare services - Outpatients visits	179 (1 study) 4 weeks	⊕⊕⊕⊖ MODERATE2 due to imprecision		The mean use of healthcare services - outpatients visits in the control groups was 0.63 visits	The mean use of healthcare services - outpatients visits in the intervention groups was 0.2 higher (0.02 lower to 0.42 higher)
Quality of life (SF36; 12 weeks) - SF36 physical component Scale from: 0 to 100.	88 (1 study) 12 weeks	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean quality of life (sf36; 12 weeks) - sf36 physical component in the control groups was 50.89	The mean quality of life (sf36; 12 weeks) - sf36 physical component in the intervention groups was 0.84 higher (2.88 lower to 4.56 higher)
Quality of life (SF36; 12 weeks) - SF36 mental	88 (1 study) 12 weeks	⊕⊖⊖⊖ VERY LOW1,2		The mean quality of life (sf36; 12 weeks) - sf36 mental component in the	The mean quality of life (sf36; 12 weeks) - sf36 mental component in the intervention groups was

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Calcium channel blockers	Risk difference with Alpha blockers (95% CI)
component Scale from: 0 to 100.		due to risk of bias, imprecision		control groups was 42.25	0.53 higher (3.84 lower to 4.9 higher)
Quality of life (EQ5D; 12 weeks) Scale from: 0 to 1.	91 (1 study) 12 weeks	⊕⊕⊕⊖ MODERATE1 due to risk of bias		The mean quality of life (eq5d; 12 weeks) in the control group was 0.894	The mean quality of life (eq5d; 12 weeks) in the intervention was 0.02 lower (0.09 lower to 005 higher)
Adverse events (discontinuation due to AE)	117 (1 study)	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision	RR 0.77 (0.31 to 1.92)	Moderate	
				157 per 1000	36 fewer per 1000 (from 108 fewer to 144 more)
Pain intensity (VAS) Scale from: 0 to 10.	114 (1 study) 4 weeks	⊕⊕⊕⊖ MODERATE2 due to imprecision		The mean pain intensity (vas) in the control groups was 1.86	The mean pain intensity (vas) in the intervention groups was 1.01 lower (1.83 to 0.19 lower)
Pain intensity (EQ5D no pain/discomfort)	91 (1 study) 12 weeks	⊕⊕⊖⊖ LOW1,2 due to risk of bias, imprecision	RR 0.84 (0.63 to 1.1)	Moderate	
				750 per 1000	120 fewer per 1000 (from 278 fewer to 75 more)
Pain intensity (EQ5D moderate pain/discomfort)	91 (1 study) 12 weeks	⊕⊕⊖⊖ LOW1,2 due to risk of bias, imprecision	RR 1.66 (0.84 to 3.26)	Moderate	
				225 per 1000	148 more per 1000 (from 36 fewer to 508 more)
Pain intensity (EQ5D extreme pain/discomfort)	91 (1 study) 12 weeks	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision	Peto OR 0.1 (0 to 5.33)	Moderate	
				25 per 1000	22 fewer per 1000 (from 25 fewer to 95 more)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Calcium channel blockers	Risk difference with Alpha blockers (95% CI)
Analgesic use (pain medication use)	116 (1 study)	⨁⨁⊖⊖ LOW1,2 due to risk of bias, imprecision	RR 0.94 (0.72 to 1.22)	Moderate	
				680 per 1000	41 fewer per 1000 (from 190 fewer to 150 more)
Analgesic use (number of days of pain medication use)	75 (1 study) 4 weeks	⨁⨁⨁⊖ MODERATE2 due to imprecision		The mean analgesic use (number of days of pain medication use) in the control groups was 13.56 days	The mean analgesic use (number of days of pain medication use) in the intervention groups was 1.58 lower (6.09 lower to 2.93 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					

1.4.5.4 Distal ureteric stones <10mm in children

Table 16: Clinical evidence summary: Alpha blockers versus placebo for distal ureteric stones <10mm in children

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Placebo	Risk difference with Alpha blockers (95% CI)
Time to stone passage (days)	98 (2 studies) (4 weeks)	⨁⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, inconsistency, imprecision		The mean time to stone passage (days) in the control groups was 12.45 days	The mean time to stone passage (days) in the intervention groups was 4.89 lower (7.73 to 2.05 lower)
Stone passage	98 (2 studies) 4 weeks	⨁⨁⊖⊖ LOW1,2 due to risk of bias, imprecision	RR 1.3 (1.04 to 1.62)	Moderate	
				690 per 1000	207 more per 1000 (from 28 more to 428 more)
				Moderate	

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Placebo	Risk difference with Alpha blockers (95% CI)
Adverse events (headaches/dizziness)	37 (1 study) 4 weeks	⊕⊕⊖⊖ LOW1,2 due to risk of bias, imprecision	Peto OR 8.82 (0.86 to 90.57)	0 per 1000	167 more per 1000 (from 21 fewer to 354 more)4
Adverse events (headaches)	61 (1 study) 4 weeks	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision	RR 0.85 (0.06 to 12.95)	Moderate	
				36 per 1000	5 fewer per 1000 (from 34 fewer to 430 more)
Adverse events (hypotension)	61 (1 study)	⊕⊖⊖⊖ VERY LOW1 due to risk of bias, imprecision	Not estimable6	Moderate	
				0 per 1000	0 fewer per 1000 (from 62 fewer to 62 more)4
Pain intensity (number of pain episodes)	98 (2 studies) 4 weeks	⊕⊖⊖⊖ VERY LOW1,2,5 due to risk of bias, inconsistency, imprecision		The mean pain intensity (number of pain episodes) in the control groups was 3.45	The mean pain intensity (number of pain episodes) in the intervention groups was 1.49 lower (3.04 lower to 0.06 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.
3 Downgraded by 1 or 2 increments because heterogeneity, I2= 73%, p= > 0.1, unexplained by subgroup analysis
4 Risk difference calculated in Review Manager
5 Downgraded by 1 or 2 increments because heterogeneity, I2= 77%, p= > 0.1, unexplained by subgroup analysis
6 Could not be calculated as there were no events in the intervention or comparison group

Table 17: Clinical evidence summary: Alpha blockers versus no treatment (pain management only) for distal ureteric stones <10mm in children

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with No treatment	Risk difference with Alpha blockers (95% CI)
Time to stone passage mean number of days for spontaneous stone passage	102 (2 studies) 3-4 weeks	⊕⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, inconsistency, imprecision		The mean time to stone passage in the control groups was 12.05	The mean time to stone passage in the intervention groups was 5.26 lower (15.16 lower to 4.63 higher)
Stone passage number of people spontaneously passing stones	147 (3 studies) 3-4 weeks	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision	RR 1.45 (1.14 to 1.84)	Moderate	
				625 per 1000	281 more per 1000 (from 87 more to 525 more)
Adverse events number of people experiencing adverse events (unspecified)	102 (2 studies) 3-4 weeks	⊕⊕⊖⊖ LOW1 due to risk of bias	Not estimable 5	Moderate	
				0 per 1000	0 more per 1000 (from 50 fewer to 50 more)4
Pain intensity (daily pain episodes) mean number of daily pain episodes during follow up	63 (1 study) 4 weeks	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean pain intensity (daily pain episodes) in the control groups was 2.5	The mean pain intensity (daily pain episodes) in the intervention groups was 0.9 lower (1.77 to 0.03 lower)
Analgesic use mean number of times analgesics were used during follow up	63 (1 study) 4 weeks	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision		The mean analgesic use in the control groups was 1.8	The mean analgesic use in the intervention groups was 1.25 lower (1.87 to 0.63 lower)

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
3 Downgraded by 1 or 2 increments because the point estimate varies widely across studies, the confidence intervals across studies show minimal or no overlap, or heterogeneity, I2=99%, p<0.04, unexplained by subgroup analysis.

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with No treatment	Risk difference with Alpha blockers (95% CI)
4 Risk difference calculated in Review Manager 5 Could not be calculated as there were no events in the intervention or comparison group					

1.4.5.5 Adjunctive therapy: distal ureteric stones <10mm in adults

Table 18: Clinical evidence summary: Alpha blockers as adjunctive therapy to shock wave lithotripsy versus shock wave lithotripsy only for distal ureteric stones <10mm in adults

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with SWL	Risk difference with Alpha blockers + SWL (95% CI)
Time to stone passage number of days for stone passage	207 (2 studies) 4-6 weeks	⊕⊖⊖⊖ VERY LOW1,3 due to risk of bias, imprecision		The mean time to stone passage in the control groups was 14.65	The mean time to stone passage in the intervention groups was 2.21 lower (3.35 to 1.08 lower)
Stone passage number of people stone free at the end of follow up	383 (5 studies) 15 days - 6 weeks	⊕⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, indirectness, imprecision	RR 1.28 (1.11 to 1.48)	Moderate	
				568 per 1000	159 more per 1000 (from 62 more to 273 more)
Hospitalisation number of people hospitalized during follow up	88 (1 study) 4 weeks	⊕⊕⊖⊖ LOW1,3 due to risk of bias, imprecision	RR 0.63 (0.35 to 1.14)	Moderate	
				432 per 1000	160 fewer per 1000 (from 281 fewer to 60 more)
Adverse events (dizziness) number of people experiencing dizziness during follow up	206 (3 studies) 15 days - 6 weeks	⊕⊕⊖⊖ LOW1 due to risk of bias	Peto OR 8.4 (1.86 to 37.87)	Moderate	
				0 per 1000	69 more per 1000 (from 17 more to 122 more)4
				Moderate	

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with SWL	Risk difference with Alpha blockers + SWL (95% CI)
Adverse events (abnormal ejaculation) number of people experiencing abnormal ejaculation during follow up	98 (2 studies) 4-6 weeks	⊕⊕⊖⊖ LOW1 due to risk of bias	Peto OR 8.56 (1.83 to 40.08)	0 per 1000	142 more per 1000 (from 40 more to 246 more)4
Adverse events (headache) number of people experiencing headache during follow up	155 (2 studies) 4-6 weeks	⊕⊖⊖⊖ VERY LOW1,3 due to risk of bias, imprecision	RR 4.03 (1.04 to 15.72)	Moderate	
				29 per 1000	88 more per 1000 (from 1 more to 427 more)
Adverse events (hypotension) number of people experiencing hypotension during follow up	67 (1 study) 6 weeks	⊕⊕⊖⊖ LOW1 due to risk of bias		Moderate	
				0 per 1000	0 more per 1000 (from 60 fewer to 60 more)4
Analgesic use mean number of times analgesics were used during follow up	88 (1 study) 4 weeks	⊕⊖⊖⊖ VERY LOW1,3 due to risk of bias, imprecision		The mean analgesic use in the control groups was 6.11	The mean analgesic use in the intervention groups was 1.72 lower (2.88 to 0.56 lower)
Analgesic use (dosage) mean dosage (mg) of Diclofenac during follow up	119 (1 study) 4 weeks	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, indirectness		The mean analgesic use (dosage) in the control groups was 116.1	The mean analgesic use (dosage) in the intervention groups was 50.27 lower (68.87 to 31.67 lower)

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 or 2 increments because the majority of the evidence included an indirect population (downgrade by one increment) or a very indirect population (downgrade by two increments)
3 Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs
4 Risk difference calculated in Review Manager

Table 19: Clinical evidence summary: Alpha blockers as adjunctive therapy to ureteroscopy versus ureteroscopy only for distal ureteric stones <10mm in adults

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with URS	Risk difference with Alpha blockers + URS (95% CI)
Stone passage number of people stone-free at the end of follow up	98 (1 study) 2 weeks	⊕⊕⊕⊖ MODERATE1 due to risk of bias	RR 1.08 (0.95 to 1.23)	Moderate	
				872 per 1000	70 more per 1000 (from 44 fewer to 201 more)
Use of healthcare services length of hospital stay	98 (1 study)	⊕⊕⊖⊖ LOW1,2 due to risk of bias, imprecision		The mean use of healthcare services in the control groups was 1.7	The mean use of healthcare services in the intervention groups was 0.5 lower (0.81 to 0.19 lower)

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 summary: Alpha blockers as adjunctive therapy to ureteroscopy versus placebo and ureteroscopy for distal ureteric stones <10mm in adults

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with placebo + URS	Risk difference with Alpha blockers + URS (95% CI)
Stone passage number of people stone free at the end of follow up	102 (1 study) 2 weeks	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision	RR 1.35 (1.11 to 1.63)	Moderate	
				700 per 1000	245 more per 1000 (from 77 more to 441 more)
Pain intensity (colic episodes) mean number of colic episodes during follow up	102 (1 study) 2 weeks	⊕⊕⊖⊖ LOW1 due to risk of bias		The mean pain intensity (colic episodes) in the control groups was 6	The mean pain intensity (colic episodes) in the intervention groups was 5 lower (5.99 to 4.01 lower)
				Moderate	

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with placebo + URS	Risk difference with Alpha blockers + URS (95% CI)
Analgesic use number of people using analgesics during follow up	102 (1 study) 2 weeks	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision	RR 0.32 (0.11 to 0.93)	240 per 1000	163 fewer per 1000 (from 17 fewer to 214 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 Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

1.4.5.6 Adjunctive therapy: distal ureteric stones 10-20mm in adults

Table 21: Clinical evidence summary: Alpha blockers as adjunctive therapy to shock wave lithotripsy versus shock wave lithotripsy only for distal ureteric stones 10-20mm in adults

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with SWL	Risk difference with Alpha blockers + SWL (95% CI)
Time to stone passage number of days for stone passage	38 (1 study) unclear	⊕⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, indirectness, imprecision		The mean time to stone passage in the control groups was 12.42	The mean time to stone passage in the intervention groups was 2.56 lower (7.78 lower to 2.66 higher)
Pain intensity (VAS) visual analogue scale. Scale from: 0 to 10.	38 (1 study) unclear	⊕⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, indirectness, imprecision		The mean pain intensity (vas) in the control groups was 4	The mean pain intensity (vas) in the intervention groups was 1.21 lower (2.88 lower to 0.46 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 or 2 increments because the majority of the evidence included an indirect population (downgrade by one increment) or a very indirect population (downgrade by two increments)
3 Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

1.4.5.7 Adjunctive therapy: mid ureteric stones 10-20mm in adults

Table 22: Clinical evidence summary: Alpha blockers as adjunctive therapy to shock wave lithotripsy versus shock wave lithotripsy only for mid ureteric stones 10-20mm in adults

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with SWL	Risk difference with Alpha blockers + SWL (95% CI)
Time to stone passage number of days for stone passage	28 (1 study) unclear	⊕⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, indirectness, imprecision		The mean time to stone passage in the control groups was 10.75	The mean time to stone passage in the intervention groups was 1.5 lower (8.23 lower to 5.23 higher)
Pain intensity (VAS) visual analogue scale. Scale from: 0 to 10.	28 (1 study) unclear	⊕⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, indirectness, imprecision		The mean pain intensity (VAS) in the control groups was 3	The mean pain intensity (VAS) in the intervention groups was 0.62 lower (3.13 lower to 1.89 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 or 2 increments because the majority of the evidence included an indirect population (downgrade by one increment) or a very indirect population (downgrade by two increments)
3 Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

1.4.5.8 Adjunctive therapy: proximal ureteric stones <10mm in adults

Table 23: Clinical evidence summary: Alpha blockers as adjunctive therapy to shock wave lithotripsy versus shock wave lithotripsy only for proximal ureteric stones <10mm in adults

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with SWL	Risk difference with Alpha blockers + SWL (95% CI)
Time to stone passage number of days for stone passage	320 (4 studies) 2-12 weeks	⊕⊖⊖⊖ VERY LOW1,2		The mean time to stone passage in the	The mean time to stone passage in the intervention groups was

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with SWL	Risk difference with Alpha blockers + SWL (95% CI)
		due to risk of bias, inconsistency		control groups was 23.12	4.32 lower (9.85 lower to 1.21 higher)
Stone passage number of people stone free at the end of follow up	405 (6 studies) 2-12 weeks	⊕⊕⊕⊖ MODERATE1 due to risk of bias	RR 1.11 (1.03 to 1.21)	Moderate	
				848 per 1000	93 more per 1000 (from 25 more to 178 more)
Hospitalisation mean number of Hospitalisations	79 (1 study) 2 weeks	⊕⊖⊖⊖ VERY LOW1,4 due to risk of bias, indirectness		The mean Hospitalisation in the control groups was 0.52	The mean Hospitalisation in the intervention groups was 0.01 lower (0.31 lower to 0.29 higher)
Use of healthcare services (ED visits) mean number of ED visits during follow up	54 (1 study) 4 weeks	⊕⊖⊖⊖ VERY LOW1,3 due to risk of bias, imprecision		The mean use of healthcare services (ED visits) in the control groups was 1.42	The mean use of healthcare services (ED visits) in the intervention groups was 0.6 lower (1.13 to 0.07 lower)
Quality of life (EQ5D) mean score on EQ5D. Scale from: 0 to 1.	54 (1 study) 4 weeks	⊕⊖⊖⊖ VERY LOW1,3 due to risk of bias, imprecision		The mean quality of life (EQ5D) in the control groups was 0.78	The mean quality of life (EQ5D) in the intervention groups was 0.04 higher (0.01 lower to 0.09 higher)
Quality of life (EQ5D VAS) mean score on EQ5D visual analogue scale . Scale from: 0 to 100.	54 (1 study) 4 weeks	⊕⊖⊖⊖ VERY LOW1,3 due to risk of bias, imprecision		The mean quality of life (EQ5D VAS) in the control groups was 73.65	The mean quality of life (EQ5D VAS) in the intervention groups was 6.71 higher (1.49 to 11.93 higher)
Adverse events (dizziness) number of people experiencing dizziness during follow up	172 (2 studies) 3-6 weeks	⊕⊖⊖⊖ VERY LOW1,3 due to risk of bias, imprecision	Peto OR 7.76 (0.8 to 75.32)	Moderate	
				0 per 1000	35 more per 1000 (from 9 fewer to 80 more)5
Adverse events (retrograde ejaculation) number of people experiencing retrograde ejaculation during follow up	84 (1 study) 6 weeks	⊕⊕⊖⊖ LOW1 due to risk of bias	Not estimable8	Moderate	
				0 per 1000	0 more per 1000 (from 45 fewer to 45 more)5

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with SWL	Risk difference with Alpha blockers + SWL (95% CI)
Pain intensity (VAS) visual analogue scale . Scale from: 0 to 10.	374 (5 studies) 2-12 weeks	⊕⊖⊖⊖ VERY LOW1,3,6 due to risk of bias, imprecision, inconsistency		The mean pain intensity (vas) in the control groups was 5.54	The mean pain intensity (vas) in the intervention groups was 0.89 lower (1.68 to 0.1 lower)
Pain intensity (renal colic episodes) mean number of renal colic episodes during follow up	54 (1 study) 4 weeks	⊕⊖⊖⊖ VERY LOW1,3 due to risk of bias, imprecision		The mean pain intensity (renal colic episodes) in the control groups was 4.92	The mean pain intensity (renal colic episodes) in the intervention groups was 2.38 lower (3.89 to 0.87 lower)
Analgesic use (dosage) mean dosage (mg) of Diclofenac used during follow up	54 (1 study) 4 weeks	⊕⊖⊖⊖ VERY LOW1,3 due to risk of bias, imprecision		The mean analgesic use (dosage) in the control groups was 431.7	The mean analgesic use (dosage) in the intervention groups was 189.7 lower (309.2 to 70.2 lower)
Analgesic use number of people using analgesia during follow up	163 (2 studies) 2-6 weeks	⊕⊖⊖⊖ VERY LOW1,3,4,7 due to risk of bias, indirectness, imprecision, inconsistency	RR 0.96 (0.49 to 1.91)	Moderate	
				492 per 1000	20 fewer per 1000 (from 251 fewer to 448 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 or 2 increments because the point estimate varies widely across studies, the confidence intervals across studies show minimal or no overlap or heterogeneity, I2=77%, p= > 0.1, unexplained by subgroup analysis.
3 Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs
4 Downgraded by 1 or 2 increments because the majority of the evidence included an indirect population (downgrade by one increment) or a very indirect population (downgrade by two increments)
5 Risk difference calculated in Review Manager
6 Downgraded by 1 or 2 increments because the point estimate varies widely across studies, the confidence intervals across studies show minimal or no overlap or heterogeneity, I2=86%, p= > 0.1, unexplained by subgroup analysis
7 Downgraded by 1 or 2 increments because the point estimate varies widely across studies, the confidence intervals across studies show minimal or no overlap or heterogeneity, I2=67%, p= > 0.1, unexplained by subgroup analysis

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with SWL	Risk difference with Alpha blockers + SWL (95% CI)
8 Could not be calculated as there were no events in the intervention or comparison group					

Table 24: Clinical evidence summary: Alpha blockers as adjunctive therapy to shock wave lithotripsy versus placebo and shock wave lithotripsy for proximal ureteric stones <10mm in adults

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Placebo + SWL	Risk difference with Alpha blockers + SWL (95% CI)
Time to stone passage number of days for stone passage	49 (1 study) 3 months	⊕⊕⊖⊖ LOW1,3 due to risk of bias, indirectness		The mean time to stone passage in the control groups was 7.5	The mean time to stone passage in the intervention groups was 3.3 lower (4.47 to 2.13 lower)
Stone passage number of people stone free at the end of follow up	49 (1 study) 3 months	⊕⊕⊖⊖ LOW1,2 due to indirectness, imprecision	RR 1.45 (1.06 to 1.97)	Moderate	
				667 per 1000	300 more per 1000 (from 40 more to 647 more)
1 Downgraded by 1 or 2 increments because the majority of the evidence included an indirect population (downgrade by one increment) or a very indirect population (downgrade by two increments) 2 Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs 3 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					

1.4.5.9 Adjunctive therapy: proximal ureteric stones 10-20mm in adults

Table 25: Clinical evidence summary: Alpha blockers as adjunctive therapy to shock wave lithotripsy versus shock wave lithotripsy only for proximal ureteric stones 10-20mm in adults

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with SWL	Risk difference with Alpha blockers + SWL (95% CI)
Time to stone passage number of days to stone passage	57 (1 study) unclear	⊕⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, indirectness, imprecision		The mean time to stone passage in the control groups was 13.54	The mean time to stone passage in the intervention groups was 6.44 lower (10.3 to 2.58 lower)
Stone passage number of people stone free at the end of follow up	57 (1 study) 3 months	⊕⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, indirectness, imprecision	RR 1.09 (0.88 to 1.35)	Moderate	
				821 per 1000	74 more per 1000 (from 99 fewer to 287 more)
Pain intensity (VAS) visual analogue scale. Scale from: 0 to 10.	57 (1 study) unclear	⊕⊖⊖⊖ VERY LOW1,2,3 due to risk of bias, indirectness, imprecision		The mean pain intensity (vas) in the control groups was 4	The mean pain intensity (vas) in the intervention groups was 1.1 lower (2.34 lower to 0.14 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 or 2 increments because the majority of the evidence included an indirect population (downgrade by one increment) or a very indirect population (downgrade by two increments)
3 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 summary: Alpha blockers as adjunctive therapy to ureteroscopy versus ureteroscopy only for proximal ureteric stones 10-20mm in adults

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with URS	Risk difference with Alpha blockers + URS (95% CI)
Time to stone passage number of days for stone passage	89 (1 study) 6 weeks	⊕⊖⊖⊖ VERY LOW1,2		The mean time to stone passage in	The mean time to stone passage in the intervention groups was

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with URS	Risk difference with Alpha blockers + URS (95% CI)
		due to risk of bias, imprecision		the control groups was 11.54	3.68 lower (6.95 to 0.41 lower)
Stone passage number of people stone free at the end of follow up	254 (2 studies) 4-6 weeks	⊕⊕⊕⊖ MODERATE1 due to risk of bias	RR 1.11 (1.02 to 1.21)	Moderate	
				865 per 1000	95 more per 1000 (from 17 more to 182 more)
Use of healthcare services (Hospitalisation time) length of hospital stay for procedure	165 (1 study) admission	⊕⊕⊖⊖ LOW1,2 due to risk of bias, imprecision		The mean use of healthcare services (Hospitalisation time) in the control groups was 1.4	The mean use of healthcare services (Hospitalisation time) in the intervention groups was 0.2 lower (0.34 to 0.06 lower)
Hospitalisation (readmission) number of people readmitted to hospital during follow up	165 (1 study) 8 weeks	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision	RR 0.62 (0.15 to 2.52)	Moderate	
				60 per 1000	23 fewer per 1000 (from 51 fewer to 91 more)
Adverse events (dizziness) number of people experiencing dizziness during follow up	89 (1 study) 6 weeks	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision	Peto OR 7.39 (0.46 to 120.11)	Moderate	
				0 per 1000	44 more per 1000 (from 28 fewer to 117 more)3
Pain intensity (ureteral colic rate) number of people experiencing ureteral colic during follow up	89 (1 study) 6 weeks	⊕⊖⊖⊖ VERY LOW1,2 due to risk of bias, imprecision	RR 0.2 (0.05 to 0.84)	Moderate	
				227 per 1000	182 fewer per 1000 (from 36 fewer to 216 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 Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs
3 Risk difference calculated in Review Manager

See appendix F for full GRADE tables.

1.5 Economic evidence

1.5.1 Included studies

One health economic study was identified in adults with the relevant comparison and has been included in this review.[153] This is summarised in the health economic evidence profile below (Table 27) and the health economic evidence table in appendix H.

No relevant health economic studies were identified in children.

1.5.2 Excluded studies

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

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

1.5.3 Summary of studies included in the economic evidence review

Table 27: Health economic evidence profile: MET (tamsulosin or nifedipine) versus placebo and tamsulosin versus nifedipine

Study	Applicability	Limitations	Other comments	Incremental cost	Incremental effects	Cost effectiveness	Uncertainty
Pickard 2015 [UK][153]	Directly applicable [(a)]	Potentially serious limitations [(b)]	Within trial analysis based on an RCT of 12 weeks. No extrapolation. Population is adult patients with ureteric stones. Interventions were MET (tamsulosin 400 µg and nifedipine 30 mg groups combined) for up to 4 weeks, and placebo. Tamsulosin versus Nifedipine also compared in the analysis. The study perspective is the NHS but also patient costs were collected from patients. These costs are difficult to be separated from the rest of NHS costs. Health related quality of life measures were collected by participant completed EQ-5D questionnaires. SF-36 also collected.	**Placebo vs MET:** £42 **Nifedipine vs Tamsulosin**: £87	**Placebo vs MET:** 0.001 **Nifedipine vs Tamsulosin**: 0.002 [(c)]	**Placebo vs MET:** £42,000 [(d)] **Nifedipine vs Tamsulosin**: £43,500 [(e)]	Used non-parametric boostrapping to get 1000 estimates of the ICERs. One-way sensitivity analyses using extreme values were performed around the QALY estimates. An alternative measure was used for QoL; SF-36 responses were mapped on the SF-6D measure using the algorithm from another study to validate the estimate of utility value for each time point derived from the EQ-5D. = Placebo now cost effective instead of MET. Tamsulosin still cost effective. Also a Sensitivity analysis using imputed EQ-5D assuming the imputed values are the highest estimates was conducted. = Placebo now cost effective instead of MET. Nifedipine now cost effective.

Abbreviations: EQ-5D: Euroqol 5 dimensions questionnaire ICER: incremental cost-effectiveness ratio; MET: Medical Expulsive Therapy QALY: quality-adjusted life years; RCT: randomised controlled trial SF:6D: (Short-Form Six-Dimension questionnaire

(a) Within trial analysis based on UK RCT. Uses an NHS perspective and EQ-5D. Included some participants costs that are not NHS costs related, and these were reported as part of NHS costs that they account for significant % of total costs of intervention ; so it is difficult to separate participants' costs from the NHS costs in order to determine whether their magnitude is significant compared to the total costs of interventions. The categories where the patient reported outcomes fall include costs that are of similar amount in both interventions (MET, placebo) , so unlikely changing the cost effectiveness results.

(b) Study didn't meet the quality criteria around the choice of time horizon being 12 weeks and not longer. That was justified by the authors as there weren't many people who still needed interventions at the end of the trial. However there were no extrapolation and therefore assumptions made about what this treatment would be which could impact incremental costs and effects because different numbers of people are stone free in each arm.

(c) Utilities for clinical response were derived using trial data and the EQ-5D questionnaire'

(d) This has been calculated by the health economist as there is an error in the study. This was reported as cost saving per QALY lost for MET versus placebo because MET was both cheaper and less effective. However for ease of interpretation in cases like this the intervention should be switched around i.e. to compare placebo versus MET so that the less effective intervention is used as the comparator and so the ICER can be interpreted as it normally would (if less than £20,000 then intervention is cost effective versus the comparison).

(e) Similar to note d. Nifedipine is less expensive and less effective than tamsulosin, so the ICER of nifedipine versus tamsulosin is presented for ease of interpretation.

1.5.4 Unit costs

Where several studies evaluated the same intervention in different doses we used the highest dose reported. Calculation for tablets and capsules for tamsulosin and nifedipine were made as capsules formulation of these drugs was identified in the cost utility analysis [153]

Table 28: UK costs of alpha blockers and calcium channel blockers

Drug	Daily dose (mg)	Cost (per unit)	Daily cost	Cost – monthly	Cost- annual	Source of dose
Alpha blockers						
Tamsulosin hydrocholoride TABLETS	0.4 per day	0.4mg tablet (Pack of 30) = £10.47	£0.35	£10.65	£127.39	Clinical review
Tamsulosin hydrocholoride CAPSULES	0.4 per day	0.4mg capsule (Pack of 30) = £3.89	£0.13	£3.94	£47.33	Pickard 2015 [153]
Alfuzosin hydrocholoride	10mg per day	10 mg tablet (pack of 30) =£12.51	£0.42	£12.68	£152.21	Clinical review
Doxazosin	4mg per day	4mg tablet (pack of 28) = £5	£0.18	£5.43	£65.18	Clinical review
Terazosin	10mg per day	10mg tablet (pack of 28) = £7.87	£0.28	£8.55	£102.59	Clinical review
Calcium channel blockers						
Nifedipine TABLETS	30mg per day	30 mg tablet (pack of 28) = £6.85	£0.24	£7.44	£89.29	Clinical review
Nifedipine CAPSULES	30mg per day	30 mg tablet (pack of 28 =£4.89	£0.17	£5.31	£63.74	Pickard 2015 [153]

Source: BNF "Drug Tariff" price, DATE; September 2017 [99]
(a) The cost of other alpha blockers, naftopodil, silodosin is not provided by BNF site

1.6 Resource costs

The recommendations made in this review are likely to have a substantial impact on resources.

Additional savings are likely to be made for the following reasons: MET are very inexpensive drugs, the cost of providing these would be outweighed by the savings from downstream resource use avoided because of the effectiveness of MET at helping stones to pass. Further work is being carried out to quantify the potential resource impact in this area.

1.7 Evidence statements

1.7.1 Clinical evidence statements

Distal ureteric stones

Thirteen studies compared alpha blockers to placebo in adults with distal ureteric stones <10mm. For the outcomes of stone passage and time to stone passage, the evidence suggested a clinically important benefit in favour of alpha blockers (6-13 studies; n=3788-5154). For the outcomes of hospitalisation, use of healthcare services (emergency department, doctor, nurse or outpatient visits) and quality of life, the evidence suggested no clinical difference (1-3 studies; n=210-580). The evidence suggested a clinically important benefit in favour of placebo in terms of unspecified adverse events, and no clinical difference for all other adverse event outcomes (2-7 studies; n=198-3728). For the outcome of pain intensity, measured by the visual analogue scale and EQ-5D, the evidence suggested no clinically important difference between interventions (1 study; n=219-279). For reducing the number of people experiencing pain episodes, the evidence suggested a clinically important benefit in favour of alpha blockers (1 study; n=150). In terms of the average number of pain episodes and pain intensity measured by verbal numeric pain scale, the evidence suggested no clinical difference (1-2 studies; n=219-367). The evidence suggested a clinically important benefit in favour of alpha blockers for reducing the number of people using analgesics and analgesic dose (Ketorolac and Diclofenac), but no clinical difference in the average number of episodes of analgesic use, days of analgesic use or Buprenorphine dose (3 studies; n=153-3693). The quality of the evidence was High to Very Low. The main reasons for downgrading the quality of the evidence were risk of bias and imprecision. In addition, four outcomes for stone passage and analgesic use (number of people using analgesics and Diclofenac dose) were downgraded for inconsistency.

Thirty-two studies compared alpha blockers to no treatment in adults with distal ureteric stones <10mm. For the outcomes of stone passage and time to stone passage, the evidence suggested a clinically important benefit in favour of alpha blockers (18-31 studies; n=1642-2530). For the outcome of adverse events (dizziness, headache, hypotension, retrograde ejaculation, and unspecified), the evidence suggested no clinical difference (2-9 studies; n=163-716). The evidence suggested a clinically important benefit in favour of alpha blockers for reducing hospitalisations, but no clinical difference between interventions in terms of reducing use of healthcare services (return to emergency department/primary care visit) (2-8-studies; n=77-587). Eleven studies reported reduction in the number of pain episodes and the evidence suggested a clinically important benefit in favour of alpha blockers (11 studies; n=1077).Three studies reported the number of people experiencing pain and this evidence also suggested a clinically important benefit in favour of alpha blockers (3 studies; n=240). In terms of colicky pain episodes, the evidence from one study suggested no clinical difference between interventions (1study; n=72). One study reported pain intensity measured by visual analogue scale and the evidence suggested a clinically important benefit in favour of no treatment (pain management only) (1 study; n=103). For reducing the number of people using analgesics, the average number of days of analgesic use, and the dose of analgesics (Diclofenac, Ketorolac and Pethidine), the evidence suggested a clinically important benefit in favour of alpha blockers (1-4 studies; n=64-301) but no clinical difference for average number of times analgesics were used or Buprenorphine dose (1-4 studies; 65-421). The quality of the evidence was Low to Very Low. The main reasons for downgrading the evidence were risk of bias, imprecision and inconsistency. One outcome for adverse events (headache) was downgraded for indirectness.

One study compared calcium channel blockers to placebo in adults with distal ureteric stones <10mm. This evidence suggested no clinical difference between interventions in terms of stone passage, time to stone passage, use of healthcare services (doctor, nurse or outpatient visits), hospitalisation and quality of life (1 study; n=113-535). For the outcome of

adverse events, the evidence suggested a clinical benefit in favour of placebo (1 study; n=315) For the outcomes of analgesic use and pain intensity, measured on the visual analogue scale and EQ-5D, the evidence suggested no clinically important difference between interventions (1 study; n=157-314). The quality of the evidence was High to Very Low. The main reasons for downgrading the quality of the evidence were risk of bias and imprecision.

Three studies compared calcium channel blockers versus no treatment in adults with distal ureteric stones <10mm. This evidence suggested a clinically important benefit in favour of calcium channel blockers for stone passage but no clinical difference for time to stone passage (1-3 studies; n=70-179). For reducing hospitalisations, the evidence suggested a clinically important benefit of calcium channel blockers (2 studies; n=129), but no clinical difference in the average number of pain episodes (1 study; n=70). For the outcome of adverse events, the evidence suggested no clinical difference in hypotension or dizziness (1 study; n=50-59). The evidence suggested a clinical benefit in favour of calcium channel blockers for reducing the dose of analgesic (Diclofenac) (1 study; n=50). The quality of the evidence was Moderate to Very Low. The main reason for downgrading the quality of the evidence was risk of bias. In addition, two outcomes for adverse events (hypotension) and pain intensity (pain episodes) were downgraded for imprecision.

Seven studies compared alpha blockers to calcium channel blockers in adults with distal ureteric stones <10mm and the evidence suggested a clinically important benefit in favour of alpha blockers for the outcome stone passage (7 studies; 4189). Two studies reported the outcome time to stone passage and this evidence suggested no clinical difference between alpha blockers and calcium channel blockers (2 studies; n=182). Reduction in the number of hospitalisations was reported by two studies and suggested a clinically important benefit in favour of alpha blockers (2 studies; n=133). For the outcome of hospitalisation in terms of excess admission days, there was no clinically important difference between alpha blockers and calcium channel blockers (1 study; n=493). For the outcomes of quality of life and use of healthcare services (doctor, nurse or outpatient visits) there was no clinically important difference between interventions (1 study; n=216-441). For the outcome of adverse events, the evidence suggested a clinically important benefit in favour of calcium channel blockers for dizziness and headache, and a clinically important benefit in favour of alpha blockers for adverse events leading to discontinuation, but no clinical difference for hypotension, flushing or unspecified adverse events (1-2 studies; n=63-3189). The evidence suggested a clinically important benefit in favour of alpha blockers for reducing the number of people using analgesia and the number of analgesic injections used, but no clinical difference in terms of days of analgesic use, analgesic dosage or the number of people using analgesia (1-2 studies; n=50-3497). One study reported reduction in the number of pain episodes and this evidence suggested a clinically important benefit of alpha blockers (1 study; n=70). The quality of the evidence was High to Very Low. The main reasons for downgrading the evidence were risk of bias and imprecision. In addition, two adverse event outcomes were downgraded for indirectness and two outcomes for stone passage and analgesic use were downgraded for inconsistency.

Mid ureteric stones

Two studies compared alpha blockers to placebo in adults with mid ureteric stones <10mm. This evidence suggested a clinically important benefit in favour of placebo for stone passage and time to stone passage (1-2 studies; n=21-126). The evidence suggested clinically important benefit of placebo for use of healthcare services in terms of nurse visits and hospitalisation (1 study; n=74-81). For the outcomes of doctor and outpatient visits, the evidence suggested no clinically important difference between interventions (1 study; n=74-85). For the outcome of quality of life, the evidence suggested a clinically important benefit of placebo in terms of the SF36 mental component summary but no clinical difference for the SF36 physical component summary or EQ-5D (1 study; n=50-56). For the outcomes of adverse events, the evidence suggested no clinically important difference between

interventions (1 study; n=63). For the outcomes of pain intensity (EQ-5D no pain/discomfort and extreme pain/discomfort) and analgesic use, the evidence suggested a clinically important benefit in favour of placebo (1 study; n=41-63), but no clinically important difference for pain intensity as measured on the visual analogue scale or EQ-5D moderate pain/discomfort (1 study; n=56-59).The quality of the evidence was Moderate to Very Low. The main reasons for downgrading the quality of the evidence were risk of bias and imprecision.

Two studies compared alpha blockers to no treatment (pain management only) in adults with mid ureteric stones <10mm. For the outcome of stone passage, the evidence showed a benefit of alpha blockers (2 studies; n=27). In terms of reducing the time to stone passage, the evidence also suggested a clinically important benefit in favour of alpha blockers (1 study; n=16). For reducing the average number of episodes of analgesic use, the evidence suggested a clinically important benefit in favour of alpha blocker (1 study; n=16). The quality of the evidence was Low to Very Low. The main reason for downgrading the quality of the evidence was risk of bias. In addition, the outcomes for stone passage and analgesic use were downgraded for imprecision.

One study compared calcium channel blockers to placebo in adults with mid ureteric stones <10mm. This evidence suggested a clinically important benefit of placebo for time to stone passage but no clinical difference between interventions for stone passage (n=24-84). For the outcomes of hospitalisation and use of healthcare services (doctor or nurse visits), the evidence suggested no clinically important difference between interventions (n=77-81), but for the outcome of use of healthcare services in terms of outpatient visits, the evidence suggested a clinically important benefit of calcium channel blockers (n=81). For adverse events and quality of life (SF36 mental component summary, and EQ-5D), the evidence suggested no clinical difference, but for the SF36 physical component summary of quality of life, the evidence suggested a clinically important benefit of placebo. For the outcome of pain intensity in terms of EQ-5D no pain/discomfort or extreme pain/discomfort, the evidence suggested a clinically important benefit of placebo (n=53). For the outcomes of adverse events, analgesic use and pain intensity in terms of EQ-5D moderate pain/discomfort, or as measured on the visual analogue scale, the evidence suggested no clinically important difference between interventions (n=36-59).The quality of the evidence was High to Very Low. The main reasons for downgrading the quality of the evidence were risk of bias and imprecision.

One study compared alpha blockers to calcium channel blockers in adults with mid ureteric stones <10mm. This evidence suggested a clinically important benefit of calcium channel blockers for stone passage but no clinical difference for time to stone passage (n=19-81). The evidence suggested a clinically important benefit of calcium channel blockers for use of healthcare services in terms of nurse and outpatient visits, but no clinical difference in terms of hospitalisation, doctor visits and quality of life (EQ-5D and the SF36 mental component summary of quality of life) (n=50-81). For the outcome of quality of life in terms of the SF36 physical component summary, the evidence suggested a clinically important benefit of alpha blockers (n=50). For the outcomes of adverse events, pain intensity and analgesic use, the evidence suggested no clinical difference between alpha blockers and calcium channel blockers (n=39-60). The quality of the evidence was High to Very Low. The main reasons for downgrading the quality of the evidence were risk of bias and imprecision.

Proximal ureteric stones

Two studies compared alpha blockers to placebo in adults with proximal ureteric stones <10mm. This evidence suggested no clinical difference between interventions for the outcomes of stone passage and time to stone passage (1-2 studies; n=23-257). For use of healthcare services in terms of outpatient visits, the evidence suggested a clinically important benefit of placebo, but in terms of hospitalisation, doctor and nurse visits, the evidence suggested no clinical difference between interventions (1 study; n=141-176). For the

outcomes of quality of life (SF36 mental component summary and EQ-5D), the evidence suggested no clinical difference, but in terms of the SF36 physical component summary, the evidence suggested a clinically important benefit of alpha blockers (1 study; n=84). For the outcomes of pain intensity in terms of EQ-5D no pain/discomfort, extreme pain/discomfort and analgesic use (pain medication use), the evidence suggested a clinically important benefit of alpha blockers (1 study; n=85). For the outcomes of adverse events and pain intensity in terms of EQ-5D moderate pain/discomfort, the evidence suggested a clinically important benefit of placebo (1 study; n=85-113). The evidence suggested no clinically important difference between interventions when analgesic use was measured by the number of days of pain medication use, and when pain intensity was measured on the visual analogue scale (1 study; n=74-111).The quality of the evidence was High to Very Low. The reasons for downgrading the quality of the evidence were risk of bias and imprecision.

Four studies compared alpha blockers to no treatment in adults with proximal ureteric stones <10mm. This evidence suggested a clinically important benefit in favour of alpha blockers for stone passage (4 studies; n=213). For reducing time to stone passage, the evidence also suggested a clinically important benefit in favour of alpha blockers (2 studies; n=133). The evidence suggested no clinical difference for outcomes of quality of life and analgesic use (1-2 studies; n=79-133). The quality of the evidence was Low to Very Low. The main reasons for downgrading the quality of the evidence were risk of bias and imprecision.

One study compared calcium channel blockers placebo in adults with proximal ureteric stones <10mm. This evidence suggested a clinically important benefit in favour of placebo for stone passage and adverse events, but no clinically important difference for time to stone passage (n=21-181). The evidence suggested a clinically important benefit of placebo for use of healthcare services in terms of outpatient visits, but for the outcomes of hospitalisation, doctor and nurse visits, and quality of life, the evidence suggested no clinically important difference between interventions (n=70-179). When analgesic use was measured as pain medication use, the evidence suggested a clinically important benefit of calcium channel blockers (n=97). For the outcomes of analgesic use (number of days of pain medication use) and pain intensity (as measured on the visual analogue scale and EQ-5D), the evidence suggested no clinical difference between interventions (n=74-97). The quality of the evidence was High to Very Low. The main reasons for downgrading the quality of the evidence were risk of bias and imprecision.

One study compared alpha blockers to calcium channel blockers in adults with proximal ureteric stones <10mm. This evidence suggested a clinically important benefit in favour of alpha blockers for stone passage but no clinically important difference for time to stone passage or adverse events (n=22-180). For the outcomes of quality of life, hospitalisation and use of healthcare services in terms of doctor, nurse and outpatient visits, the evidence suggested no clinically important difference between interventions (n=88-179). The evidence suggested a clinically important benefit of alpha blockers for pain intensity as measured on the visual analogue scale and EQ-5D no pain/discomfort, but a clinically important benefit of calcium channel blockers for moderate pain/discomfort (n=91-114). For the outcomes of analgesic use and pain intensity in terms of EQ-5D extreme pain/discomfort, the evidence suggested no clinically important difference between interventions (n=75-116). The quality of the evidence was High to Very Low. The main reasons for downgrading the quality of the evidence were risk of bias and imprecision.

Children

Two studies compared alpha blockers to placebo in children with distal ureteric stones <10mm. This evidence suggested a clinically important benefit in favour of alpha blockers for stone passage, time to stone passage and the number of pain episodes (2 studies; n=98). The evidence suggested a clinically important benefit in favour of placebo for headaches/dizziness, but no clinical difference between the interventions for headaches or hypotension (1 study; 1=37-61). The quality of the evidence was Low to Very Low. The main

reasons for downgrading the quality of the evidence were risk of bias and imprecision. In addition, outcomes for time to stone passage and pain intensity were downgraded for inconsistency.

Three studies compared alpha blockers to no treatment in children with distal ureteric stones <10mm. This evidence suggested a clinically important benefit in favour of alpha blockers for stone passage, time to stone passage and analgesic use (average number of episodes of analgesic use) (1-3 studies; n=63-147). The evidence suggested no clinical difference between interventions in terms of unspecified adverse events (2 studies; n=102). The evidence also suggested no clinical difference in average number of daily pain episodes (1 study; n=63). The quality of the evidence was Low to Very Low. The main reasons for downgrading the quality of the evidence were risk of bias and imprecision. In addition, the outcome for time to stone passage was downgraded for inconsistency.

MET as an adjunctive therapy to surgery

Distal ureteric stones

Five studies compared alpha blockers as adjunctive therapy to shock wave lithotripsy versus shock wave lithotripsy only in adults with distal ureteric stones <10mm. This evidence suggested a clinically important benefit in favour of alpha blockers for stone passage, but no clinical difference in time to stone passage (2-5 studies; n=207-383). For the outcome of adverse events, the evidence suggested a clinically important benefit of SWL only for dizziness, abnormal ejaculation and headache, but no clinical difference for hypotension (1-2 studies; n=67-206). For reducing hospitalisations, the evidence suggested a clinically important benefit in favour of alpha blockers (1 study; n=88). The evidence suggested a clinically important benefit in favour of alpha blockers for reducing analgesic use (average number of episodes of analgesic use and dose of Diclofenac) (1 study; n=88-119). The quality of the evidence was Low to Very Low. The main reasons for downgrading the quality of the evidence were risk of bias and imprecision. In addition, the outcomes for stone passage and analgesic use (dose of Diclofenac) were downgraded for indirectness.

One study compared alpha blockers as adjunctive therapy to shock wave lithotripsy versus shock wave lithotripsy only in adults with distal ureteric stones 10-12mm. This evidence suggested no clinical difference between interventions in terms of the time to stone passage or pain intensity measured by visual analogue scale(n=38). The quality of the evidence was Very Low. The main reasons for downgrading the quality of the evidence were risk of bias, indirectness and imprecision.

One study compared alpha blockers as adjunctive therapy to ureteroscopy versus ureteroscopy only in adults with distal ureteric stones <10mm. This evidence suggested a clinically important benefit in favour of alpha blockers for stone passage (n=98). The evidence also showed a benefit of alpha blockers for reducing length of hospital stay (n=98). The quality of the evidence was Moderate to Low. The main reasons for downgrading the quality of the evidence were risk of bias and imprecision.

One study compared alpha blockers as adjunctive therapy to ureteroscopy versus placebo and ureteroscopy in adults with distal ureteric stones <10mm. This evidence suggested a clinically important benefit in favour of alpha blockers for stone passage and reducing the number of people using analgesics (n=102). The evidence also suggested a clinically important benefit in favour of alpha blockers for reducing the average number of pain episodes (n=102). The quality of the evidence was Low to Very Low. The main reasons for downgrading the quality of the evidence were risk of bias and imprecision.

Mid ureteric stones

One study compared alpha blockers as adjunctive therapy to shock wave lithotripsy versus shock wave lithotripsy only in adults with mid ureteric stones 10-20mm. This evidence suggested no clinical difference between interventions in terms of the time to stone passage

or pain intensity measured by visual analogue scale (n=28). The quality of the evidence was Very Low. The main reasons for downgrading the quality of the evidence were risk of bias, indirectness and imprecision.

Proximal ureteric stones

Six studies compared alpha blockers as adjunctive therapy to shock wave lithotripsy versus shock wave lithotripsy only in adults with proximal ureteric stones <10mm. This evidence a clinically important benefit in favour of alpha blockers for stone passage (6 studies; n=405). The evidence also suggested a clinically important benefit in favour of alpha blockers in terms of outcomes for quality of life, emergency department visits, pain intensity (visual analogue scale and average number of pain episodes) and analgesic dose (Diclofenac) (1-6 studies; n=54-405), but no clinical difference in terms of the time to stone passage, hospitalisation or the number of people using analgesia (1-4 studies; n=54-320). For the outcome of adverse events, the evidence suggested no clinically important difference between interventions in terms of retrograde ejaculation or dizziness (1-2 studies; n=84-172). The quality of the evidence was Moderate to Very Low. The main reasons for downgrading the quality of the evidence were risk of bias and imprecision. In addition, outcomes for time to stone passage and pain intensity were downgraded for inconsistency, and analgesic use (in terms of the number of people using analgesia) was downgraded for inconsistency and indirectness.

Two studies compared alpha blockers as adjunctive therapy to shock wave lithotripsy versus shock wave lithotripsy only in adults with proximal ureteric stones 10-20mm. This evidence suggested a clinically important benefit in favour of alpha blockers for time to stone passage and stone passage, but no clinical difference in pain intensity (visual analogue scale) (1-2 studies; n=57). The quality of the evidence was Very Low. The main reasons for downgrading the quality of the evidence were risk of bias, indirectness and imprecision.

One study compared alpha blockers as adjunctive therapy to shock wave lithotripsy versus placebo and shock wave lithotripsy in adults with proximal ureteric stones <10mm. This evidence suggested a clinically important benefit in favour of alpha blockers for stone passage and time to stone passage (n=49). The quality of the evidence was Low. The main reasons for downgrading the quality of the evidence were risk of bias, indirectness and imprecision.

Two studies compared alpha blockers as adjunctive therapy to ureteroscopy versus ureteroscopy only in adults with proximal ureteric stones 10-20mm. This evidence suggested a clinically important benefit in favour of alpha blockers for stone passage (2 studies; n=254). For the outcomes of time to stone passage and hospitalisation, the evidence suggested no clinical difference between interventions (1-2 studies; n=89-165). The evidence suggested no clinical difference between interventions for dizziness, but a clinically important benefit in favour of alpha blockers for reducing the number of people experiencing pain episodes (1 study; n=89). The quality of the evidence was Moderate to Very Low. The main reasons for downgrading the quality of the evidence were risk of bias and imprecision.

1.7.2 Health economic evidence statements

- Interventions studied only in separate pairwise analyses:
  - One cost-utility analysis found that placebo was not cost effective compared to MET in people with symptomatic ureteric stones of ≤ 10 mm (ICER: £42,000 per QALY gained).
  - One cost-utility analysis found that Nifedipine was not cost effective compared to Tamsulosin in people with symptomatic ureteric stones of ≤ 10 mm (ICER: £43,500 per QALY gained)

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 time to stone passage, stone passage, use of healthcare services/hospitalisation, quality of life, and adverse events (hypotension, dizzy spells, falls, floppy iris, retrograde ejaculation, headaches, flushing) were the outcomes that were critical for decision-making. Pain intensity and analgesic use were also considered as an important outcome.

Evidence was reported for all of the critical and important outcomes.

1.8.1.2 The quality of the evidence

For the majority of evidence included in this review, the quality ranged from a GRADE rating of high to very low. This was due to lack of blinding, presence of selection bias, missing data and drop out, and risk of measurement 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 the presence of heterogeneity for some outcomes, further downgraded the quality of the evidence. It was also difficult to classify several studies according to the strata specified in the protocols, because the results were not stratified by stone size; for this reason, some of the evidence was downgraded for indirectness.

1.8.1.3 Benefits and harms

Evidence for people with both symptomatic and asymptomatic stones was searched for, however only 1 study included a population of people with asymptomatic stones, and this evidence suggested that there was no difference in the outcomes between people with symptomatic or asymptomatic stones. As there was no other evidence for people with asymptomatic stones, the committee were not confident that those with asymptomatic stones can be treated the same as those with symptomatic stones. They concluded that the recommendations should only apply to those with symptomatic stones.

It is important to note that the population that MET would be appropriate for would generally be people who were symptomatic but whose pain is not ongoing after treatment with analgesia.

Medication versus each other/placebo/no treatment

Distal ureteric stones <10mm

Alpha blockers

When alpha blockers were compared to placebo, the committee noted that there was a benefit of alpha blockers in terms of stone passage, time to stone passage, pain when measured as the number of people experiencing pain episodes, and analgesic use when measured as the number of people using analgesics during follow-up and average ketorolac or diclofenac dose. There was no difference between the groups in terms of all other pain and analgesic use outcomes, quality of life, use of healthcare services or hospitalisation. In terms of adverse events, there was a benefit of placebo in terms of unspecified adverse events, but no difference between interventions for all other outcomes. This suggests that alpha blockers are not associated with an increased risk of experiencing adverse effects.

When compared to no treatment (pain relief only), there was a benefit of alpha blockers in terms of stone passage and time to stone passage based on two meta-analyses of 32 and 18 studies respectively. There was also a benefit of alpha blockers in terms of

hospitalisation, and analgesic use (number of people using analgesics and average dose of analgesia). The committee noted that evidence from one study demonstrated a potential benefit of no treatment (pain relief only) in terms of pain intensity when measured on a visual analogue scale, but that this conflicted with other meta-analyses demonstrating a benefit of alpha blockers in terms of the number of pain episodes and the number of people experiencing pain. The committee considered that overall, there was some evidence that alpha blockers may have an analgesic effect as well as improving stone passage, which may have implications for the patient as well as from a resource use perspective, as it may reduce the amount of analgesia required. There was no difference between the interventions in terms of adverse events, which again demonstrated that alpha blockers are not associated with an increased risk of adverse effects. The committee agreed that this evidence suggests that there is a benefit of treating people with distal ureteric stones <10mm with alpha blockers compared to no treatment.

Calcium channel blockers

When compared to placebo, there was no difference between interventions in terms of stone passage or time to stone passage. There was no difference between the intervention in terms of quality of life, hospitalisation, use of healthcare services or any pain and analgesic use outcomes, but more people discontinued from the study due to adverse events in the calcium channel blocker group compared to placebo. The committee noted that this evidence was from a single study; however they did consider that this study is from the UK and has been influential in terms of shaping current practice.

When calcium channel blockers were compared to no treatment, there was a benefit of calcium channel blockers for stone passage, hospitalisation, and analgesic use (Diclofenac dose). There was no clinical difference between interventions in terms of time to stone passage or adverse events. The committee considered that compared to no treatment, there did seem to be a benefit of calcium channel blockers. When compared to placebo, the evidence was less convincing, but they committee noted that the evidence was from a single study.

Alpha blockers versus calcium channel blockers

The committee noted that there were more stones passed, fewer patients requiring hospitalisation, fewer people discontinuing due to adverse events, fewer diclofenac injections and fewer people using analgesia for those receiving alpha blockers, compared to calcium channel blockers. The committee noted that the group receiving calcium channel blockers experienced fewer episodes of dizziness and headaches, but there was no difference between the interventions in terms of other reported outcomes, such as time to stone passage, all other adverse events, quality of life, hospitalisation, use of healthcare services, and analgesic use in terms of length of use and dose. The committee considered that the only outcomes demonstrating a clinical benefit of calcium channel blockers over alpha blockers were dizziness and headaches, and agreed that these were not very serious adverse events. The committee discussed that the benefits of alpha blockers in terms of increased stone passage, less hospitalisation and less pain, outweighed the experience of dizziness and headache. The committee considered that these benefits would reduce requirements for pain medication and may reduce the need for surgical intervention.

The committee noted that current practice is partly based on the findings of the SUSPEND trial, a large UK study which showed no benefit of alpha blocker or calcium channel blockers when compared to placebo. They considered that this is the only UK study included in the review, and so may best represent UK practice and the UK population. However, they also noted that including this study in the analysis still led to an overall benefit of alpha blockers. Therefore they agreed that this single study does not outweigh the body of evidence suggesting that alpha blockers and calcium channel blockers may be beneficial, especially considering that there are no significant harms associated with either drug. The committee also considered that the strategy of the present review, as set out in the protocol, was to

stratify the population into three groups; less than 10mm, 10-20mm and more than 20mm. However, some evidence in this area has used smaller size subgroups, of less than 5mm and 5-10mm, and the evidence suggests that there may be differences between these smaller sub groups that this review was unable to assess. This means that there is uncertainty in terms of the population of stones that may derive benefit of alpha blockers which meant that the committee were not confident enough in the evidence to make a strong recommendation. Therefore they agreed that alpha blockers should be considered for people with small distal ureteric stones. The committee considered the evidence for calcium channel blockers and noted that although there did seem to be evidence of a benefit when compared to no treatment, there was no benefit when compared to placebo. They also considered that in the head-to-head comparison with alpha blockers, alpha blockers were favoured. As placebo-controlled evidence is commonly considered the gold standard in pharmacological studies, the committee agreed that more weight should be placed on this evidence, compared to the no treatment comparison. Based on this, the committee agreed not to recommend calcium channel blockers.

Mid ureteric stones <10mm

Alpha blockers

When compared to placebo, there was a harm of alpha blockers for stone passage, time to stone passage, some quality of life measures, hospitalisation and analgesic use. There was no difference between the intervention and placebo for use of healthcare services in terms of doctor and outpatient visits, but more nurse visits in those taking alpha blockers. There were also more people with extreme pain or discomfort, and less people with no pain or discomfort in those taking alpha blockers. However the committee noted concerns regarding the quality and limited evidence with only two studies with 126 participants found for this comparator.

Compared to no treatment (pain relief only), there was a benefit of alpha blockers for all of the reported outcomes, including stone passage, time to stone passage, and analgesic use. The committee noted that the evidence came from a very small single study of just 16 people, and was low and very low quality, and agreed that based on this, they did not have confidence in extrapolating this data to clinical practice.

Calcium channel blockers

When compared to placebo, there was no difference between interventions for stone passage or time to stone passage. There were less outpatient visits in those taking calcium channel blockers, but no difference in terms of hospitalisation, doctor or nurse visits. Those taking calcium channel blockers also had poorer quality of life scores, and more people had extreme pain or discomfort than the placebo group. The committee noted that this evidence came from a single study.

Alpha blockers versus calcium channel blockers

There was a benefit of calcium channel blockers for stone passage, nurse and outpatient visits, and a benefit of alpha blockers for the quality of life physical component score. There was no difference between interventions for use of healthcare services in terms of doctor visits. The committee discussed that this evidence was from a single study of 81 participants and some of the evidence was of low quality, and therefore they agreed that they did not have confidence in the findings.

The committee noted that much of the evidence for the mid ureteric stones population was of low or very low quality, and that all of the evidence came from a very small number of studies with very small participant numbers. The committee therefore agreed that there was a lack of sufficient convincing evidence to make a recommendation. The committee also discussed that this population would be a small number of cases in clinical practice, and that there is no consensus on how these stones should be treated. Based on this, the committee decided not to make a recommendation.

Proximal ureteric stones <10mm

Alpha blockers

When compared to placebo, there was no clinical difference between the two groups in terms stone passage or time to stone passage. In the alpha blockers group there were better quality of life scores on the physical component subscale, and less people reporting pain or discomfort, but there were more outpatient visits and discontinuations due to adverse events. There was no difference between the intervention and placebo for use of healthcare services in terms of doctor and nurse visits.

When compared to no treatment, there was a benefit of alpha blockers for stone passage and time to stone passage. There was no clinical difference for quality of life (EuroQoL) and analgesic use (mean number of times analgesics were used). The committee noted that the evidence involved a small number of participants.

Calcium channel blockers

When compared to placebo, there was a benefit of placebo for stone passage, fewer outpatient visits and discontinuation due to adverse events. Those taking calcium channel blockers reported less analgesia use, and there were no differences between the interventions for all other outcomes. The committee noted that the evidence came from a single study.

Alpha blockers versus calcium channel blockers

The committee noted that alpha blockers appeared to be more clinically effective than calcium channel blockers in terms of stone passage and some pain outcomes. However, there were more people with only moderate pain or discomfort in the calcium channel blockers group. There were no differences for all other outcomes. The committee considered that this evidence came from a single study and included some low quality evidence; therefore, the committee agreed that the evidence was not strong enough to draw conclusions from.

The committee noted that the majority of comparisons for this population were based on evidence from small studies or single studies. They discussed that the evidence for alpha blockers versus calcium channel blockers suggested a benefit of alpha blockers, and that there was a lot of uncertainty surrounding the outcomes due to low quality evidence and small participant numbers. They agreed that overall, there was a lack of convincing evidence, and so no recommendation could be made for this group.

Children and young people, distal ureteric stones <10mm

Alpha blockers

The committee considered the evidence for children, and noted that all of the evidence was for distal ureteric stones <10mm. When alpha blockers (tamsulosin and doxazosin) were compared to no treatment (pain management only), the evidence suggested a benefit of alpha blockers in terms of stone passage, time to stone passage and analgesic use but no difference between the groups in terms of the number of pain episodes and unspecified adverse events. The committee noted from clinical experience that children may spontaneously pass stones more easily than adults.

When compared to placebo, there was a benefit of alpha blockers in terms of stone passage, time to stone passage and the number of pain episodes. There was a benefit of placebo in terms of headaches/dizziness, but no difference between interventions for all other adverse events.

The committee also considered that current practice for alpha blockers is varied, but that they are considered much safer for children than calcium channel blockers. Overall, the

committee considered that this evidence suggests that conservative management is more likely to succeed with the use of alpha blockers, which may make the need for surgery less likely. The committee agreed that given the benefits of alpha blockers in terms of increasing stone passage and reducing the time to stone passage, as well as the potential analgesic effects and implications in terms of reducing the need for further intervention and no evidence of increased risk of harms, alpha blockers should be offered to children and young people with distal ureteric stones <10 mm.

MET as an adjunctive therapy to surgery

The committee considered the evidence for MET as an adjunctive therapy to surgery. It was noted that for all comparisons, the MET was alpha blockers, and there was no evidence for calcium channel blockers or other MET drugs. It was also noted that all of the evidence for MET as adjunctive was in an adult population, and there was no evidence for the paediatric population.

Distal ureteric stones <10mm

Alpha blockers as adjunctive to SWL versus SWL

When MET was adjunctive to SWL in people with stones less than 10mm, the committee noted that there was a benefit of alpha blockers as adjunctive to SWL for outcomes relating to stone passage, hospitalisation and pain, but a benefit of SWL alone for most adverse events outcomes. The committee considered that because the adverse events were not serious, the benefit of adjuvant alpha blockers in terms of stone passage outweighed the experience of such adverse events.

The committee agreed to make a recommendation to consider alpha blockers as adjuvant therapy when people are having SWL. This was because the added potential benefit of MET was potentially significant, and there was a lack of serious associated harms. Current practice for people with these stones is SWL without the use of MET, and therefore use of MET would be a change in practice.

Alpha blockers as adjunctive to URS versus URS

The committee also considered the evidence for alpha blockers as adjunctive to URS. The evidence demonstrated a benefit of alpha blockers as adjuvant to URS for stone passage and length of stay, compared to URS alone. The committee discussed that the evidence for stone passage was unusual, as it was agreed that when performing a URS most UK surgeons would either fragment the stones to fragments <2-3mm, which would be expected to pass, or remove all the fragments during the procedure. Therefore the committee agreed that the use of adjuvant alpha blockers is likely to add very little benefit to UK practice. They also considered that the evidence came from a single study of 98 people.

Alpha blockers as adjunctive to URS versus placebo + URS

Evidence also demonstrated a benefit of alpha blockers as adjuvant to URS when compared to placebo as adjuvant to URS, in terms of stone passage and pain related outcomes. The committee were concerned that the evidence was based on a single study and was low and very low quality. It was further noted that the study used a ballistic method during URS, rather than laser, which does not reflect UK practice and may make stone fragments more difficult to pass, therefore potentially overestimate the effect of alpha blockers.

Overall, the committee agreed that evidence for alpha blockers as adjunctive to URS (with or without placebo) was not convincing and not sufficient on which to base a recommendation. They considered that a research recommendation investigating the use of alpha blockers as adjunctive to URS may be beneficial in terms of providing high quality evidence to help address this gap in the evidence and inform future practice.

Distal ureteric stones 10-20mm

Alpha blockers as adjunctive to SWL versus SWL

The committee noted that evidence from a single study of 38 participants demonstrated no difference between the interventions. Further, this evidence was very low quality. Therefore the committee agreed that there was not convincing evidence of a benefit of adjuvant MET for people with 10-20mm stones, and decided not make a recommendation.

Mid ureteric stones 10-20mm

Alpha blockers as adjunctive to SWL versus SWL

There was evidence from one study in a population of mid ureteric stones. This study demonstrated no clinical difference between alpha blockers as adjunctive therapy to SWL and SWL only. The committee considered that this evidence came from a single study of 28 people, and was very low quality. The committee also considered that this was a small patient group and are not normally treated with SWL in UK clinical practice. They agreed that there was insufficient evidence to make a recommendation for this population.

Proximal ureteric stones <10mm

Alpha blockers as adjunctive to SWL versus SWL

When MET as adjunctive to SWL was compared to SWL alone in people with <10mm proximal ureteral stones, the committee noted a clinical benefit for alpha blockers for stone passage outcomes, quality of life outcomes, most pain outcomes, and use of healthcare services in terms of the number of ED visits at follow up. There was no clinical difference between interventions in terms retrograde ejaculation, dizziness, analgesic use and hospitalisation. The committee considered that the two adverse events are not serious and would not outweigh the benefits of increased stone passage and improved pain and quality of life.

Overall, the committee considered that the evidence for stone passage came from a number of studies and was of moderate quality; this was a key outcome of success and would lead to reduced downstream resource use. The benefits of the treatment were also thought to far outweigh any minor risks, therefore the committee made a consider recommendation for ureteric stones <10mm.

Alpha blockers as adjunctive to SWL versus placebo + SWL

When alpha blockers adjuvant to SWL was compared to placebo + SWL, the evidence demonstrated a clinical benefit for alpha blockers in terms of stone passage and time to stone passage. Although the evidence came from a single study, the committee noted that this supported the evidence for the comparison of alpha blockers adjuvant to SWL versus SWL alone.

Proximal ureteric stones 10-20mm

Alpha blockers as adjunctive to SWL versus SWL

Alpha blockers as adjuvant to SWL were also compared to SWL alone in people with 10-20mm stones. For this comparison the committee noted that the evidence was not conclusive. Although there was a clinical benefit of alpha blockers in terms of time to stone passage and stone passage, there was no difference between interventions in terms of pain. The committee noted that this was based on single studies and very low quality evidence. They agreed not to make a recommendation for alpha blockers as adjunctive to SWL for this stone size.

Alpha blockers as adjunctive to URS versus URS

When alpha blockers as adjuvant to URS were compared to URS alone in people with stones between 10-20mm, the committee noted that there was conflicting evidence. There was a suggested benefit of alpha blockers for stone passage and colic episodes, but no difference in terms of time to stone passage and outcomes relating to hospitalisation. The committee considered the evidence and discussed that usually during URS, the surgeon either removes all residual stones, or breaks them down to <2-3mm fragments to pass spontaneously. Therefore alpha blockers may increase the passage rate of residual stones when the latter method is used. The committee considered that although alpha blockers may be beneficial in terms in reducing the need for pain relief and increasing passage of residual stones, most of the evidence was from single studies, which limited the degree of confidence the committee could place in the results.

The committee agreed that as with the <10mm group, the evidence for MET as an adjunct to URS was not considered sufficient to make recommendations, and is not commonly used in current practice, so a research recommendation would be beneficial to inform future practice. They agreed that the research recommendation should include all stones less than 20 mm, and include any location within the ureter.

1.8.2 Cost effectiveness and resource use

One cost utility analysis (Pickard 2015) was identified from the literature and presented to the committee. This was a within trial, cost utility analysis based on SUSPEND, an RCT conducted in the UK, that compared two medical expulsive therapies (tamsulosin or nifedipine) to each other and then combined the groups to compare medical expulsive therapy, in general, to placebo. There was no economic evidence identified for the use of medical expulsive therapy as adjunctive to surgery.

The study was assessed as directly applicable, as it was a UK cost utility analysis taking the NHS perspective. The study also reported values of health effects expressed in terms of QALYs and used EQ-5D data collected directly from patients. The study was rated as having potentially serious limitations because the time horizon was only the 12 week period of the RCT and no extrapolation of study results took place beyond that period; so effects and costs from any stones that might have needed treatment after this period wouldn't be captured by the analysis. Also, the estimates of relative treatment effects and resource use were not derived from a systematic literature review but from the study effectiveness data and records.

The study found that the use of medical expulsive therapy was associated with cost savings but also less QALYs (only slightly, so a negligible difference in QALYs). The cost savings are because the resource use involved in the MET group was overall lower (e.g. admission days, interventions undertaken), and is consistent with what we would think about the intervention, because if more people are passing their stone with MET, then there is less downstream resource use being consumed, such as time in hospital or other interventions.

We can change round the comparators for ease of interpretation of the ICER, so the more expensive and effective alternative (placebo – with its slightly higher QALYs) is compared to the less effective alternative (MET). This shows that the use of placebo compared to medical expulsive therapy was not cost effective (ICER of £42,000), therefore the alternative of medical expulsive therapy is a cost effective option because we are only comparing two alternatives, so if placebo is not cost effective according to the NICE threshold then that means the comparator is the cost effective choice. In effect, the placebo strategy involved more resource use overall (making it more costly), and there was a negligible difference in quality of life between the two strategies. When comparing tamsulosin to nifedipine, the study also found that tamsulosin was associated with cost savings but also less QALYs (again a negligible difference in QALYs). Tamsulosin was a cost effective option compared to nifedipine. The study results were sensitive to any changes in QoL values.

The Pickard study was included in the clinical review, and provided a conservative estimate of medical expulsive therapy's effectiveness when compared to the other studies pooled in the review for the stone passage of alpha blockers versus placebo. The point estimate was very close to the no difference line, while the pooled estimate was further on the left, favouring alpha blockers. Higher effectiveness of alpha blockers could impact cost effectiveness of medical expulsive therapy compared to placebo, making the choice of alpha blockers (MET) even more cost effective than what the Pickard study estimated. The committee agreed that the magnitude of cost effectiveness of medical expulsive therapy compared to placebo is likely to be higher than the Pickard study demonstrated if the effectiveness of alpha blockers is in fact higher.

Unit costs of the interventions identified from the clinical review divided into alpha blockers and calcium blockers were presented using BNF prices and doses from clinical review data. Costs were presented monthly because from the trials people tended to take MET for around 4 weeks (although the committee noted that 2 weeks is also used in practice). The drug formulation was that of modified release tablets or capsules with alpha blockers represented by more drug options and calcium channel blockers represented only by nifedipine. There were differences between drug prices between the two categories and an attempt to identify the most and least expensive drug from the unit costs data was made; doxazosin (alpha blocker) was found to be the cheapest option and alfuzosin (alpha blocker) the most expensive one among alpha blockers. The GC members highlighted that the most commonly prescribed alpha blocker, tamsulosin was shown to be less expensive than nifedipine in the capsules formulation, but more expensive as a tablet.

Resource impact data were also presented, using an average monthly cost of medical expulsive therapy of £10.65 (similar to the tamsulosin tablet monthly cost), and the population with ureteric stones from HES hospital admitted activity 2015-16 data (calculus of ureter finished consultant episodes; 24,589). Even at the extreme scenario of medical expulsive therapy that would be recommended for use for all the people diagnosed with ureteric stones at hospitals, the resource impact wasn't expected to meet the NICE threshold of 'significant', as the results showed that the annual NHS spending would be around £262,000. The data from HES may well underestimate the population with ureteric stones because there may be people coping with their stone who haven't been admitted to hospital, but on the other hand the HES data is probably a mix of stone sizes whereas the recommendations are mainly for smaller stone size groups.

Passing the stone earlier will also have a QoL improvement, as an individual does not have a stone anymore (e.g. if pass a stone at 2 weeks instead of 4 weeks then that is an extra 2 weeks where the individual has returned to their normal QoL level). The time to stone passage for alpha blockers versus placebo was also shown to be clinically significant. The issue around short term pain and any associated improvement in quality of life from passing a stone earlier (or conversely the loss in quality of life from having a stone for a few more days if they didn't have MET to pass the stone earlier) was discussed. An ICER example was provided using data from the clinical review showing MET (alpha blockers specifically) would help you pass your stone on average 4 days quicker (given 4 weeks of treatment costing around £10); using quality of life data derived from the Health Survey for England 2014 as the utility level for those who don't have a stone (0.874), and the utility of patients with stones was from baseline data in the Pickard study (0.684 –(EQ-5D)). This showed that helping you pass your stone 4 days earlier would have an ICER of around £5,000. This is cost effective taking into account only a few days of pain avoided, and this is because the drug is so cheap. It was highlighted that avoiding pain of short duration wasn't expected to contribute a significant improvement in the quality of life for people achieving stone passage, therefore the committee agreed with the incremental QALY estimates presented that were very small. Discussion indicated that in practice the cheapest drug is likely to be given, which is Tamsulosin in a capsule form, and is much cheaper than the tablet form (£4 a month versus £10 a month respectively), therefore the estimates used above are likely to be overestimates.

The above example has only taken into account the people who would pass their stone *quicker* with the drug, but not the large proportion of people who would pass their stone if they used MET (compared to if they didn't), and what downstream treatment they could therefore avoid. The committee recognised that the use of MET could contribute in avoiding further downstream costs, such as surgery, from more people that passed their stone using MET.

More specifically; using as a reference point the clinical review data for the stone passage achieved with alpha blockers compared to no treatment for distal ureteric stones <10mm in adults (Table 4 in the evidence report);

- 327 more patients per 1000 that used alpha blockers passed their stones compared to the no treatment group.
- It was assumed otherwise these 327 patients would undergo a lithotripsy (a conservative estimate, as some of the patients would undergo URS that is more costly, but some patients given more time may just pass the stone and not need treatment).
- Therefore the cost from the interventions avoided considering a unit cost of £452 for an SWL session, were estimated to be £452 x 327 = £147,084.This is a conservative estimate considering only the cost of the intervention, without any retreatment or ancillary procedure cost needed for an unsuccessful first lithotripsy.
- The cost of providing alpha blockers for 1 month for 1000 people, to avoid the 327 lithotripsies, would be around £10,000 (a conservative estimate assuming a cost of the drug of £10 a month, but this could be less as mentioned in the previous paragraph).
- This makes an overall incremental saving from those additional people passing their stone with MET equal to £147,084 – £10,000 = £137,084 for every 1,000 people that medical expulsive therapy is provided for.

This saving would actually allow MET to be provided to over 13,000 people. The committee were confident that this recommendation has potential to be a cost saving recommendation because of the costs offset. Not everyone in the under 10mm stone size group would go on to need an intervention to clear their stone as some may pass spontaneously with more time. The Pickard study reported that for the placebo arm the proportion requiring no further intervention at 4 weeks was 86% in the <=5mm group and 61% in the >5mm group. Breaking this down even further by size was not possible but committee opinion was that stones of between 4-7mm are the ones where clinicians would be uncertain if they would pass, and <4mm would be given more time to pass and >7mm would usually require intervention. If treating 1000 people with MET costs £10,000, then this only has to avoid 22 sessions of SWL (which would be for 2.5% of the 1000 people (assuming one session per person)) or around 5 URS's to make the intervention cost neutral. This is likely to be achievable given the low numbers, and so even if only a proportion of people go on to avoid treatment it is still likely that MET is cost saving.

The above is an illustrative calculation which is rather simplistic. As well as the interventions unit costs, the cost of other resources should be considered; such as appointments with staff including GPs and consultants, for review of medication therapy and any monitoring of adverse events. Additionally, the clinical review showed that MET was associated with fewer hospitalisations when compared to no treatment. MET had more adverse events, but mainly dizziness and headache, which the committee considered to be minor adverse events.

Used as an adjunct to surgery, alpha blockers were also shown to be effective at improving stone passage, which means further treatments could be avoided.

The committee agreed that MET is likely to be a cost effective if not cost saving treatment. However, the committee discussed that although for pragmatism the guideline clinical review broke down the stone subgroups into 10mm, new evidence in the field has sub grouped by

smaller gradations (<5mm, and 5-10mm). Given the uncertainty around the effectiveness of MET in these smaller subgroups, the committee were not confident enough in the evidence to make a strong recommendation, and thus recommended that alpha blockers be considered for adults and children with distal ureteric stones less than 10mm. a consider recommendation was also made for alpha blockers as an adjunct to SWL.

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A recommendation on nifedipine for adults was also discussed, but the committee felt that only the no treatment comparison showed effect, and not the placebo controlled trials. Although no treatment would be the real life comparison, and placebo is acknowledged to have an effect, the criteria that is commonly followed with pharmacological treatments is for placebo controlled trials to be the gold standard of proving efficacy. And as that isn't the case for calcium channel blockers, the committee felt that the intervention didn't meet the criteria of being effective that has been applied to alpha blockers for example.

1.8.3 Other factors the committee took into account

The committee noted that both alpha blockers and calcium channel blockers are not licensed specifically for renal stones, but they are licensed for other conditions. Alpha blockers are mainly used for men with symptomatic lower urinary tract symptoms and the management of acute retention of urine, with some also indicated for hypertension. Calcium channel blocker nifedipine is primarily licensed for Raynaud's syndrome. Alpha blockers and calcium channel blockers are not licensed for children.

The committee noted that the evidence included studies that used Silodosin, and that this is not available in the UK.

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Appendices

Appendix A: Review protocols

Table 29: Review protocol: Medical expulsive therapy

Field	Content
Review question	Is medical expulsive therapy clinically and cost-effective in managing people with ureteric 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 determine whether medical expulsive therapy enhances stone passage in people with ureteric stones. Key issues and questions from the scope: 2 Pharmacological management of symptomatic renal and ureteric stones (for example, non-steroidal anti-inflammatory drugs, opioids and alpha-blockers). 2.1 What are the most clinical and cost-effective drugs for managing symptomatic renal or ureteric stones? 4 Managing asymptomatic renal and ureteric stones. 4.1 What is the most clinically and cost-effective management (surgical and non-surgical) of asymptomatic renal and ureteric stones?
Eligibility criteria – population / disease / condition / issue / domain	People (adults, children and young people) with symptomatic and asymptomatic ureteric stones
Eligibility criteria – intervention(s) / exposure(s) / prognostic factor(s)	Medical expulsive therapy: • Alpha blockers (Tamsulosin, Alfuzosin, Doxazosin, Naftopidil, Silodosin, Terazosin) • Calcium channel blocker (Nifedipine)
Eligibility criteria – comparator(s) / control or reference (gold) standard	Compared to: • Each other • Placebo • No treatment • Steroids
Outcomes and prioritisation	Critical outcomes: • Time to stone passage • Stone passage • Use of healthcare services/Hospitalisation • Quality of life • Adverse events (hypotension, dizzy spells, falls, floppy iris, retrograde ejaculation, headaches, flushing) Important outcomes: • Pain intensity (visual analogue scale, verbal ratings, descriptive scales, time to pain relief, need to rescue medication) • Analgesic use
Eligibility criteria – study design	Randomised controlled trials (RCTs), systematic reviews of RCTs. If no RCT evidence is available, non-randomised comparative studies, prospective and retrospective search for observational studies.

Field	Content
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:
	• Population
	  ○ Adults (≥16 years)
	  ○ Children and young people (<16 years)
	• Stone size:
	  ○ <10 mm
	  ○ 10-20 mm
	  ○ >20 mm
	• Stone site:
	  ○ Distal ureteric stone
	  ○ Mid ureteric stone
	  ○ Proximal ureteric stone
	Subgroups:
	• 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 were performed using Cochrane Review Manager (RevMan5). GRADEpro was 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

Field	Content
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. [Consider exploring publication bias for review questions where it may be more common, such as pharmacological questions, certain disease areas, etc. Describe any steps taken to mitigate against publication bias, such as examining trial registries.]
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 30: 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.[145] **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 31: Database date parameters and filters used

Database	Dates searched	Search filter used
Medline (OVID)	1946 – 21 March 2018	Exclusions Randomised controlled trials Systematic review studies Observational studies
Embase (OVID)	1974 – 21 March 2018	Exclusions Randomised controlled trials Systematic review studies Observational studies
The Cochrane Library (Wiley)	Cochrane Reviews to 2018 Issue 3 of 12 CENTRAL to 2018 Issue 2 of 12 DARE, and NHSEED to 2015 Issue 2 of 4 HTA to 2016 Issue 2 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.	(expuls* adj3 (therap* or treatment* or intervention*)).ti,ab.
28.	((calculus or calculi or stone*) adj3 (expuls* or pass*)).ti,ab.
29.	exp Adrenergic alpha-Antagonists/ or exp Adrenergic alpha-1 Receptor Antagonists/ or exp Adrenergic alpha-2 Receptor Antagonists/
30.	(alpha* adj3 blocker*).ti,ab.
31.	(tamsulosin or alfuzosin or doxazosin).ti,ab.
32.	(Positam or Contiflo or Diffundox or Faramsil or Flectone or Flomax or Flomaxtra or Galebon or Losinate or Pamsvax or Petyme or Pinexel or Prosurin or Tabphyn or Tamfrex or Tamurex or Combodart or Urimax or Vesomni or Besavar or Uroxatral or Xatral or Fuzatal or Varsan or Larbex or Cardozin or Cardura or Doxadura or Raporsin or Slocinx).ti,ab.
33.	exp Calcium Channel Blockers/
34.	(calcium channel blocker* or c-channel blocker* or Ca channel blocker* or CCB).ti,ab.
35.	exp Nifedipine/
36.	nifedipine.ti,ab.
37.	(Adalat or Adipine or Calchan or Coracten or Cordipin or Cordipine or Corinfar or Fenigidin or Fortipine or Korinfar or Nifangin or Nifedipress or Nimodrel or Procardia or Tenif or Tensipine or Valni or Vascard).ti,ab.
38.	or/27-37
39.	26 and 38
40.	randomized controlled trial.pt.
41.	controlled clinical trial.pt.

42.	randomi#ed.ti,ab.
43.	placebo.ab.
44.	randomly.ti,ab.
45.	Clinical Trials as topic.sh.
46.	trial.ti.
47.	or/40-46
48.	39 and 47
49.	Meta-Analysis/
50.	exp Meta-Analysis as Topic/
51.	(meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
52.	((systematic* or evidence*) adj3 (review* or overview*)).ti,ab.
53.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
54.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
55.	(search* adj4 literature).ab.
56.	(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.
57.	cochrane.jw.
58.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
59.	or/49-58
60.	39 and 59
61.	Epidemiologic studies/
62.	Observational study/
63.	exp Cohort studies/
64.	(cohort adj (study or studies or analys* or data)).ti,ab.
65.	((follow up or observational or uncontrolled or non randomi#ed or epidemiologic*) adj (study or studies or data)).ti,ab.
66.	((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys* or cohort* or data)).ti,ab.
67.	Controlled Before-After Studies/
68.	Historically Controlled Study/
69.	Interrupted Time Series Analysis/
70.	(before adj2 after adj2 (study or studies or data)).ti,ab.
71.	or/61-70
72.	exp case control study/
73.	case control*.ti,ab.
74.	or/72-73
75.	71 or 74
76.	Cross-sectional studies/
77.	(cross sectional and (study or studies or review or analys* or cohort* or data)).ti,ab.
78.	or/76-77
79.	71 or 78
80.	71 or 74 or 78
81.	39 and 80
82.	48 or 60
83.	81 or 82

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.	(expuls* adj3 (therap* or treatment* or intervention*)).ti,ab.
26.	((calculus or calculi or stone*) adj3 (expuls* or pass*)).ti,ab.
27.	exp alpha adrenergic receptor blocking agent/ or exp alpha 1 adrenergic receptor blocking agent/ or exp alpha 2 adrenergic receptor blocking agent/
28.	(alpha* adj3 blocker*).ti,ab.
29.	(tamsulosin or alfuzosin or doxazosin).ti,ab.
30.	(Flomax or Flomaxtra or Urimax or Besavar or Uroxatral or Xatral or Cardozin or Cardura or Doxadura or Raporsin or Slocinx).ti,ab.
31.	exp calcium channel blocking agent/
32.	(calcium channel blocker* or c-channel blocker* or Ca channel blocker* or CCB).ti,ab.
33.	exp nifedipine/
34.	nifedipine.ti,ab.
35.	(Adalat or Adipine or Calchan or Coracten or Cordipin or Cordipine or Corinfar or Fenigidin or Fortipine or Korinfar or Nifangin or Nifedipress or Nimodrel or Procardia or Tensipine or Valni or Vascard).ti,ab.
36.	or/25-35
37.	24 and 36
38.	random*.ti,ab.
39.	factorial*.ti,ab.
40.	(crossover* or cross over*).ti,ab.

41.	((doubl* or singl*) adj blind*).ti,ab.
42.	(assign* or allocat* or volunteer* or placebo*).ti,ab.
43.	crossover procedure/
44.	single blind procedure/
45.	randomized controlled trial/
46.	double blind procedure/
47.	or/38-46
48.	37 and 47
49.	systematic review/
50.	meta-analysis/
51.	(meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
52.	((systematic* or evidence*) adj3 (review* or overview*)).ti,ab.
53.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
54.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
55.	(search* adj4 literature).ab.
56.	(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.
57.	cochrane.jw.
58.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
59.	or/49-58
60.	37 and 59
61.	Clinical study/
62.	Observational study/
63.	family study/
64.	longitudinal study/
65.	retrospective study/
66.	prospective study/
67.	cohort analysis/
68.	follow-up/
69.	cohort*.ti,ab.
70.	68 and 69
71.	(cohort adj (study or studies or analys* or data)).ti,ab.
72.	((follow up or observational or uncontrolled or non randomi#ed or epidemiologic*) adj (study or studies or data)).ti,ab.
73.	((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys* or cohort* or data)).ti,ab.
74.	(before adj2 after adj2 (study or studies or data)).ti,ab.
75.	or/61-67,70-74
76.	exp case control study/
77.	case control*.ti,ab.
78.	or/76-77
79.	75 or 78
80.	cross-sectional study/
81.	(cross sectional and (study or studies or review or analys* or cohort* or data)).ti,ab.
82.	or/80-81

83.	75 or 82
84.	75 or 78 or 82
85.	37 and 84
86.	48 or 60
87.	85 or 86

Cochrane Library (Wiley) search terms

#1.	MeSH descriptor: [Urolithiasis] explode all trees
#2.	(nephrolitiasis or nephrolith or nephroliths or urolithias?s or ureterolithias?s):ti,ab
#3.	((renal or kidney* or urinary or ureter* or urethra*) near/3 (stone* or calculi or calculus or calculosis or lithiasis or c?olic*)):ti,ab
#4.	stone disease*:ti,ab
#5.	((calculi or calculus or calcium oxalate or cystine) near/3 (crystal* or stone* or lithiasis)):ti,ab
#6.	(or #1-#5)
#7.	(expuls* near/3 (therap* or treatment* or intervention*)):ti,ab
#8.	((calculus or calculi or stone*) near/3 (expuls* or pass*)):ti,ab
#9.	MeSH descriptor: [Adrenergic alpha-Antagonists] explode all trees
#10.	MeSH descriptor: [Adrenergic alpha-1 Receptor Antagonists] explode all trees
#11.	MeSH descriptor: [Adrenergic alpha-2 Receptor Antagonists] explode all trees
#12.	(alpha* near/3 blocker*):ti,ab
#13.	(tamsulosin or alfuzosin or doxazosin):ti,ab
#14.	(Cositam or Contiflo or Diffundox or Faramsil or Flectone or Flomax or Flomaxtra or Galebon or Losinate or Pamsvax or Petyme or Pinexel or Prosurin or Tabphyn or Tamfrex or Tamurex or Combodart or Urimax or Vesomni or Besavar or Uroxatral or Xatral or Fuzatal or Varsan or Larbex or Cardozin or Cardura or Doxadura or Raporsin or Slocinx):ti,ab
#15.	MeSH descriptor: [Calcium Channel Blockers] explode all trees
#16.	(calcium channel blocker* or c-channel blocker* or Ca channel blocker* or CCB):ti,ab
#17.	MeSH descriptor: [Nifedipine] explode all trees
#18.	nifedipine:ti,ab
#19.	(Adalat or Adipine or Calchan or Coracten or Cordipin or Cordipine or Corinfar or Fenigidin or Fortipine or Korinfar or Nifangin or Nifedipress or Nimodrel or Procardia or Tenif or Tensipine or Valni or Vascard):ti,ab
#20.	(or #7-#19)
#21.	#6 and #20

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 32: Database date parameters and filters used

Database	Dates searched	Search filter used
Medline	2014 – 9 March 2018	Exclusions Health economics studies

Database	Dates searched	Search filter used
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/

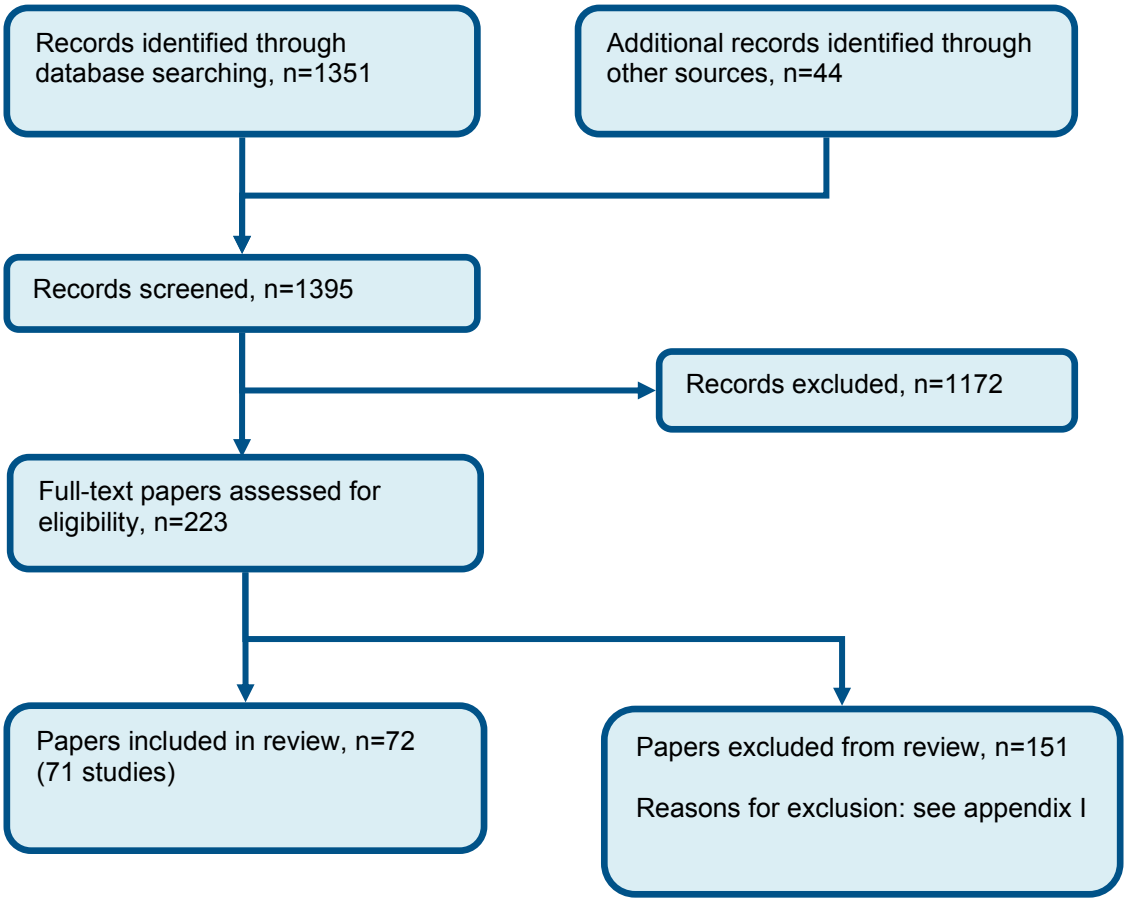
30.	funding/
31.	budget*.ti,ab.
32.	cost*.ti.
33.	(economic* or pharmaco?economic*).ti.
34.	(price* or pricing*).ti,ab.
35.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
36.	(financ* or fee or fees).ti,ab.
37.	(value adj2 (money or monetary)).ti,ab.
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 medical expulsive therapy



Appendix D: Clinical evidence tables

Study	Abdelaziz 2017[3]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=98)
Countries and setting	Conducted in Saudi Arabia; Setting: not reported
Line of therapy	Adjunctive to current care
Duration of study	Intervention + follow up: 1 week + 2 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: medical history, physical examination and laboratory investigations, abdominal x-rays for KUB, urinary ultrasonography, intravenous urography and/or abdominal computed tomography
Stratum	Adults (≥16 years), ureteric stone <1 cm: NA
Subgroup analysis within study	Not applicable: NA
Inclusion criteria	≥18 years; single, radio opaque, lower ureteral stone, 5-10mm in maximum diameter
Exclusion criteria	pregnant women; history of endoscopic or open ureteral surgery, persistent renal pain; urinary tract infection; renal impairment; solitary kidney; bilateral ureteral stones; high grade hydronephrosis; hypersensitivity to alpha-blockers
Recruitment/selection of patients	consecutive patients meeting the inclusion criteria during recruitment period
Age, gender and ethnicity	Age - Mean (SD): 36.27 (6.7). Gender (M:F): 64/34. Ethnicity: not reported
Further population details	1. Kidney pole: Not applicable 2. Neuropathic/ cerebral-palsy /immobility: Not applicable 3. Obesity /skin-to-stone distance: Not applicable 4. Pregnant women: Non-pregnant 5. Stone composition/hounsfield units: Not applicable 6. Ureteric stone: Lower ureteric stones
Indirectness of population	No indirectness: NA
Interventions	(n=51) Intervention 1: Alpha blockers and URS. Tamsulosin 0.4mg daily before URS. Duration 1 week. Concurrent medication/care: ureterorenoscopy and NSAIDs. Indirectness: No indirectness; Indirectness comment: NA (n=47) Intervention 2: Surgery - URS. URS. Duration procedure time. Concurrent medication/care: NSAIDs. Indirectness: No indirectness; Indirectness comment: NA

Funding	No funding
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: ALPHA BLOCKERS AND URS versus URS Protocol outcome 1: Hospitalisation/ Use of healthcare services - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: length of stay at during Hospitalisation; Group 1: mean 1.2 days (SD 0.6); n=51, Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: no significant differences in age, sex, stone location (left/right) or size; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 2: Stone passage - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: stone free rate at 2 weeks ; Group 1: 48/51, Group 2: 41/47 Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: no significant differences in age, sex, stone location (left/right) or size; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Quality of life; Adverse events; Pain intensity; Analgesic use; Time to stone passage

Study	Abdel-Meguid 2010[1]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=150)
Countries and setting	Conducted in Saudi Arabia; Setting: Department of Urology, University Hospital
Line of therapy	1st line
Duration of study	Intervention + follow up: 4 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Adults (≥16 years), ureteric stone <1 cm
Subgroup analysis within study	Not applicable
Inclusion criteria	>18 years; single, unilateral, newly diagnosed, 4-10mm in transverse diameter, distal ureteral stones; in paired kidneys patients with minimal or no ipsilateral hydronephrosis, normal contralateral kidney and normal overall renal functions; stones evident in either KUB x-ray or ultrasonography or both
Exclusion criteria	history of ipsilateral ureteral endoscopic or surgical manipulations or ESWL; patients with symptomatic urinary tract infections; pregnant or lactating women; patients already receiving alpha blockers, beta blockers, calcium channel antagonists or corticosteroids; patients with serious medical conditions
Recruitment/selection of patients	not reported
Age, gender and ethnicity	Age - Median (range): Group A 36 years (19-72), Group B 34 years (20-67). Gender (M:F): 103/47. Ethnicity: not reported
Further population details	1. Kidney pole: Not applicable 2. Neuropathic/ cerebral-palsy /immobility: Not applicable 3. Obesity /skin-to-stone distance: Not applicable 4. Pregnant women: Non-pregnant 5. Stone composition/hounsfield units: Not applicable 6. Ureteric stone: Lower ureteric stones
Indirectness of population	No indirectness
Interventions	(n=75) Intervention 1: Alpha blockers - Tamsulosin. Tamsulosin 0.4mg oral tablets once daily. Duration up to 4 weeks. Concurrent medication/care: hydration and analgesia (diclofenac 100mg) as needed, patients with non-symptomatic urinary tract infections were given antibiotics. Indirectness: No indirectness (n=75) Intervention 2: Placebo. Placebo. Duration up to 4 weeks. Concurrent medication/care: hydration and analgesia (diclofenac 100mg) as needed, patients with non-symptomatic urinary tract infections were given antibiotics. Indirectness: No indirectness
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: TAMSULOSIN versus PLACEBO

Protocol outcome 1: Stone passage
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: spontaneous stone passage at 4 weeks ; Group 1: 61/75, Group 2: 42/75
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 ; Baseline details: comparable for sex, age and stone size ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 2: Pain intensity
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: episodes of renal colic at 4 weeks ; Group 1: 20/75, Group 2: 58/75
Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: comparable for sex, age and stone size ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcomes not reported by the study	Quality of life; Time to stone passage; Adverse events; Analgesic use ; Hospitalisation/ Use of healthcare services

Study	**Agrawal 2009[6]**
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=102)
Countries and setting	Conducted in India; Setting: Not reported
Line of therapy	1st line
Duration of study	Follow up (post intervention): 4 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Plain x-rays of the abdomen, ultrasonography of the urinary system, intravenous urography and non-contrast CT in selected patients
Stratum	Adults (≥16 years), ureteric stone <1 cm
Subgroup analysis within study	Not applicable
Inclusion criteria	Patients presenting with stone <1cm in size located in the distal part of the ureter (juxtavesical part and ureterovesical junction)
Exclusion criteria	Urinary tract infection, sever hydroureteronephrosis, diabetes mellitus, multiple stones, hypotension, pregnancy, previous spontaneous stone expulsion, distal ureteral surgery and history of intake of any of the following: warfarin, α-adrenergic blockers, calcium antagonist, steroids, cimetidine

Recruitment/selection of patients	Not reported
Age, gender and ethnicity	Age - Range: 15-60. Gender (M:F): 78/24. Ethnicity: Not reported
Further population details	1. Kidney pole: Not applicable 2. Neuropathic/ cerebral-palsy /immobility: Not stated / Unclear 3. Obesity /skin-to-stone distance: Not stated / Unclear 4. Pregnant women: Not stated / Unclear 5. Stone composition/hounsfield units: Not stated / Unclear 6. Ureteric stone: Lower ureteric stones
Indirectness of population	No indirectness
Interventions	(n=68) Intervention 1: Alpha blockers - Tamsulosin. Tamsulosin once daily 0.4mg or 10mg alfuzosin once daily. Duration 4 weeks. Concurrent medication/care: Instructions to drink at least 3 L of fluids daily, diclofenac injection (75mg) intramuscularly on demand for pain relief. Indirectness: No indirectness (n=34) Intervention 2: Placebo. Placebo. Duration 4 weeks. Concurrent medication/care: Instructions to drink at least 3 L of fluids daily, diclofenac injection (75mg) intramuscularly on demand for pain relief. Indirectness: No indirectness
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: TAMSULOSIN/ALFUZOSIN versus PLACEBO

Protocol outcome 1: Stone passage at Define
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: Stone expulsion at 4 weeks; Group 1: 52/68, Group 2: 12/34
Risk of bias: All domain - High, Selection - High, Blinding - Low, 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: Adverse events at Define
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: Postural hypotension at 4 weeks; Group 1: 0/68, Group 2: 0/34
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: Retrograde ejaculation at 4 weeks; Group 1: 3/68, Group 2: 0/34
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: Dizziness at 4 weeks; Group 1: 9/68, Group 2: 2/34
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing:
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: Headache at 4 weeks; Group 1: 8/68, Group 2: 1/34
Risk of bias: All domain - High, Selection - High, Blinding - Low, 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; Time to stone passage at Define; Pain intensity at Define; Analgesic use at Define; Hospitalisation/ Use of healthcare services at Define

Study	**Agarwal 2009[5]**
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=40)
Countries and setting	Conducted in India; Setting: department of urology, single centre
Line of therapy	Adjunctive to current care
Duration of study	Intervention + follow up: 3 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: radiological and metabolic evaluation
Stratum	Adults (≥16 years), ureteric stone <1 cm: NA
Subgroup analysis within study	Not applicable: NA
Inclusion criteria	single upper ureteric stone <15mm electing SWL
Exclusion criteria	extremes of ages; serum creatinine >2mg/dL; concomitant stones in ipsilateral kidney; radiolucent stones; history of previous unsuccessful SWL; active urinary tract infection; diabetes; concomitant treatment with calcium channel blockers, alpha-blockers and/or corticosteroids; previous pyeloureteral surgery; severe vertebral malformation; morbid obesity; pregnancy; aortic and/or renal artery aneurysm; uncorrected coagulopathy; ureteral stent
Recruitment/selection of patients	not reported
Age, gender and ethnicity	Age - Mean (SD): intervention group: 32.4 (8.7), control group: 35.5 (15.4). Gender (M:F): 31/9. Ethnicity: not reported
Further population details	1. Kidney pole: Not applicable 2. Neuropathic/ cerebral-palsy /immobility: Not applicable 3. Obesity /skin-to-stone distance: Not applicable 4. Pregnant women: Non-pregnant 5. Stone composition/hounsfield units: Not applicable 6. Ureteric stone: Upper ureteric stones
Indirectness of population	Serious indirectness: included 14 patients with stones <10mm, 20 with 10mm stones and 10 with stones >10mm
Interventions	(n=20) Intervention 1: Alpha blockers and SWL. Tamsulosin 0.4mg daily starting from the day of SWL, just before the session. SWL performed up to a maximum of 4 sessions for any significant ureteric fragment, ureteroscopy offered if stone did not show adequate fragmentation after 2 sessions. Duration up to 3

	months. Concurrent medication/care: over-the-counter NSAIDs, antispasmodics or Tramadol on demand. Indirectness: No indirectness; Indirectness comment: NA (n=20) Intervention 2: Surgery - SWL. SWL performed up to a maximum of 4 sessions for any significant ureteric fragment, ureteroscopy offered if stone did not show adequate fragmentation after 2 sessions. Duration up to 5 weeks. Concurrent medication/care: over-the-counter NSAIDs, antispasmodics or Tramadol on demand. Indirectness: No indirectness; Indirectness comment: NA
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: ALPHA BLOCKERS AND SWL versus SWL

Protocol outcome 1: Stone passage
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: stone clearance at the end of the study at study duration ; Group 1: 19/20, Group 2: 18/20
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: no significant differences in age, sex, weight, height, BMI or stone size ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 2: Time to stone passage
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: days to stone clearance at study duration ; Group 1: mean 30.7 days (SD 19.6); n=20,
Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: no significant differences in age, sex, weight, height, BMI or stone size ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 3: Pain intensity
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: VAS at unclear; Group 1: mean 25.3 (SD 17.9); n=20,
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: no significant differences in age, sex, weight, height, BMI or stone size ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcomes not reported by the study	Quality of life; Adverse events; Analgesic use ; Hospitalisation/ Use of healthcare services

Study	Ahmad 2015[7]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=100)
Countries and setting	Conducted in Pakistan; Setting: Armed Forces Institute of Urology
Line of therapy	1st line
Duration of study	Intervention time: 4 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Adults (≥16 years), ureteric stone <1 cm
Subgroup analysis within study	Not applicable
Inclusion criteria	age >18 years; stone size 8mm or smaller in distal third of the ureter
Exclusion criteria	ureteric obstruction; distal ureteric stricture; previous ureteral surgery; solitary kidney; aberrant ureteral anatomy; urinary tract infection; radiolucent stone
Recruitment/selection of patients	consecutive meeting the inclusion/exclusion criteria during the study period (10 months)
Age, gender and ethnicity	Age - Mean (range): . Gender (M:F): not reported . Ethnicity: not reported
Further population details	1. Kidney pole: Not applicable 2. Neuropathic/ cerebral-palsy /immobility: Not applicable 3. Obesity /skin-to-stone distance: Not applicable 4. Pregnant women: Not stated / Unclear 5. Stone composition/hounsfield units: Not applicable 6. Ureteric stone: Lower ureteric stones
Indirectness of population	No indirectness
Interventions	(n=50) Intervention 1: Alpha blockers - Tamsulosin. Tamsulosin 0.4mg daily. Duration up to 4 weeks. Concurrent medication/care: Diclofenac Sodium 50mg 8 hourly on required basis. Indirectness: No indirectness (n=50) Intervention 2: Placebo. Placebo 1 capsule daily. Duration up to 4 weeks. Concurrent medication/care: Diclofenac Sodium 50mg 8 hourly on required basis. Indirectness: No indirectness
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: TAMSULOSIN versus PLACEBO

Protocol outcome 1: Hospitalisation/ Use of healthcare services
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: number requiring hospitalisation at 4 weeks ; Group 1: 0/49, Group 2: 1/48
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High,

Crossover - Low, Subgroups - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, stone size and stone lateralisation; Group 1 Number missing: 1; Group 2 Number missing: 2 Protocol outcome 2: Stone passage - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: expulsion rate at 4 weeks ; Group 1: 42/49, Group 2: 26/48 Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low, Subgroups - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, stone size and stone lateralisation; Group 1 Number missing: 1; Group 2 Number missing: 2 Protocol outcome 3: Adverse events - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: drug side effects at 4 weeks ; Group 1: 0/49, Group 2: 0/48 Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low, Subgroups - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, stone size and stone lateralisation; Group 1 Number missing: 1; Group 2 Number missing: 2 Protocol outcome 4: Analgesic use - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: number requiring analgesic (diclofenac) at 4 weeks ; Group 1: 9/49, Group 2: 19/48 Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low, Subgroups - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, stone size and stone lateralisation; Group 1 Number missing: 1; Group 2 Number missing: 2	
Protocol outcomes not reported by the study	Quality of life; Pain intensity; Time to stone passage

Study	Ahmed 2017[9]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=183)
Countries and setting	Conducted in Saudi Arabia; Setting: department of urology, 3 centres
Line of therapy	Adjunctive to current care
Duration of study	Intervention + follow up: 1 week + 8 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: unenhanced abdominal CT
Stratum	Adults (≥16 years), ureteric stone 1-2 cm: NA
Subgroup analysis within study	Not applicable: NA
Inclusion criteria	adult patients (≥18 years); proximal ureteral stones ≥10mm; scheduled for URS lithotripsy
Exclusion criteria	pregnancy; persistent moderate/severe pain; bilateral ureteral stones; solitary kidney; renal impairment; ureteral stricture and/or history of previous ureteral surgery or endoscopy
Recruitment/selection of patients	consecutive patients meeting the inclusion criteria during the recruitment period
Age, gender and ethnicity	Age - Mean (SD): 36.7 (11.1). Gender (M:F): 98/67. Ethnicity: not reported
Further population details	1. Kidney pole: Not applicable 2. Neuropathic/ cerebral-palsy /immobility: Not applicable 3. Obesity /skin-to-stone distance: Not applicable 4. Pregnant women: Non-pregnant 5. Stone composition/hounsfield units: Not applicable 6. Ureteric stone: Upper ureteric stones
Indirectness of population	No indirectness: NA
Interventions	(n=91) Intervention 1: Alpha blockers and URS. Tamsulosin 0.4mg daily before URS. Duration 1 week. Concurrent medication/care: not reported. Indirectness: No indirectness; Indirectness comment: NA (n=92) Intervention 2: Surgery - URS. URS. Duration procedure time. Concurrent medication/care: not reported. Indirectness: No indirectness; Indirectness comment: NA
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: ALPHA BLOCKERS AND URS versus URS

Protocol outcome 1: Hospitalisation/ Use of healthcare services
- Actual outcome for Adults (≥16 years), ureteric stone 1-2 cm: Hospitalisation time at initial procedure ; Group 1: mean 1.2 days (SD 0.3); n=81, Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: no significant differences in age, sex, BMI, stone density,

	stone size or location (left/right); Group 1 Number missing: 10, Reason: non-compliance with medication (4), lost to follow up/did not complete investigation (6); Group 2 Number missing: 8, Reason: lost to follow up/did not complete investigations (8) - Actual outcome for Adults (≥16 years), ureteric stone 1-2 cm: readmission at 8 weeks ; Group 1: 3/81, Group 2: 5/84 Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: no significant differences in age, sex, BMI, stone density, stone size or location (left/right); Group 1 Number missing: 10, Reason: non-compliance with medication (4), lost to follow up/did not complete investigation (6); Group 2 Number missing: 8, Reason: lost to follow up/did not complete investigations (8) Protocol outcome 2: Stone passage - Actual outcome for Adults (≥16 years), ureteric stone 1-2 cm: stone free rate at 4 weeks ; Group 1: 74/81, Group 2: 67/84 Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: no significant differences in age, sex, BMI, stone density, stone size or location (left/right); Group 1 Number missing: 10, Reason: non-compliance with medication (4), lost to follow up/did not complete investigation (6); Group 2 Number missing: 8, Reason: lost to follow up/did not complete investigations (8)
Protocol outcomes not reported by the study	Quality of life; Adverse events; Pain intensity; Analgesic use ; Time to stone passage

Study	**Al-ansari 2010[14]**
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=100)
Countries and setting	Conducted in Qatar; Setting: Department of Urology, single centre
Line of therapy	1st line
Duration of study	Intervention time: 4 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Adults (≥16 years), ureteric stone <1 cm
Subgroup analysis within study	Not applicable
Inclusion criteria	ureteral stones 10mm or smaller located below the common iliac vessels as assessed on non-contrast computed tomography

Exclusion criteria	age <18 years; non-radiopaque stones; multiple stones; urinary tract infections; severe hydronephrosis; pregnancy; hypotension; peptic ulcer; history of endoscopic or open ureteral surgery; taking calcium antagonist medications; refusal to participate
Recruitment/selection of patients	consecutive patients meeting the inclusion/exclusion criteria during the study period
Age, gender and ethnicity	Age - Mean (SD): 36.7 (9.35), range 21-55 years. Gender (M:F): 67/33. Ethnicity: not reported
Further population details	1. Kidney pole: Not applicable 2. Neuropathic/ cerebral-palsy /immobility: Not applicable 3. Obesity /skin-to-stone distance: Not applicable 4. Pregnant women: Non-pregnant 5. Stone composition/hounsfield units: Not applicable 6. Ureteric stone: Lower ureteric stones
Indirectness of population	No indirectness
Interventions	(n=50) Intervention 1: Alpha blockers - Tamsulosin. Tamsulosin 0.4mg once daily. Duration up to 4 weeks. Concurrent medication/care: Diclofenac 75mg injection on demand and advice to drink a minimum of 2 L of water daily. Indirectness: No indirectness (n=50) Intervention 2: Placebo. Placebo. Duration up to 4 weeks. Concurrent medication/care: Diclofenac 75mg injection on demand and advice to drink a minimum of 2 L of water daily. Indirectness: No indirectness
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: TAMSULOSIN versus PLACEBO

Protocol outcome 1: Stone passage
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: expulsion rate at 4 weeks ; Group 1: 41/50, Group 2: 28/46
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low; Indirectness of outcome: No indirectness ; Baseline details: comparable regarding age, sex, stone size and stone location; Group 1 Number missing: 0; Group 2 Number missing: 4

Protocol outcome 2: Time to stone passage
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: day the patient reported the passage of the stone, confirmed by absence of radiopaque calculi shadow on x-ray at 4 weeks ; Group 1: mean 6.4 days (SD 2.77); n=50,
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low; Indirectness of outcome: No indirectness ; Baseline details: comparable regarding age, sex, stone size and stone location; Group 1 Number missing: 0; Group 2 Number missing: 4

Protocol outcome 3: Adverse events
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: retrograde ejaculation at 4 weeks ; Group 1: 1/32, Group 2: 0/35
Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High,

Crossover - Low, Subgroups - Low; Indirectness of outcome: No indirectness ; Baseline details: comparable regarding age, sex, stone size and stone location; Group 1 Number missing: 0; Group 2 Number missing: 4 - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: dizziness at 4 weeks ; Group 1: 2/50, Group 2: 2/46 Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low, Subgroups - Low; Indirectness of outcome: No indirectness ; Baseline details: comparable regarding age, sex, stone size and stone location; Group 1 Number missing: 0; Group 2 Number missing: 4 - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: headache at 4 weeks ; Group 1: 2/50, Group 2: 2/46 Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low, Subgroups - Low; Indirectness of outcome: No indirectness ; Baseline details: comparable regarding age, sex, stone size and stone location; Group 1 Number missing: 0; Group 2 Number missing: 4 - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: postural hypotension at 4 weeks ; Group 1: 1/50, Group 2: 0/46 Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low, Subgroups - Low; Indirectness of outcome: No indirectness ; Baseline details: comparable regarding age, sex, stone size and stone location; Group 1 Number missing: 0; Group 2 Number missing: 4 Protocol outcome 4: Pain intensity - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: number of pain episodes at 4 weeks ; Group 1: mean 1.6 pain episodes (SD 1.3); n=50, Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low, Subgroups - Low; Indirectness of outcome: No indirectness ; Baseline details: comparable regarding age, sex, stone size and stone location; Group 1 Number missing: 0; Group 2 Number missing: 4 Protocol outcome 5: Analgesic use - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: need for Diclofenac injection at 4 weeks ; Group 1: mean 0.9 (SD 0.93); n=50, Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low; Indirectness of outcome: No indirectness ; Baseline details: comparable regarding age, sex, stone size and stone location; Group 1 Number missing: 0; Group 2 Number missing: 4 - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: dose of Diclofenac injection at 4 weeks ; Group 1: mean 67.5 mg (SD 69.8); n=50, Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low; Indirectness of outcome: No indirectness ; Baseline details: comparable regarding age, sex, stone size and stone location; Group 1 Number missing: 0; Group 2 Number missing: 4	
Protocol outcomes not reported by the study	Quality of life; Hospitalisation/ Use of healthcare services

Study	Aldaqadossi 2015[15]
Study type	RCT (randomised; Parallel)
Number of studies (number of participants)	1 (n=67)
Countries and setting	Conducted in Egypt; Setting: not reported
Line of therapy	1st line
Duration of study	Intervention + follow up: 4 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Children (<16 years)
Subgroup analysis within study	Not applicable
Inclusion criteria	children presenting with a distal ureteric stone of <1cm below the common iliac vessels as assessed by enhanced CT
Exclusion criteria	bilateral ureteric stones, multiple stones, marked hydronephrosis, urinary tract infection, urinary tract abnormalities, voiding dysfunction, any previous open or endoscopic ureteric surgery
Recruitment/selection of patients	not reported
Age, gender and ethnicity	Age - Mean (SD): Tamsulosin group 7.7 years (3.02), control group 7.25 years (2.7). Gender (M:F): 36/27. Ethnicity: not reported
Further population details	1. Kidney pole: Not applicable 2. Neuropathic/ cerebral-palsy /immobility: Not applicable 3. Obesity /skin-to-stone distance: Not applicable 4. Pregnant women: Non-pregnant 5. Stone composition/hounsfield units: Not applicable 6. Ureteric stone: Lower ureteric stones
Indirectness of population	No indirectness
Interventions	(n=31) Intervention 1: Alpha blockers - Tamsulosin. Tamsulosin 0.4mg for patients >5 years and 0.2mg for younger patients. Duration up to 4 weeks. Concurrent medication/care: Ibuprofen 4-10mg/kg orally every 6-8 hours as needed; in the case of intractable pain, Ketorolac 0.5-1mg/kg intramuscularly. Indirectness: No indirectness (n=32) Intervention 2: Pain management only - NSAIDs. Ibuprofen 4-10mg/kg every 6-8 hours as needed; in the case of intractable pain Ketorolac 0.5-1mg/kg intramuscularly. Duration 4 weeks. Concurrent medication/care: NA. Indirectness: No indirectness
Funding	No funding
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: TAMSULOSIN versus NSAIDS	

Protocol outcome 1: Stone passage - Actual outcome for Children (<16 years): stone-free rate at 4 weeks ; Group 1: 25/31, Group 2: 20/32; Comments: numbers calculated from percentages Risk of bias: All domain - Very 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: Time to stone passage - Actual outcome for Children (<16 years): time to stone expulsion (days) at 4 weeks ; Group 1: mean 7.7 days (SD 1.9); n=31, Risk of bias: All domain - Very 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: Adverse events - Actual outcome for Children (<16 years): major side effects at 4 weeks ; Group 1: 0/31, Group 2: 0/32 Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 4: Pain intensity - Actual outcome for Children (<16 years): daily pain episodes at 4 weeks ; Group 1: mean 1.6 mean number of daily pain episodes (SD 1.6); n=31, Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 5: Analgesic use - Actual outcome for Children (<16 years): mean number of Ketorolac injections during the study at 4 weeks ; Group 1: mean 0.55 (SD 0.8); n=31, Risk of bias: All domain - Very 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; Hospitalisation/ Use of healthcare services

Study	Aldemir 2011[16]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=90)
Countries and setting	Conducted in Turkey; Setting: Department of Urology, single centre
Line of therapy	1st line
Duration of study	Intervention time: 10 days
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Adults (≥16 years), ureteric stone <1 cm
Subgroup analysis within study	Not applicable
Inclusion criteria	older than 17 years; stones located in the distal ureter with a size of <10mm in largest diameter
Exclusion criteria	urinary tract infection; solitary kidney; severe hydronureteroephrosis; renal insufficiency; diabetes; multiple stones; bilateral stones; hypotension; pregnancy; previous spontaneous stone expulsion; previous distal ureteral surgery; history of intake of nifedipine, alpha-adrenergic blockers, calcium antagonists or steroids
Recruitment/selection of patients	not reported
Age, gender and ethnicity	Age - Mean (SD): Tamsulosin group: 42.4 (16.1), control group: 43.5 (16.6). Gender (M:F): 58/32. Ethnicity: not reported
Further population details	1. Kidney pole: Not applicable 2. Neuropathic/ cerebral-palsy /immobility: Not applicable 3. Obesity /skin-to-stone distance: Not applicable 4. Pregnant women: Non-pregnant 5. Stone composition/hounsfield units: Not applicable 6. Ureteric stone: Lower ureteric stones
Indirectness of population	No indirectness
Interventions	(n=31) Intervention 1: Alpha blockers - Tamsulosin. Tamsulosin 0.4mg once daily. Duration up to 10 days. Concurrent medication/care: Diclofenac as needed and advice to drink at least 2 L of water daily. Indirectness: No indirectness (n=29) Intervention 2: Pain management only - NSAIDs. Diclofenac 100mg once daily. Duration up to 10 days. Concurrent medication/care: advice to drink at least 2 L of water daily. Indirectness: No indirectness
Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: TAMSULOSIN versus NSAIDS Protocol outcome 1: Stone passage	

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: stone expulsion rate at 10 days ; Group 1: 25/31, Group 2: 11/29; Comments: numbers calculated from percentages Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, gender, stone size, stone location or stone site; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 2: Adverse events - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: significant adverse events at 10 days ; Group 1: 0/31, Group 2: 0/29 Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: Serious indirectness ; Baseline details: no significant difference in age, gender, stone size, stone location or stone site; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 3: Pain intensity - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: incidence of ureteral colic at 10 days ; Group 1: 20/31, Group 2: 23/29 Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, gender, stone size, stone location or stone site; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 4: Analgesic use - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: additional analgesic requirement at 10 days ; Group 1: 10/31, Group 2: 18/29 Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, gender, stone size, stone location or stone site; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Quality of life; Time to stone passage; Hospitalisation/ Use of healthcare services

Study	Alizadeh 2014[17]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=96)
Countries and setting	Conducted in Iran; Setting: Clinic of Urology, Radiology Centre or emergency department at a single centre
Line of therapy	1st line
Duration of study	Intervention time: 4 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Adults (≥16 years), ureteric stone <1 cm
Subgroup analysis within study	Not applicable
Inclusion criteria	18-60 years of age; renal colic (3-6mm ureteral stone of distal ureteral or UVj)
Exclusion criteria	urinary tract infection; radiolucent stones on KUB; acute hydronephrosis (grades 2 and 3) in sonography; diabetes; history of peptic ulcer disease; systolic blood pressure <100; taking calcium antagonist medications; history of surgery on the distal ureter; single renal patients; creatinine >1.4 for males and >1.2 for females; pain resistant to conservative treatment; NSAID intolerance or adverse effects of Tamsulosin; withdrawal; unforeseen complications during the study; pregnancy
Recruitment/selection of patients	not reported
Age, gender and ethnicity	Age - Range: 19-54. Gender (M:F): 61/35. Ethnicity: not reported
Further population details	1. Kidney pole: Not applicable 2. Neuropathic/ cerebral-palsy /immobility: Not applicable 3. Obesity /skin-to-stone distance: Not applicable 4. Pregnant women: Non-pregnant 5. Stone composition/hounsfield units: Not applicable 6. Ureteric stone: Lower ureteric stones
Indirectness of population	No indirectness
Interventions	(n=50) Intervention 1: Alpha blockers - Tamsulosin. Tamsulosin 0.4mg daily. Duration up to 4 weeks. Concurrent medication/care: Indomethacin 100mg as needed and advice to drink 2 L of water daily. Indirectness: No indirectness (n=46) Intervention 2: Pain management only - NSAIDs. Indomethacin 100mg as needed. Duration up to 4 weeks. Concurrent medication/care: advice to drink 2 L of water daily. Indirectness: No indirectness
Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: TAMSULOSIN versus NSAIDS	

Protocol outcome 1: Stone passage - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: spontaneous expulsion at 4 weeks ; Group 1: 41/50, Group 2: 30/46 Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age or stone size ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 2: Time to stone passage - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: expulsion time at 4 weeks ; Group 1: mean 3.7 days (SD 5.07); n=50, Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age or stone size ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 3: Adverse events - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: symptoms such as UTI, fever, severe obstructive uropathy, worsening of symptoms and side effects of Tamsulosin or Indomethacin that require discontinuation at 4 weeks ; Group 1: 0/50, Group 2: 0/46 Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: Serious indirectness ; Baseline details: no significant difference in age or stone size ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 4: Analgesic use - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: average analgesic consumption at 4 weeks ; Group 1: mean 1.48 number of times (SD 2.15); n=50, Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age or stone size ; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Quality of life; Pain intensity; Hospitalisation/ Use of healthcare services

Study	Arrabal-martin 2010[20]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=70)
Countries and setting	Conducted in Spain; Setting: Department of Urology, single centre
Line of therapy	1st line
Duration of study	Intervention + follow up: 30 days
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Adults (≥16 years), ureteric stone <1 cm
Subgroup analysis within study	Not applicable
Inclusion criteria	ureteral lithiasis below the S3 and S4 levels and a calculus size of 4-10mm
Exclusion criteria	urinary infection; abdominal alterations; multiple lithiases; urinary derivation (double-J catheter in the ureter or percutaneous nephrostomy); other factors hindering the removal of calculi
Recruitment/selection of patients	not reported
Age, gender and ethnicity	Age - --: . Gender (M:F): not reported . Ethnicity: not reported
Further population details	1. Kidney pole: Not applicable 2. Neuropathic/ cerebral-palsy /immobility: Not applicable 3. Obesity /skin-to-stone distance: Not applicable 4. Pregnant women: Not stated / Unclear 5. Stone composition/hounsfield units: Not applicable 6. Ureteric stone: Lower ureteric stones
Indirectness of population	No indirectness
Interventions	(n=35) Intervention 1: Alpha blockers - Tamsulosin. Tamsulosin 0.4mg daily. Duration 3 weeks. Concurrent medication/care: Ibuprofen 600mg every 12 hours, 2 L of water daily and Tramadol in case of pain. Indirectness: No indirectness (n=35) Intervention 2: Pain management only - NSAIDs. Ibuprofen 600mg every 12 hours. Duration 3 weeks. Concurrent medication/care: 2 L of water daily and Tramadol in case of pain. Indirectness: No indirectness
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: TAMSULOSIN versus NSAIDS

Protocol outcome 1: Stone passage
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: stone expulsion at 30 days ; Group 1: 30/35, Group 2: 19/35
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low,

Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in sex, age or lithiasis size ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 2: Adverse events - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: fever >37.5•c or side effects concerning Tamsulosin at 30 days ; Group 1: 0/35, Group 2: 0/35 Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - High, Measurement - High, Crossover - Low; Indirectness of outcome: Serious indirectness ; Baseline details: no significant difference in sex, age or lithiasis size ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 3: Analgesic use - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: use of Tramadol at 30 days ; Group 1: 9/35, Group 2: 21/35; Comments: numbers calculated from percentages Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in sex, age or lithiasis size ; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Quality of life; Time to stone passage; Pain intensity; Hospitalisation/ Use of healthcare services

Study	**Ates 2012[21]**
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=79)
Countries and setting	Conducted in Turkey; Setting: 4 urology departments at 3 centres
Line of therapy	Adjunctive to current care
Duration of study	Intervention + follow up: 2 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: history, physical evaluation, urinary analysis, laboratory findings, ultrasonography
Stratum	Adults (≥16 years), ureteric stone <1 cm: NA
Subgroup analysis within study	Not applicable: NA
Inclusion criteria	radio-opaque upper ureteral stones

Exclusion criteria	abnormal renal anatomy and function; use of medications that may lead to stone formation; pregnancy or suspicion of pregnancy; distal obstruction; history of previous urinary stone surgery; hydronephrosis >grade 1; presence of coagulopathy; active urinary tract infection; history of hypersensitivity to Doxazosin; serum creatinine level >2mg/dL; existence of >1 ureteral stone; hypotension; pain that could not be controlled with an analgesic
Recruitment/selection of patients	not reported
Age, gender and ethnicity	Age - Mean (SD): Doxazosin group: 38.35 (11.41), control group: 30.95 (9.68). Gender (M:F): 58/21. Ethnicity: not reported
Further population details	1. Kidney pole: Not applicable 2. Neuropathic/ cerebral-palsy /immobility: Not applicable 3. Obesity /skin-to-stone distance: Not applicable 4. Pregnant women: Non-pregnant 5. Stone composition/hounsfield units: Not applicable 6. Ureteric stone: Upper ureteric stones
Indirectness of population	Serious indirectness: includes stones < and > 10mm
Interventions	(n=35) Intervention 1: Alpha blockers and SWL. Doxazosin controlled release 4mg daily within 24 hours before SWL, if stone was not influenced or fragmented into pieces ≥6mm a second session was performed 3 days after the first procedure. Duration up to 14 days. Concurrent medication/care: oral Diclofenac on demand and advice to drink at least 2L of fluid daily. Indirectness: No indirectness; Indirectness comment: NA (n=44) Intervention 2: Surgery - SWL. SWL, if stone was not influenced or fragmented into pieces ≥6mm a second session was performed 3 days after the first procedure. Duration procedure time. Concurrent medication/care: oral Diclofenac on demand and advice to drink at least 2 L of fluid daily. Indirectness: No indirectness; Indirectness comment: NA
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: ALPHA BLOCKERS AND SWL versus SWL

Protocol outcome 1: Hospitalisation/ Use of healthcare services
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: number of hospital admissions at 14 days ; Group 1: mean 0.51 admissions (SD 0.7); n=35, Group 2: mean 0.52 admissions (SD 0.62); n=44; VAS 0-10 Top=High is poor outcome
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: Doxazosin group were older; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 2: Stone passage
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: stone free rate at 14 days ; Group 1: 33/35, Group 2: 35/44

Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: Doxazosin group were older; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 3: Time to stone passage - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: time to stone passage at 14 days ; Group 1: mean 4.14 days (SD 1.78); n=35, Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: Doxazosin group were older; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 4: Pain intensity - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: VAS at unclear; Group 1: mean 6.89 (SD 1.02); n=35, Group 2: mean 6.59 (SD 1.58); n=44; VAS 0-10 Top=High is poor outcome Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: Doxazosin group were older; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 5: Analgesic use - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: need for analgesics at 14 days ; Group 1: 29/35, Group 2: 30/44 Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: Doxazosin group were older; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Quality of life; Adverse events

Study (subsidiary papers)	Autorino 2005[22] (De sio 2006[49])
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=64)
Countries and setting	Conducted in Italy; Setting: Department of Urology, single centre
Line of therapy	1st line
Duration of study	Intervention + follow up: 4 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: unenhanced CT scan
Stratum	Adults (≥16 years), ureteric stone <1 cm
Subgroup analysis within study	Not applicable
Inclusion criteria	unilateral distal ureteral calculi
Exclusion criteria	urinary tract infection; severe hydronephrosis; diabetes; ulcer; hypotension or hypertension when in treatment with alpha-blockers or calcium-antagonists; pregnancy; multiple stones; history of spontaneous stone expulsion or ureteral stricture
Recruitment/selection of patients	consecutive patients meeting the inclusion/exclusion criteria during the study period
Age, gender and ethnicity	Age - Other: Tamsulosin group mean: 45, control group mean: 43. Gender (M:F): 62/34. Ethnicity: not reported
Further population details	1. Kidney pole: Not applicable 2. Neuropathic/ cerebral-palsy /immobility: Not applicable 3. Obesity /skin-to-stone distance: Not applicable 4. Pregnant women: Non-pregnant 5. Stone composition/hounsfield units: Not applicable 6. Ureteric stone: Lower ureteric stones
Indirectness of population	No indirectness
Interventions	(n=50) Intervention 1: Alpha blockers - Tamsulosin. Tamsulosin 0.4mg daily. Duration up to 2 weeks. Concurrent medication/care: Diclofenac 100mg daily, Aescin 80mg daily, advice to drink 2 L of water daily, Omeprazole 20mg daily for the treatment period and Levofloxacin 250mg daily for the first week. Indirectness: No indirectness (n=46) Intervention 2: Pain management only - NSAIDs. Diclofenac 100mg daily and Aescin 80mg daily. Duration up to 2 weeks. Concurrent medication/care: advice to drink 2 L of water daily, Omeprazole 20mg daily for the treatment period and Levofloxacin 250mg daily for the first week . Indirectness: No indirectness
Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: TAMSULOSIN versus NSAIDS	

Protocol outcome 1: Hospitalisation/ Use of healthcare services
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: hospitalisation for recurrent colic at 2 weeks ; Group 1: 5/50, Group 2: 11/46
Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, gender or stone size ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 2: Stone passage
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: stone expulsion rate at 2 weeks ; Group 1: 45/50, Group 2: 27/46
Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, gender or stone size ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 3: Time to stone passage
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: expulsion time at 2 weeks ; Group 1: mean 4.4 days (SD 2.1); n=50,
Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, gender or stone size ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 4: Adverse events
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: dizziness at 2 weeks ; Group 1: 1/50, Group 2: 0/46
Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, gender or stone size ; Group 1 Number missing: ; Group 2 Number missing:
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: hypotension at 2 weeks ; Group 1: 2/50, Group 2: 0/46
Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, gender or stone size ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 5: Analgesic use
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: number of patients requiring different analgesics from those used in the standard treatment regimen at 2 weeks ; Group 1: 5/50, Group 2: 17/46
Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, gender or stone size ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcomes not reported by the study	Quality of life; Pain intensity

Study	Aydogdu 2009[24]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=39)
Countries and setting	Conducted in Turkey; Setting: paediatric urology unit, single centre
Line of therapy	1st line
Duration of study	Intervention time: up to 3 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Children (<16 years)
Subgroup analysis within study	Not applicable
Inclusion criteria	radiopaque lower ureteral stones 2-10mm in diameter
Exclusion criteria	anatomical abnormalities; previously diagnosed reflux; voiding dysfunction; history of ureteral surgery or steinstrasse formed after ESWL; receiving calcium channel blockers
Recruitment/selection of patients	not reported
Age, gender and ethnicity	Age - Mean (SD): 5.6 (2.6). Gender (M:F): 21/18. Ethnicity: not reported
Further population details	1. Kidney pole: Not applicable 2. Neuropathic/ cerebral-palsy /immobility: Not applicable 3. Obesity /skin-to-stone distance: Not applicable 4. Pregnant women: Non-pregnant 5. Stone composition/hounsfield units: Not applicable 6. Ureteric stone: Lower ureteric stones
Indirectness of population	No indirectness
Interventions	(n=19) Intervention 1: Alpha blockers - Doxazosin. Doxazosin 0.03mg/kg once daily administered at bedtime. Duration up to 3 weeks. Concurrent medication/care: Ibuprofen 20mg/kg daily divided in 2 equal doses for pain episodes. Indirectness: No indirectness (n=20) Intervention 2: Pain management only - NSAIDs. Ibuprofen 20mg/kg daily divided in 2 equal doses for pain episodes. Duration up to 3 weeks. Concurrent medication/care: none. Indirectness: No indirectness
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: DOXAZOSIN versus NSAIDS

Protocol outcome 1: Stone passage
- Actual outcome for Children (<16 years): stone expulsion at 3 weeks ; Group 1: 16/19, Group 2: 14/20
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High,

Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, gender or stone size; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 2: Time to stone passage - Actual outcome for Children (<16 years): time to expulsion at 3 weeks ; Group 1: mean 5.9 days (SD 2.1); n=19, Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, gender or stone size; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 3: Adverse events - Actual outcome for Children (<16 years): adverse events including hypotension, asthenia, syncope and palpitations at 3 weeks ; Group 1: 0/19, Group 2: 0/20 Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: Serious indirectness ; Baseline details: no significant difference in age, gender or stone size; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Quality of life; Pain intensity; Analgesic use ; Hospitalisation/ Use of healthcare services

Study	**Bajwa 2013[28]**
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=60)
Countries and setting	Conducted in Pakistan; Setting: Department of Urology, single centre
Line of therapy	1st line
Duration of study	Intervention time: 4 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Adults (≥16 years), ureteric stone <1 cm
Subgroup analysis within study	Not applicable
Inclusion criteria	lower ureteric stone <1cm; sterile urine; symptom free
Exclusion criteria	obstruction; stone size >1cm; urinary tract infection
Recruitment/selection of patients	not reported

Age, gender and ethnicity	Age - Mean (SD): 33.15 (8.97). Gender (M:F): 37/23. Ethnicity: not reported
Further population details	1. Kidney pole: Not applicable 2. Neuropathic/ cerebral-palsy /immobility: Not applicable 3. Obesity /skin-to-stone distance: Not applicable 4. Pregnant women: Not stated / Unclear 5. Stone composition/hounsfield units: Not applicable 6. Ureteric stone: Lower ureteric stones
Indirectness of population	No indirectness
Interventions	(n=30) Intervention 1: Alpha blockers - Tamsulosin. Tamsulosin 0.4mg once daily. Duration up to 4 weeks. Concurrent medication/care: not reported. Indirectness: No indirectness (n=30) Intervention 2: Pain management only - NSAIDs. Diclofenac 50mg 12 hourly. Duration up to 4 weeks. Concurrent medication/care: not reported. Indirectness: No indirectness
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: TAMSULOSIN versus NSAIDS

Protocol outcome 1: Stone passage
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: stone discharged at 4 weeks ; Group 1: 23/30, Group 2: 11/30
Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: comparable for age, gender and stone size ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 2: Time to stone passage
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: expulsion time at 4 weeks ; Group 1: mean 15.7 days (SD 3.72); n=30,
Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: comparable for age, gender and stone size ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcomes not reported by the study	Quality of life; Adverse events; Pain intensity; Analgesic use; Hospitalisation/ Use of healthcare services

Study	Balci 2014[29]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=75)
Countries and setting	Conducted in Turkey; Setting: Department of Urology, single centre
Line of therapy	1st line
Duration of study	Intervention time: up to 4 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Adults (≥16 years), ureteric stone <1 cm
Subgroup analysis within study	Not applicable
Inclusion criteria	stones of 5-10mm diameter in the lower third of the ureter (below the common iliac vessels)
Exclusion criteria	proximal or intramural part of the ureteral stone; active urinary tract infection; ureterohydronephrosis; acute renal failure; fever; multiple ureteral stones; history of surgery or endoscopic procedures for urolithiasis; chronic renal failure; diabetes; peptic ulcer; concomitant treatment with alpha-blocker and beta-blocker, calcium antagonists or nitrates; pregnancy; lactation; patient desire for immediate stone removal
Recruitment/selection of patients	not reported
Age, gender and ethnicity	Age - Mean (SD): 36.8 (11.3). Gender (M:F): 53/22. Ethnicity: not reported
Further population details	1. Kidney pole: Not applicable 2. Neuropathic/ cerebral-palsy /immobility: Not applicable 3. Obesity /skin-to-stone distance: Not applicable 4. Pregnant women: Non-pregnant 5. Stone composition/hounsfield units: Not applicable 6. Ureteric stone: Lower ureteric stones
Indirectness of population	No indirectness
Interventions	(n=25) Intervention 1: Alpha blockers - Tamsulosin. Tamsulosin 0.4mg daily. Duration up to 4 weeks. Concurrent medication/care: Diclofenac 50mg when required and advice to drink 2-2.5 L of water daily. Indirectness: No indirectness (n=25) Intervention 2: Calcium channel blockers - Nifedipine. Nifedipine 30mg daily. Duration up to 4 weeks. Concurrent medication/care: Diclofenac 50mg when required and advice to drink 2-2.5 L of water daily. Indirectness: No indirectness (n=25) Intervention 3: Pain management only - NSAIDs. Diclofenac 50mg when required. Duration up to 4 weeks. Concurrent medication/care: advice to drink 2-2.5 L of water daily. Indirectness: No indirectness
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: TAMSULOSIN versus NIFEDIPINE

Protocol outcome 1: Stone passage
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: expulsion rate at 4 weeks ; Group 1: 19/25, Group 2: 16/25
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, gender, stone size and Hounsfield Units ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 2: Adverse events
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: dizziness at 4 weeks ; Group 1: 2/25, Group 2: 0/25
Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, gender, stone size and Hounsfield Units ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 3: Analgesic use
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: analgesic use at 4 weeks ; Group 1: mean 544 mg (SD 493); n=25,
Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, gender, stone size and Hounsfield Units ; Group 1 Number missing: ; Group 2 Number missing:

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: TAMSULOSIN versus NSAIDS

Protocol outcome 1: Stone passage
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: expulsion rate at 4 weeks ; Group 1: 19/25, Group 2: 9/25
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, gender, stone size and Hounsfield Units ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 2: Adverse events
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: dizziness at 4 weeks ; Group 1: 2/25, Group 2: 0/25
Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, gender, stone size and Hounsfield Units ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 3: Analgesic use
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: analgesic use at 4 weeks ; Group 1: mean 544 mg (SD 493); n=25,
Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High,

Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, gender, stone size and Hounsfield Units ; Group 1 Number missing: ; Group 2 Number missing: RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: NIFEDIPINE versus NSAIDS Protocol outcome 1: Stone passage - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: expulsion rate at 4 weeks ; Group 1: 16/25, Group 2: 9/25 Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, gender, stone size and Hounsfield Units ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 2: Adverse events - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: dizziness at 4 weeks ; Group 1: 0/25, Group 2: 0/25 Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, gender, stone size and Hounsfield Units ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 3: Analgesic use - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: analgesic use at 4 weeks ; Group 1: mean 602 mg (SD 434); n=25, Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, gender, stone size and Hounsfield Units ; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Quality of life; Time to stone passage; Pain intensity; Hospitalisation/ Use of healthcare services

Study	Basri 2013[30]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=123)
Countries and setting	Conducted in Turkey; Setting: single centre
Line of therapy	Adjunctive to current care
Duration of study	Intervention + follow up: 4 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: plain x-ray of the KUB and/or ultrasound imaging
Stratum	Adults (≥16 years), ureteric stone 1-2 cm: NA
Subgroup analysis within study	Not applicable: NA
Inclusion criteria	solitary ureteral stone 6-15mm located in the upper, middle or lower ureter
Exclusion criteria	<18 years of age; weight <50kg or >100kg; severe skeletal malformation; pregnancy; aortic and/or renal artery aneurysm; history of drug or alcohol abuse; long-term use of drugs such as antidepressants, histamine blockers or anxiolytics; allergy to the study medications; concomitant treatment with calcium antagonists and/or an alpha adrenergic antagonist; concomitant renal stones; previous unsuccessful attempts at SWL; elevated serum creatinine >2 mg/dL; urinary tract infection; diabetes; peptic ulcer; history of spontaneous stone expulsion; hypotension; coagulopathy; urinary congenital abnormalities; previous nephroureteral surgery
Recruitment/selection of patients	not reported
Age, gender and ethnicity	Age - Mean (SD): Tamsulosin group: 44.66 (13.25), control group: 42.19 (13.17). Gender (M:F): 98/25. Ethnicity: not reported
Further population details	1. Kidney pole: Not applicable 2. Neuropathic/ cerebral-palsy /immobility: Not applicable 3. Obesity /skin-to-stone distance: Not applicable 4. Pregnant women: Non-pregnant 5. Stone composition/hounsfield units: Not applicable 6. Ureteric stone: Not stated / Unclear
Indirectness of population	Serious indirectness: included stones < and >10mm
Interventions	(n=59) Intervention 1: Alpha blockers and SWL. Tamsulosin 0.4mg daily immediately after SWL. Duration up to 4 weeks. Concurrent medication/care: Diclofenac 75mg injected intramuscularly on demand, gastro protective therapy 40mg Pantoprazole once daily and instruction to drink a minimum of 2L of water daily. Indirectness: No indirectness; Indirectness comment: NA (n=64) Intervention 2: Surgery - SWL. SWL. Duration unclear. Concurrent medication/care: Diclofenac 75mg injected intramuscularly on demand, gastro protective therapy 40mg Pantoprazole daily and instruction to a

	minimum of 2L of water daily. Indirectness: No indirectness; Indirectness comment: NA
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: ALPHA BLOCKERS AND SWL versus SWL

Protocol outcome 1: Time to stone passage
- Actual outcome for Adults (≥16 years), ureteric stone 1-2 cm: time to stone clearance (upper stones) at unclear ; Group 1: mean 7.1 days (SD 6.4); n=29,
Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: no significant differences in age, sex or stone size; Group 1 Number missing: ; Group 2 Number missing:
- Actual outcome for Adults (≥16 years), ureteric stone 1-2 cm: time to stone clearance (middle stones) at unclear ; Group 1: mean 9.25 days (SD 9.95); n=16,
Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: no significant differences in age, sex or stone size; Group 1 Number missing: ; Group 2 Number missing:
- Actual outcome for Adults (≥16 years), ureteric stone 1-2 cm: time to stone clearance (lower stones) at unclear ; Group 1: mean 9.86 days (SD 6.94); n=14,
Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: no significant differences in age, sex or stone size; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 2: Pain intensity
- Actual outcome for Adults (≥16 years), ureteric stone 1-2 cm: VAS (upper stones) at unclear ; Group 1: mean 2.9 (SD 2.19); n=29, Group 2: mean 4 (SD 2.58); n=28; VAS 0-10 Top=High is poor outcome
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: no significant differences in age, sex or stone size; Group 1 Number missing: ; Group 2 Number missing:
- Actual outcome for Adults (≥16 years), ureteric stone 1-2 cm: VAS (middle stones) at unclear ; Group 1: mean 2.38 (SD 2.42); n=16, Group 2: mean 3 (SD 3.91); n=12; VAS 0-10 Top=High is poor outcome
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: no significant differences in age, sex or stone size; Group 1 Number missing: ; Group 2 Number missing:
- Actual outcome for Adults (≥16 years), ureteric stone 1-2 cm: VAS (lower stones) at unclear ; Group 1: mean 2.79 (SD 2.42); n=14, Group 2: mean 4 (SD 2.71); n=24; VAS 0-10 Top=High is poor outcome
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: no significant differences in age, sex or stone size; Group 1

Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Quality of life; Stone passage; Adverse events; Analgesic use; Hospitalisation/ Use of healthcare services

Study	**Bayraktar 2017[31]**
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=124)
Countries and setting	Conducted in Turkey; Setting: Not reported
Line of therapy	1st line
Duration of study	Follow up (post intervention): 4 weeks
Method of assessment of guideline condition	Method of assessment /diagnosis not stated
Stratum	Adults (≥16 years), ureteric stone <1 cm
Subgroup analysis within study	Not applicable
Inclusion criteria	Males with radiopaque distal ureter stones 5-10mm
Exclusion criteria	Not reported
Recruitment/selection of patients	Not reported
Age, gender and ethnicity	Age - Mean (SD): Alpha blocker group 34.4 (13.5); control group 36.92 (12.4). Gender (M:F): All male. Ethnicity: Not reported
Further population details	1. Kidney pole: Not applicable 2. Neuropathic/ cerebral-palsy /immobility: Not stated / Unclear 3. Obesity /skin-to-stone distance: Not stated / Unclear 4. Pregnant women: Non-pregnant 5. Stone composition/hounsfield units: Not stated / Unclear 6. Uteric stone: Lower ureteric stones
Indirectness of population	No indirectness
Interventions	(n=70) Intervention 1: Alpha blockers - Tamsulosin. Tamsulosin 0.4mg daily as a single dose. Duration Unclear. Concurrent medication/care: As a standard medical therapy, all patients were recommended a daily intake of liquids to urinate at least 1.5-2 litres, and 75mg of diclofenac was injected when needed. Indirectness: No indirectness (n=71) Intervention 2: Pain management only - NSAIDs. No treatment. Duration Unclear. Concurrent medication/care: As a standard medical therapy, all patients were recommended a daily intake of liquids to urinate at least 1.5-2 litres, and 75mg of diclofenac was injected when needed. Indirectness: No indirectness

Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: TAMSULOSIN versus NSAIDS

Protocol outcome 1: Stone passage at Define
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: Stone expulsion at 2 weeks; Group 1: 42/60, Group 2: 18/64
Risk of bias: All domain - High, Selection - Very high, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 11; Group 2 Number missing: 6
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: Stone expulsion at 4 weeks; Group 1: 49/60, Group 2: 33/64
Risk of bias: All domain - High, Selection - Very high, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 11; Group 2 Number missing: 6

Protocol outcome 2: Time to stone passage at Define
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: Expulsion time at 4 weeks; Group 1: mean 9.3 days (SD 5.8); n=60, Group 2: mean 8.7 days (SD 6.4); n=64
Risk of bias: All domain - High, Selection - Very high, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 11; Group 2 Number missing: 6

Protocol outcome 3: Pain intensity at Define
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: Number of NSAID injections at 4 weeks; Group 1: mean 1.3 (SD 0.4); n=60, Group 2: mean 1.4 (SD 0.4); n=64
Risk of bias: All domain - Very high, Selection - Very high, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Group 1 Number missing: 11; Group 2 Number missing: 6

Protocol outcomes not reported by the study	Quality of life at Define; Adverse events at Define; Analgesic use at Define; Hospitalisation/ Use of healthcare services at Define

Study	Chau 2011[42]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=67)
Countries and setting	Conducted in China; Setting: Urology division, Surgery, single centre
Line of therapy	1st line
Duration of study	Intervention + follow up: 5 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: non-contrast computerised tomography used to confirm presence of radio-opaque stone
Stratum	Adults (≥16 years), ureteric stone <1 cm
Subgroup analysis within study	Not applicable
Inclusion criteria	acute ureteric stone 5-10mm
Exclusion criteria	radiolucent stone; paper thin cortex; non-functioning kidney; intolerance to Alfuzosin; renal insufficiency (serum creatinine >160umol/L); concurrent alpha-blocker/calcium channel blocker/steroid/Furosemide usage; pregnancy; hypotension; history of ureteral stricture; history of ureteric stone treatment; allergic reaction to the study medication; patient on double-J ureteric stenting or percutaneous nephrostomy drainage; uncontrolled urosepsis
Recruitment/selection of patients	consecutive
Age, gender and ethnicity	Age - Mean (SD): 47.7 (12.3). Gender (M:F): 41/26. Ethnicity: not reported
Further population details	1. Kidney pole: Not applicable 2. Neuropathic/ cerebral-palsy /immobility: Not applicable 3. Obesity /skin-to-stone distance: Not applicable 4. Pregnant women: Non-pregnant 5. Stone composition/hounsfield units: Not applicable 6. Ureteric stone: Not stated / Unclear
Indirectness of population	No indirectness
Interventions	(n=33) Intervention 1: Alpha blockers - Alfuzosin. Alfuzosin slow release 10mg daily. Duration 4 weeks. Concurrent medication/care: Dologesic (Paracetamol + Dextropropoxyphene) four tablets daily on demand for 2 weeks and Diclofenac slow release 100mg daily on demand for 2 weeks in case of suboptimal pain control by Dologesic . Indirectness: No indirectness (n=34) Intervention 2: Pain management only - Opioids. Dologesic (Paracetamol + Dextropropoxyphene) four tablets daily on demand for 2 weeks and Diclofenac slow release 100mg daily on demand for 2 weeks in case of suboptimal pain control by Dologesic . Duration 2 weeks. Concurrent medication/care: not reported. Indirectness: No indirectness
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: ALFUZOSIN versus OPIOIDS

Protocol outcome 1: Stone passage
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: stone passage (upper ureteral stones) at 5 weeks ; Group 1: 8/11, Group 2: 3/14
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: difference in serum creatinine level; Group 1 Number missing: ; Group 2 Number missing:
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: stone passage (lower ureteral stones) at 5 weeks ; Group 1: 19/22, Group 2: 14/20
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: difference in serum creatinine level; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 2: Adverse events
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: dizziness at 5 weeks ; Group 1: 2/33, Group 2: 0/34
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: difference in serum creatinine level; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcomes not reported by the study	Quality of life; Time to stone passage; Pain intensity; Analgesic use; Hospitalisation/ Use of healthcare services

Study	**Cho 2013[43]**
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=90)
Countries and setting	Conducted in South Korea; Setting: urology department, single centre
Line of therapy	Adjunctive to current care
Duration of study	Intervention + follow up: up to 42 days
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: plain KUB x-ray, urinalysis, physical examination, non-contrast CT
Stratum	Adults (≥16 years), ureteric stone <1 cm: NA
Subgroup analysis within study	Not applicable: NA
Inclusion criteria	radio-opaque ureter stones; 5-10mm in diameter

Exclusion criteria	radiolucent stones; paper-thin cortex; non-functional kidney; previous genitourinary tract surgery; elevated serum creatinine >1.5mg/dL; severe obesity; pregnancy; concurrent alpha-blocker/calcium channel blocker/steroid/Frusemide usage; aortic or renal artery aneurysm; contraindications to alpha AR antagonist treatment
Recruitment/selection of patients	consecutive patients meeting the inclusion criteria during the recruitment period
Age, gender and ethnicity	Age - Mean (SD): Alfuzosin group: 47.4 (12.6), control group: 47.7 (12.1). Gender (M:F): 60/24. Ethnicity: not reported
Further population details	1. Kidney pole: Not applicable 2. Neuropathic/ cerebral-palsy /immobility: Not applicable 3. Obesity /skin-to-stone distance: Not applicable 4. Pregnant women: Non-pregnant 5. Stone composition/hounsfield units: Not applicable 6. Ureteric stone: Upper ureteric stones
Indirectness of population	Serious indirectness: included mainly upper but some lower stones
Interventions	(n=41) Intervention 1: Alpha blockers and SWL. ESWL then Alfuzosin 10mg daily, if the ureter stone remained and was larger than 5mm at the next follow up visit then additional ESWL was performed. Duration up to 42 days. Concurrent medication/care: Loxoprofen 68.1mg as needed and recommendation to drink at least 2L hydration daily. Indirectness: No indirectness; Indirectness comment: NA (n=43) Intervention 2: Surgery - SWL. ESWL, if the ureter stone remained and was larger than 5mm at the next follow up visit then additional ESWL was performed. Duration up to 42 days. Concurrent medication/care: Loxoprofen 68.1mg as needed and recommendation to drink at least 2L hydration daily. Indirectness: No indirectness; Indirectness comment: NA
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: ALPHA BLOCKERS AND SWL versus SWL

Protocol outcome 1: Stone passage
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: stone free rate at 42 days; Group 1: 39/41, Group 2: 40/43
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, Comments: NA; Baseline details: no significant differences in age, sex, stone size or stone location (left/right, upper/lower); Group 1 Number missing: 4, Reason: migration/discontinuation of medication/lost to follow up; Group 2 Number missing: 2, Reason: migration/lost to follow up

Protocol outcome 2: Time to stone passage
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: time to stone free at 42 days ; Group 1: mean 9.5 days (SD 4.8); n=41,
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: no significant differences in age, sex, stone size or stone

location (left/right, upper/lower); Group 1 Number missing: 4, Reason: migration/discontinuation of medication/lost to follow up; Group 2 Number missing: 2, Reason: migration/lost to follow up Protocol outcome 3: Adverse events - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: dizziness at 42 days ; Group 1: 2/41, Group 2: 0/43 Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: no significant differences in age, sex, stone size or stone location (left/right, upper/lower); Group 1 Number missing: 4, Reason: migration/discontinuation of medication/lost to follow up; Group 2 Number missing: 2, Reason: migration/lost to follow up - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: retrograde ejaculation at 42 days ; Group 1: 0/41, Group 2: 0/43 Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: no significant differences in age, sex, stone size or stone location (left/right, upper/lower); Group 1 Number missing: 4, Reason: migration/discontinuation of medication/lost to follow up; Group 2 Number missing: 2, Reason: migration/lost to follow up Protocol outcome 4: Pain intensity - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: VAS at unclear; Group 1: mean 5.33 (SD 1.22); n=41, Group 2: mean 6.43 (SD 1.36); n=43; VAS 0-10 Top=High is poor outcome 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, Comments: NA; Baseline details: no significant differences in age, sex, stone size or stone location (left/right, upper/lower); Group 1 Number missing: 4, Reason: migration/discontinuation of medication/lost to follow up; Group 2 Number missing: 2, Reason: migration/lost to follow up Protocol outcome 5: Analgesic use - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: number of patients requiring analgesics at 42 days; Group 1: 8/41, Group 2: 13/43 Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: no significant differences in age, sex, stone size or stone location (left/right, upper/lower); Group 1 Number missing: 4, Reason: migration/discontinuation of medication/lost to follow up; Group 2 Number missing: 2, Reason: migration/lost to follow up
Protocol outcomes not reported by the study	Quality of life; Hospitalisation/ Use of healthcare services

Study	El said 2015[57]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=54)
Countries and setting	Conducted in Egypt; Setting: Urology outpatient department, single centre
Line of therapy	1st line
Duration of study	Intervention time: 4 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: full medical history, physical and laboratory evaluation
Stratum	Adults (≥16 years), ureteric stone <1 cm
Subgroup analysis within study	Not applicable
Inclusion criteria	>18 years; presenting with radio-opaque stones ≤10mm and located in the distal third of the ureter
Exclusion criteria	urinary tract infections; ureteral strictures; renal impairment; solitary functioning kidney; hepatic insufficiency; severe hydronephrosis; multiple stones; peptic ulcers; diabetes; hypotension; pregnancy; lactation; sensitivity to alpha-blockers; receiving alpha-blockers, nitrates, calcium channel blockers, steroids, beta blockers, sildenafil, ketoconazole, itraconazole or ritonavir
Recruitment/selection of patients	not reported
Age, gender and ethnicity	Age - Mean (SD): Alfuzosin group: 32.8 (9.5), control group 32.1 (9.2). Gender (M:F): 34/20. Ethnicity: not reported
Further population details	1. Kidney pole: Not applicable 2. Neuropathic/ cerebral-palsy /immobility: Not applicable 3. Obesity /skin-to-stone distance: Not applicable 4. Pregnant women: Non-pregnant 5. Stone composition/hounsfield units: Not applicable 6. Ureteric stone: Lower ureteric stones
Indirectness of population	No indirectness
Interventions	(n=28) Intervention 1: Alpha blockers - Alfuzosin. Alfuzosin sustained release 5mg twice daily after meals. Duration up to 4 weeks. Concurrent medication/care: oral hydration with ≥2 L of water daily, Diclofenac 75mg intramuscularly on demand and education from the clinical pharmacist about potential adverse events, methods of reporting adverse events, self-reporting of pain on the visual analogue scale, importance of adherence to medications and daily water intake. Indirectness: No indirectness (n=26) Intervention 2: Pain management only - NSAIDs. Oral hydration with ≥2 L of water daily and Diclofenac 75mg intramuscularly on demand. Duration up to 4 weeks. Concurrent medication/care: education by the clinical pharmacist on potential adverse events, methods of reporting adverse events, self-reporting of pain on the visual analogue scale, importance of adherence to medications and daily water

	intake. Indirectness: No indirectness
Funding	No funding
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: ALFUZOSIN versus NSAIDS Protocol outcome 1: Hospitalisation/ Use of healthcare services - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: Hospitalisation at 4 weeks ; Group 1: 0/28, Group 2: 3/26 Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, stone size or stone location ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 2: Stone passage - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: stone expulsion rate at 4 weeks ; Group 1: 15/28, Group 2: 7/26 Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, stone size or stone location ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 3: Adverse events - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: adverse events at 4 weeks ; Group 1: 4/28, Group 2: 0/26; Comments: adverse events: headache (2), dizziness (1), hypotension (3) - all tolerable and did not result in discontinuation Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, stone size or stone location ; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Quality of life; Pain intensity; Analgesic use; Time to stone passage

Study	**Elgalaly 2017[58]**
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=40)
Countries and setting	Conducted in Egypt; Setting: Not reported
Line of therapy	1st line
Duration of study	Intervention + follow up: 4 weeks

Method of assessment of guideline condition	Adequate method of assessment/diagnosis: All patients were evaluated by complete history taking and a thorough physical examination. Laboratory investigations included urine analysis and serum creatinine. Radiological assessment with plain abdominal radiograph of the kidneys, ureters and bladder (KUB) and abdomino-pelvic ultrasonography was done
Stratum	Children (<16 years)
Subgroup analysis within study	Not applicable
Inclusion criteria	Paediatric patients who presented with single, radiopaque DUS, age <18 years, single unilateral radiopaque DUS, and largest stone diameter of ≤10 mm
Exclusion criteria	Multiple, bilateral or recurrent stones, radiolucent stone, largest stone diameter >10 mm, UTI or urosepsis, anomalies of the ureter or the kidney, previous urinary tract endoscopy or surgery, marked hydronephrosis, and abnormal renal function
Recruitment/selection of patients	Not reported
Age, gender and ethnicity	Age - Mean (SD): Alpha blocker group 8.4 (3.1); placebo group 7.7 (2.3). Gender (M:F): 27/13. Ethnicity: Not reported
Further population details	1. Kidney pole: 2. Neuropathic/ cerebral-palsy /immobility: 3. Obesity /skin-to-stone distance: 4. Pregnant women: 5. Stone composition/hounsfield units: 6. Uteric stone:
Indirectness of population	No indirectness
Interventions	(n=20) Intervention 1: Alpha blockers - Silodosin. Silodosin 4 mg given at bed-time. For those who could not swallow the capsule, the capsule contents were emptied into a small amount of water or juice. Duration Unclear. Concurrent medication/care: Ibuprofen (20 mg/kg/day) was divided into two doses for pain episodes. Children were encouraged to take plenty of fluids. Indirectness: No indirectness (n=20) Intervention 2: Placebo. Placebo. Duration Unclear. Concurrent medication/care: Ibuprofen (20 mg/kg/day) was divided into two doses for pain episodes. Children were encouraged to take plenty of fluids. Indirectness: No indirectness
Funding	No funding

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: SILODOSIN versus PLACEBO

Protocol outcome 1: Stone passage at Define
- Actual outcome for Children (<16 years): Stone free at 2 weeks; Group 1: 13/18, Group 2: 11/19
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: 2; Group 2 Number missing: 1
- Actual outcome for Children (<16 years): Stone free at 4 weeks; Group 1: 16/18, Group 2: 14/19

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: 2; Group 2 Number missing: 1 Protocol outcome 2: Time to stone passage at Define - Actual outcome for Children (<16 years): Time to stone expulsion at 4 weeks; Group 1: mean 7 days (SD 4.3); n=18, Group 2: mean 10.4 days (SD 4.7); n=19 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: 2; Group 2 Number missing: 1 Protocol outcome 3: Adverse events at Define - Actual outcome for Children (<16 years): Headache and dizziness at 4 weeks; Group 1: 3/18, Group 2: 0/19 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: 2; Group 2 Number missing: 1 Protocol outcome 4: Pain intensity at Define - Actual outcome for Children (<16 years): Number of pain episodes at 4 weeks; Group 1: mean 2.3 (SD 1.4); n=18, Group 2: mean 4.7 (SD 2.6); n=19 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: 2; Group 2 Number missing: 1	
Protocol outcomes not reported by the study	Quality of life at Define; Analgesic use at Define; Hospitalisation/ Use of healthcare services at Define

Study	Elkoushy 2012[60]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=126)
Countries and setting	Conducted in Egypt; Setting: Department of Urology, single centre
Line of therapy	Adjunctive to current care
Duration of study	Intervention + follow up: 3 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: full history, clinical examination, laboratory investigations, plain abdominal film KUB, intravenous urography
Stratum	Adults (≥16 years), ureteric stone <1 cm: mean stone size 9.7 (2.6), 8.6 (1.7)
Subgroup analysis within study	Not applicable: NA
Inclusion criteria	single radio-opaque renal or upper ureteral stones <2cm in largest diameter
Exclusion criteria	age <18 years; multiple stones; radiolucent stones; stones >2cm in largest diameter; previous SWL failure; history of spontaneous stone expulsion; urinary tract infection; distal obstruction; congenital renal or ureteral anomalies; serum creatinine ≥2mg/dl; uncorrectable bleeding disorders; hypotension; morbid obesity; pregnancy; concomitant use of calcium channel-blockers, alpha-adrenergic antagonists or corticosteroids
Recruitment/selection of patients	not reported
Age, gender and ethnicity	Age - Mean (SD): Tamsulosin group: 52.8 (8.2), control group: 49.4 (11.3). Gender (M:F): 72/54. Ethnicity: not reported
Further population details	1. Kidney pole: Not applicable 2. Neuropathic/ cerebral-palsy /immobility: Not applicable 3. Obesity /skin-to-stone distance: Not applicable 4. Pregnant women: Non-pregnant 5. Stone composition/hounsfield units: Not applicable 6. Ureteric stone: Upper ureteric stones
Indirectness of population	Serious indirectness: includes stones < and > 10mm
Interventions	(n=63) Intervention 1: Alpha blockers and SWL. SWL repeated every 3 weeks until the patient became stone free, Tamsulosin 0.4mg daily starting immediately after SWL. Duration up to 3 months. Concurrent medication/care: Diclofenac 50mg tablets or 75mg intramuscular injection on demand. Indirectness: No indirectness; Indirectness comment: NA (n=63) Intervention 2: Surgery and placebo - SWL and placebo. SWL repeated every 3 weeks until the patient became stone free, placebo daily starting immediately after SWL. Duration up to 3 months. Concurrent medication/care: Diclofenac 50mg tablets or 75mg intramuscular injection on demand. Indirectness: No indirectness; Indirectness comment: NA
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: ALPHA BLOCKERS AND SWL versus SWL AND PLACEBO

Protocol outcome 1: Stone passage
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: stone-free rate at 3 months ; Group 1: 27/28, Group 2: 14/21; Comments: numbers calculated from percentages
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, Comments: NA; Baseline details: no significant difference in age, sex, BMI, stone size or stone location ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 2: Time to stone passage
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: time to clearance at 3 months ; Group 1: mean 4.2 weeks (SD 1.7); n=28,
Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: no significant difference in age, sex, BMI, stone size or stone location ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcomes not reported by the study	Quality of life; Adverse events; Pain intensity; Analgesic use; Hospitalisation/ Use of healthcare services

Study	Erturhan 2007[63]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=120)
Countries and setting	Conducted in Turkey; Setting: Department of Urology, single centre
Line of therapy	1st line
Duration of study	Intervention + follow up: 4 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Adults (≥16 years), ureteric stone <1 cm
Subgroup analysis within study	Not applicable
Inclusion criteria	distal ureteral stones <10mm and allowing urinary flow
Exclusion criteria	severe hydronephrosis; solitary kidney; extra stone in urinary system; previous surgery for urinary system stone; nonopaque stone; diseases such as diabetes or hypertension; pregnant; renal reserve reduced by >50%
Recruitment/selection of patients	not reported
Age, gender and ethnicity	Age - Mean (range): 31.5 (19-51). Gender (M:F): 64/56. Ethnicity: not reported
Further population details	1. Kidney pole: Not applicable 2. Neuropathic/ cerebral-palsy /immobility: Not applicable 3. Obesity /skin-to-stone distance: Not applicable 4. Pregnant women: Non-pregnant 5. Stone composition/hounsfield units: Not applicable 6. Ureteric stone: Lower ureteric stones
Indirectness of population	No indirectness
Interventions	(n=30) Intervention 1: Alpha blockers - Tamsulosin. Tamsulosin 0.4mg daily. Duration up to 3 weeks. Concurrent medication/care: prophylactic antibiotic therapy (Ceforoxime axetil 250mg daily) and 2.5 L hydration daily, injectable Diclofenac (max 200mg/day) recommended for routine use during pain episodes. Indirectness: No indirectness (n=30) Intervention 2: Pain management only - NSAIDs. Injectable Diclofenac (max 200mg/day) recommended for routine use during pain episodes. Duration up to 3 weeks. Concurrent medication/care: prophylactic antibiotic therapy (Cefuroxime axetil 250mg daily) and 2.5 L hydration daily. Indirectness: No indirectness
Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: TAMSULOSIN versus NSAIDS	

Protocol outcome 1: Hospitalisation/ Use of healthcare services
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: hospitalisation at 4 weeks ; Group 1: 1/30, Group 2: 2/30
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, stone size or stone location (left/right) ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 2: Stone passage
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: expulsion rate at 4 weeks ; Group 1: 22/30, Group 2: 12/30
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, stone size or stone location (left/right) ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 3: Adverse events
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: withdrawal from the study due to side effects caused by the medications at 4 weeks ; Group 1: 0/30, Group 2: 0/30
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, stone size or stone location (left/right) ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcomes not reported by the study	Quality of life; Pain intensity; Analgesic use; Time to stone passage

Study	**Erturhan 2013[62]**
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=50)
Countries and setting	Conducted in Turkey; Setting: Department of Urology, single centre
Line of therapy	1st line
Duration of study	Intervention time: 3 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Children (<16 years)
Subgroup analysis within study	Not applicable

Inclusion criteria	single radiopaque lower ureteral stone
Exclusion criteria	history of ureteral and/or bladder surgery; anatomic urinary system abnormality; vesicoureteral reflux; neurogenic/non-neurogenic voiding dysfunction; bilateral or nonopaque ureteral stones; severe hydronephrosis; colic pain attacks; use of diuretic and/or calcium channel blockers
Recruitment/selection of patients	not reported
Age, gender and ethnicity	Age - Mean (SD): 6.65 (3.78). Gender (M:F): 24/26. Ethnicity: not reported
Further population details	1. Kidney pole: Not applicable 2. Neuropathic/ cerebral-palsy /immobility: Not applicable 3. Obesity /skin-to-stone distance: Not applicable 4. Pregnant women: Non-pregnant 5. Stone composition/hounsfield units: Not applicable 6. Ureteric stone: Lower ureteric stones
Indirectness of population	No indirectness
Interventions	(n=25) Intervention 1: Alpha blockers - Doxazosin. Doxazosin 0.03mg/kg daily. Duration up to 3 weeks. Concurrent medication/care: Ibuprofen 20mg/kg daily divided in to 2 equal doses or a maximum 40mg/kg daily divided in to 4 equal doses in the case of intractable pain. Indirectness: No indirectness (n=25) Intervention 2: Pain management only - NSAIDs. Ibuprofen 20mg/kg daily divided in to 2 equal doses or a maximum of 40mg/kg daily divided in to 4 equal doses in the case of intractable pain. Duration up to 3 weeks. Concurrent medication/care: NA. Indirectness: No indirectness
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: DOXAZOSIN versus NSAIDS

Protocol outcome 1: Stone passage
- Actual outcome for Children (<16 years): expulsion rate at 3 weeks ; Group 1: 17/24, Group 2: 6/21
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, body weight, or stone size ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcomes not reported by the study	Quality of life; Time to stone passage; Adverse events; Pain intensity; Analgesic use; Hospitalisation/ Use of healthcare services

Study	Eryildirim 2016[65]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=80)
Countries and setting	Conducted in Turkey; Setting: urology clinic, single centre
Line of therapy	Adjunctive to current care
Duration of study	Intervention + follow up: 4 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: history, uro-genital examination, biochemical evaluation, urinalysis tests, non-contrast CT
Stratum	Adults (≥16 years), ureteric stone <1 cm: NA
Subgroup analysis within study	Not applicable: NA
Inclusion criteria	5-10mm single radio-opaque upper ureteral stones
Exclusion criteria	multiple stones; previous stone-related procedures; obstruction; stent placement; auxiliary procedures; congenital anomalies; active urinary tract infection; pregnancy; renal insufficiency
Recruitment/selection of patients	not reported
Age, gender and ethnicity	Age - Mean (SD): 39.41 (12.99). Gender (M:F): 36/18. Ethnicity: not reported
Further population details	1. Kidney pole: Not applicable 2. Neuropathic/ cerebral-palsy /immobility: Not applicable 3. Obesity /skin-to-stone distance: Not applicable 4. Pregnant women: Non-pregnant 5. Stone composition/hounsfield units: Not applicable 6. Ureteric stone: Upper ureteric stones
Indirectness of population	No indirectness: NA
Interventions	(n=40) Intervention 1: Alpha blockers and SWL. SWL and Tamsulosin 0.4mg daily. Duration up to 4 weeks. Concurrent medication/care: Diclofenac 75mg if needed. Indirectness: No indirectness; Indirectness comment: NA (n=40) Intervention 2: Surgery - SWL. SWL. Duration up to 4 weeks. Concurrent medication/care: Diclofenac 75mg if needed. Indirectness: No indirectness; Indirectness comment: NA
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: ALPHA BLOCKERS AND SWL versus SWL

Protocol outcome 1: Quality of life
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: EQ5D at 4 weeks ; Group 1: mean 0.82 (SD 0.11); n=28, Group 2: mean 0.78 (SD 0.09); n=26; EQ5D 0-1 Top=High is good outcome

Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: no significant difference in age, BMI, stone size, hounsfeld unit or degree of hydronephrosis ; Group 1 Number missing: 12, Reason: 7 required DJ stent placement; Group 2 Number missing: 14, Reason: 5 required DJ stent placement
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: EQ5D VAS at 4 weeks ; Group 1: mean 80.36 (SD 11.05); n=28, Group 2: mean 73.65 (SD 8.43); n=26; EQ5D VAS 0-100 Top=High is good outcome
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: no significant difference in age, BMI, stone size, hounsfeld unit or degree of hydronephrosis ; Group 1 Number missing: 12, Reason: 7 required DJ stent placement; Group 2 Number missing: 14, Reason: 5 required DJ stent placement

Protocol outcome 2: Hospitalisation/ Use of healthcare services
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: number of ED visits at 4 weeks ; Group 1: mean 0.82 (SD 0.9); n=28,
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: no significant difference in age, BMI, stone size, hounsfeld unit or degree of hydronephrosis ; Group 1 Number missing: 12, Reason: 7 required DJ stent placement; Group 2 Number missing: 14, Reason: 5 required DJ stent placement

Protocol outcome 3: Stone passage
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: stone free rate at 4 weeks ; Group 1: 20/28, Group 2: 17/26
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: no significant difference in age, BMI, stone size, hounsfeld unit or degree of hydronephrosis ; Group 1 Number missing: 12, Reason: 7 required DJ stent placement; Group 2 Number missing: 14, Reason: 5 required DJ stent placement

Protocol outcome 4: Pain intensity
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: number of renal colic at 4 weeks ; Group 1: mean 2.54 (SD 2.55); n=28,
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: no significant difference in age, BMI, stone size, hounsfeld unit or degree of hydronephrosis ; Group 1 Number missing: 12, Reason: 7 required DJ stent placement; Group 2 Number missing: 14, Reason: 5 required DJ stent placement
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: VAS during pain at 4 weeks ; Group 1: mean 5.86 (SD 1.41); n=28, Group 2: mean 6.65 (SD 1.57); n=26; visual analogue pain scale 0-10 Top=High is poor outcome
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: no significant difference in age, BMI, stone size, hounsfeld unit or degree of hydronephrosis ; Group 1 Number missing: 12, Reason: 7 required DJ stent placement; Group 2 Number missing: 14, Reason: 5 required DJ stent placement

Protocol outcome 5: Analgesic use - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: analgesic required at 4 weeks ; Group 1: mean 242 mg (SD 196.6); n=28, Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: no significant difference in age, BMI, stone size, hounsfeld unit or degree of hydronephrosis ; Group 1 Number missing: 12, Reason: 7 required DJ stent placement; Group 2 Number missing: 14, Reason: 5 required DJ stent placement	
Protocol outcomes not reported by the study	Adverse events; Time to stone passage

Study	**Ferre 2009[68]**
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=80)
Countries and setting	Conducted in USA; Setting: Department of Emergency Medicine, single centre
Line of therapy	1st line
Duration of study	Intervention + follow up: 14 days
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: computed tomography confirmed diagnosis
Stratum	Adults (≥16 years), ureteric stone <1 cm
Subgroup analysis within study	Not applicable
Inclusion criteria	≥18 years of age; able to provide written informed consent; CT confirmed diagnosis of a single calculus in the distal third of the ureter (distal to the internal iliac vessels) inconsistent with phleboliths as determined by a board-certified radiologist
Exclusion criteria	allergy/sensitivity to the study drug; sulfa/sulfonamide allergy; lithiasis of the ureteral intramural tract; acute or chronic renal failure; fever; presence of multiple ureteral stones; peptic ulcer disease; liver failure; pregnancy; breastfeeding; history of urinary surgery; history of endoscopic treatment; concomitant treatment with alphalytic dugs, calcium channel antagonists, nitrates or vardenafil hydrochloride; inability to use the study pain scale; inability to read, write and speak the English language
Recruitment/selection of patients	convenience sampling
Age, gender and ethnicity	Age - Mean (SD): Tamsulosin 47 (14), standard therapy 45 (12). Gender (M:F): 56/21. Ethnicity: white race Tamsulosin group 92.1%, standard therapy group 97.4%

Further population details	1. Kidney pole: Not applicable 2. Neuropathic/ cerebral-palsy /immobility: Not applicable 3. Obesity /skin-to-stone distance: Not applicable 4. Pregnant women: Non-pregnant 5. Stone composition/hounsfield units: Not applicable 6. Ureteric stone: Lower ureteric stones
Indirectness of population	No indirectness
Interventions	(n=39) Intervention 1: Alpha blockers - Tamsulosin. Tamsulosin 0.4mg daily. Duration 10 days. Concurrent medication/care: Ibuprofen 800mg 3 times a day and Oxycodone 5010mg every 4-6 hours as needed for pain. Indirectness: No indirectness (n=41) Intervention 2: Pain management only - Opioids. Ibuprofen 800mg 3 times a day and Oxycodone 5-10mg every 4-6 hours as needed for pain. Duration up to 14 days. Concurrent medication/care: NA. Indirectness: No indirectness
Funding	Academic or government funding (academic grant from the Maine Medical Center Mentored Research Committee)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: TAMSULOSIN versus OPIOIDS

Protocol outcome 1: Hospitalisation/ Use of healthcare services
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: return to emergency department or unscheduled visit with primary care provider at 14 days ; Group 1: 6/38, Group 2: 8/39
Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: more males in study group, no significant difference in race, age, BMI, stone size or emergency department length of stay ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 2: Stone passage
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: spontaneous passage at 14 days ; Group 1: 27/38, Group 2: 24/39
Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: more males in study group, no significant difference in race, age, BMI, stone size or emergency department length of stay ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 3: Adverse events
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: adverse medication effects (nausea, vomiting, dizziness, hypotension, ejaculatory abnormalities, diarrhea, headache, arthralgia, rash) at 14 days ; Group 1: 0/38, Group 2: 0/39
Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: more males in study group, no significant difference in race, age, BMI, stone size or emergency department length of stay ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 4: Pain intensity - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: colicky pain episodes at 14 days ; MD; -0.05 (95%CI -4.81 to 4.7); Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: more males in study group, no significant difference in race, age, BMI, stone size or emergency department length of stay ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 5: Analgesic use - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: opioid used (days) at 14 days ; MD; -4.94 (95%CI -12.04 to 2.15); Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: more males in study group, no significant difference in race, age, BMI, stone size or emergency department length of stay ; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Quality of life; Time to stone passage
Study	**Furyk 2016[69]**
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=393)
Countries and setting	Conducted in Australia; Setting: 5 emergency departments
Line of therapy	1st line
Duration of study	Intervention time: 4 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: computed tomography of KUB
Stratum	Adults (≥16 years), ureteric stone <1 cm
Subgroup analysis within study	Not applicable
Inclusion criteria	>18 years; symptoms suggestive of ureteric colic; calculus demonstrated in the distal ureter (distal to the sacroiliac joint)
Exclusion criteria	temperature >38 degrees; estimated glomerula filtration rate of <60mL/minute per 1.73m²; calculus >10mm; solitary kidney; transplanted kidney; history of ureteral stricture; known allergy to the study medication; current calcium channel blocker or alpha-blocker use; hypotension; pregnant or planning pregnancy
Recruitment/selection of patients	opportunity sampling by medical staff and screening of ED databases for any patient meeting inclusion/exclusion criteria during the recruitment period
Age, gender and ethnicity	Age - Median (IQR): Tamsulosin group: 45.5 (35-55), placebo group: 46 (37-55). Gender (M:F): 320/73. Ethnicity: not reported

Further population details	1. Kidney pole: Not applicable 2. Neuropathic/ cerebral-palsy /immobility: Not applicable 3. Obesity /skin-to-stone distance: Not applicable 4. Pregnant women: Non-pregnant 5. Stone composition/hounsfield units: Not applicable 6. Ureteric stone: Lower ureteric stones
Indirectness of population	No indirectness
Interventions	(n=198) Intervention 1: Alpha blockers - Tamsulosin. Tamsulosin 0.4mg daily. Duration up to 4 weeks. Concurrent medication/care: analgesia at the discretion of the treating physician - recommended regimens were Indomethacin 25-50mg 3 times daily and Oxycodone 5-10mg 3 times daily as required for breakthrough. Indirectness: No indirectness (n=195) Intervention 2: Placebo. Placebo. Duration up to 4 weeks. Concurrent medication/care: analgesia at the discretion of the treating physician - recommended regimens were Indomethacin 25-50mg 3 times daily and Oxycodone 5-10mg 3 times daily as required for breakthrough. Indirectness: No indirectness
Funding	Academic or government funding (grant from the Queensland Emergency Medicine Research Foundation)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: TAMSULOSIN versus PLACEBO

Protocol outcome 1: Hospitalisation/ Use of healthcare services
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: re-presentation to ED at 4 weeks ; Group 1: 31/198, Group 2: 35/195
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 ; Baseline details: no significant difference in age, sex, stone size, stone location or urine culture result ; Group 1 Number missing: ; Group 2 Number missing:
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: admission to hospital at 4 weeks ; Group 1: 20/198, Group 2: 23/195
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 ; Baseline details: no significant difference in age, sex, stone size, stone location or urine culture result ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 2: Stone passage
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: stone passage at 4 weeks ; Group 1: 140/161, Group 2: 127/155
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 ; Baseline details: no significant difference in age, sex, stone size, stone location or urine culture result ; Group 1 Number missing: 37; Group 2 Number missing: 40

Protocol outcome 3: Pain intensity
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: pain score >0 at 1 week; Group 1: 142/185, Group 2: 143/182; Comments: verbal numeric pain scale
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 ; Baseline details: no significant difference in age, sex, stone size, stone location or urine culture result ; Group 1 Number missing: 13; Group 2 Number missing: 13 - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: pain score >0 at 2 weeks; Group 1: 60/176, Group 2: 58/177 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 ; Baseline details: no significant difference in age, sex, stone size, stone location or urine culture result ; Group 1 Number missing: 22; Group 2 Number missing: 18 - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: pain score >0 at 3 weeks; Group 1: 34/170, Group 2: 37/173 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 ; Baseline details: no significant difference in age, sex, stone size, stone location or urine culture result ; Group 1 Number missing: 28; Group 2 Number missing: 22 - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: pain score >0 at 4 weeks; Group 1: 26/173, Group 2: 28/174 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 ; Baseline details: no significant difference in age, sex, stone size, stone location or urine culture result ; Group 1 Number missing: 25; Group 2 Number missing: 21	
Protocol outcomes not reported by the study	Quality of life; Adverse events; Analgesic use; Time to stone passage

Study	Gandhi 2013[70]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=128)
Countries and setting	Conducted in Nepal; Setting: Department of General Surgery, single centre
Line of therapy	1st line
Duration of study	Intervention time: 4 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: abdominal ultrasonography, IVU or CT when necessary
Stratum	Adults (≥16 years), ureteric stone <1 cm
Subgroup analysis within study	Not applicable
Inclusion criteria	solitary stone in the distal ureter at the juxtavesical tract or vesico-ureteric junction of 5-15mm
Exclusion criteria	urinary tract infection; gross hydronephrosis; diabetes; peptic ulcer disease; hypersensitivity to Nifedipine or corticosteroid; history of spontaneous stone expulsion and hypotension; pregnant women; children
Recruitment/selection of patients	not reported
Age, gender and ethnicity	Age - Mean (SD): Nifedipine group: 30.4 (11.36), Tamsulosin group: 34 (12.83). Gender (M:F): Nifedipine group: 1.48:1, Tamsulosin group 1.28:1 . Ethnicity: not reported
Further population details	1. Kidney pole: Not applicable 2. Neuropathic/ cerebral-palsy /immobility: Not applicable 3. Obesity /skin-to-stone distance: Not applicable 4. Pregnant women: Non-pregnant 5. Stone composition/hounsfield units: Not applicable 6. Ureteric stone: Lower ureteric stones
Indirectness of population	Serious indirectness: included stones < and > 10mm
Interventions	(n=64) Intervention 1: Calcium channel blockers - Nifedipine. Nifedipine 30mg slow-release daily. Duration up to 4 weeks. Concurrent medication/care: oral prednisolone 30mg daily for a maximum of 10 days, Diclofenac 75mg intramuscularly on demand and ≥2 L of water daily . Indirectness: No indirectness (n=64) Intervention 2: Alpha blockers - Tamsulosin. Tamsulosin 0.4mg. Duration up to 4 weeks. Concurrent medication/care: oral prednisolone 30mg daily for a maximum of 10 days, Diclofenac 75mg intramuscularly on demand and ≥2 L of water daily . Indirectness: No indirectness
Funding	No funding
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: TAMSULOSIN versus NIFEDIPINE Protocol outcome 1: Stone passage	

- Actual outcome for Adults (≥16 years), ureteric stone 1-2 cm: expulsion at 4 weeks ; Group 1: 51/64, Group 2: 32/58 Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, duration of pain, stone size or stone location (left/right); Group 1 Number missing: 0; Group 2 Number missing: 6 Protocol outcome 2: Adverse events - Actual outcome for Adults (≥16 years), ureteric stone 1-2 cm: headache at 4 weeks ; Group 1: 32/64, Group 2: 25/58 Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, duration of pain, stone size or stone location (left/right); Group 1 Number missing: 0; Group 2 Number missing: 6 - Actual outcome for Adults (≥16 years), ureteric stone 1-2 cm: dizziness at 4 weeks ; Group 1: 16/64, Group 2: 3/58 Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, duration of pain, stone size or stone location (left/right); Group 1 Number missing: 0; Group 2 Number missing: 6 - Actual outcome for Adults (≥16 years), ureteric stone 1-2 cm: flushing at 4 weeks ; Group 1: 0/64, Group 2: 3/58 Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, duration of pain, stone size or stone location (left/right); Group 1 Number missing: 0; Group 2 Number missing: 6 Protocol outcome 3: Analgesic use - Actual outcome for Adults (≥16 years), ureteric stone 1-2 cm: analgesic use at 4 weeks ; Group 1: mean 0.42 (SD 0.14); n=64, Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, duration of pain, stone size or stone location (left/right); Group 1 Number missing: 0; Group 2 Number missing: 6	
Protocol outcomes not reported by the study	Quality of life; Time to stone passage; Pain intensity; Hospitalisation/ Use of healthcare services

Study	Gravas 2007[76]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=61)
Countries and setting	Conducted in Greece; Setting: Department of Urology, single centre
Line of therapy	Adjunctive to current care
Duration of study	Intervention + follow up: 4 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: plain KUB x-ray
Stratum	Adults (≥16 years), ureteric stone <1 cm: stone size range 6-13mm
Subgroup analysis within study	Not applicable: NA
Inclusion criteria	single radiopaque distal ureteral stone (below the sacral-iliac joint); ≥6mm in diameter undergoing ESWL for the first time
Exclusion criteria	hypotension; ulcer; therapy of benign prostatic obstruction with alpha-blockers; presence of a double J stent previously placed
Recruitment/selection of patients	consecutive patients meeting the inclusion criteria during the recruitment period
Age, gender and ethnicity	Age - Mean (range): Tamsulosin group: 48.8 (27-73), control group: 49.2 (30-72). Gender (M:F): 38/23. Ethnicity: not reported
Further population details	1. Kidney pole: Not applicable 2. Neuropathic/ cerebral-palsy /immobility: Not applicable 3. Obesity /skin-to-stone distance: Not applicable 4. Pregnant women: Not stated / Unclear 5. Stone composition/hounsfield units: Not applicable 6. Ureteric stone: Lower ureteric stones
Indirectness of population	Serious indirectness: includes stones < and > 10mm
Interventions	(n=30) Intervention 1: Alpha blockers and SWL. ESWL then Tamsulosin 0.4mg daily. Duration up to 4 weeks. Concurrent medication/care: hydration of at least 2 L daily and Diclofenac 50mg on demand. Indirectness: No indirectness; Indirectness comment: NA (n=31) Intervention 2: Surgery - SWL. ESWL. Duration up to 4 weeks. Concurrent medication/care: hydration of at least 2 L daily and Diclofenac 50mg on demand. Indirectness: No indirectness; Indirectness comment: NA
Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: ALPHA BLOCKERS AND SWL versus SWL	

Protocol outcome 1: Stone passage - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: stone free rate at 4 weeks ; Group 1: 19/30, Group 2: 16/31 Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: no significant difference in age, sex, stone size or number of shock waves; Group 1 Number missing: 1; Group 2 Number missing: 2 Protocol outcome 2: Adverse events - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: dizziness at 4 weeks ; Group 1: 2/30, Group 2: 0/31 Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: no significant difference in age, sex, stone size or number of shock waves; Group 1 Number missing: 1; Group 2 Number missing: 2	
Protocol outcomes not reported by the study	Quality of life; Time to stone passage; Pain intensity; Analgesic use; Hospitalisation/ Use of healthcare services

Study	Hermanns 2009[86]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=100)
Countries and setting	Conducted in Switzerland; Setting: Department of Urology, single centre
Line of therapy	1st line
Duration of study	Intervention time: 3 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: non-contrast-enhanced abdominal computed tomography
Stratum	Adults (≥16 years), ureteric stone <1 cm
Subgroup analysis within study	Not applicable
Inclusion criteria	≥18 years; acute renal colic; single ureteral stone ≤7mm below the common iliac vessels as assessed by CT
Exclusion criteria	multiple ureteral stones; renal insufficiency; urinary tract infection; solitary kidney; pregnancy; history of ureteral surgery or previous endoscopic procedures; hypersensitivity to Tamsulosin; current alpha-blocker, calcium antagonist or corticosteroid medication
Recruitment/selection of patients	consecutive
Age, gender and ethnicity	Age - Median (IQR): Tamsulosin group 36 (30-44), placebo group 41 (33-54). Gender (M:F): 75/15. Ethnicity: not reported
Further population details	1. Kidney pole: Not applicable 2. Neuropathic/ cerebral-palsy /immobility: Not applicable 3. Obesity /skin-to-stone distance: Not applicable 4. Pregnant women: Non-pregnant 5. Stone composition/hounsfield units: Not applicable 6. Ureteric stone: Lower ureteric stones
Indirectness of population	No indirectness
Interventions	(n=50) Intervention 1: Alpha blockers - Tamsulosin. Tamsulosin 0.4mg daily. Duration up to 3 weeks. Concurrent medication/care: after initial analgesia for acute pain management, no regular analgesic medication was maintained. Oral Diclofenac (up to 3 X 50mg) as first line and oral Metamizole (up to 4 X 1g) as second line on-demand analgesics were prescribed. Indirectness: No indirectness (n=50) Intervention 2: Placebo. Placebo. Duration up to 3 weeks. Concurrent medication/care: after initial analgesia for acute pain management, no regular analgesic medication was maintained. Oral Diclofenac (up to 3 X 50mg) as first-line and oral Metamizole (up to 4 X 1g) as second-line on demand analgesics were prescribed. Indirectness: No indirectness
Funding	No funding

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: TAMSULOSIN versus PLACEBO

Protocol outcome 1: Hospitalisation/ Use of healthcare services
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: hospital readmission with consecutive intervention and discontinuation of medication due to uncontrollable pain or side effects at 3 weeks ; Group 1: 6/45, Group 2: 2/45
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 ; Baseline details: no significant difference in age, sex, stone size or stone location; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 2: Stone passage
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: spontaneous stone expulsion rate at 3 weeks ; Group 1: 39/45, Group 2: 40/45
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 ; Baseline details: no significant difference in age, sex, stone size or stone location; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 3: Time to stone passage
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: time to stone passage at 3 weeks ; HR; 0.99 (95%CI 0.55 to 1.79) (p value : 0.97) , Comments: multiple cox regression analysis for predictive factors - therapy ;
Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, stone size or stone location; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 4: Adverse events
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: retrograde ejaculation at 3 weeks ; Group 1: 2/39, Group 2: 0/36
Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, stone size or stone location; Group 1 Number missing: ; Group 2 Number missing:
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: dizziness at 3 weeks ; Group 1: 0/45, Group 2: 1/45
Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, stone size or stone location; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcomes not reported by the study	Quality of life; Analgesic use; Pain intensity

Study	Ibrahim 2013[92]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=150)
Countries and setting	Conducted in Iraq; Setting: Not reported
Line of therapy	1st line
Duration of study	Intervention + follow up: 4 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Urinary ultrasonography (US) and a plain abdominal X-ray. IVU or CT was used in a few patients depending on specific indications
Stratum	Adults (≥16 years), ureteric stone <1 cm
Subgroup analysis within study	Not stratified but pre-specified: Mid, upper and proximal stone location
Inclusion criteria	Symptomatic ureteric stone of <10 mm in diameter
Exclusion criteria	Acute infection, a solitary kidney, elevated levels in renal functional tests at presentation, severe hydronephrosis, bilateral ureteric stones, pregnancy or lactation, current use of a-blockers, calcium-channel blockers or steroids, age <18 years, and any allergic reaction to the study medication
Recruitment/selection of patients	Not reported
Age, gender and ethnicity	Age - Mean (SD): Alpha blocker group 37.34 (13.15); control 36.71 (11.64). Gender (M:F): 91/21. Ethnicity: Not reported
Further population details	1. Kidney pole: Not applicable 2. Neuropathic/ cerebral-palsy /immobility: Not stated / Unclear 3. Obesity /skin-to-stone distance: Not stated / Unclear 4. Pregnant women: Non-pregnant 5. Stone composition/hounsfield units: Not stated / Unclear 6. Uteric stone: Upper ureteric stones
Indirectness of population	No indirectness
Interventions	(n=22) Intervention 1: Alpha blockers - Tamsulosin. Tamsulosin capsule of 0.4 mg daily (n=30) or alfuzosin 10 mg daily (n=40). Duration 4 weeks. Concurrent medication/care: All the patients were given diclofenac potassium orally 50 mg and/or diclofenac sodium as an intramuscular injection of 75 mg on demand. Indirectness: No indirectness (n=4) Intervention 2: Pain management only - NSAIDs. No alpha blockers. Duration 4 weeks. Concurrent medication/care: All the patients were given diclofenac potassium orally 50 mg and/or diclofenac sodium as an intramuscular injection of 75 mg on demand. Indirectness: No indirectness (n=6) Intervention 3: Alpha blockers - Tamsulosin. As above. Duration 4 weeks. Concurrent medication/care: As above. Indirectness: No indirectness

	(n=5) Intervention 4: Pain management only - NSAIDs. As above. Duration 4 weeks. Concurrent medication/care: As above. Indirectness: No indirectness (n=23) Intervention 5: Pain management only - NSAIDs. As above. Duration 4 weeks. Concurrent medication/care: As above. Indirectness: No indirectness (n=52) Intervention 6: Alpha blockers - Tamsulosin. As above. Duration 4 weeks. Concurrent medication/care: As above. Indirectness: No indirectness
Funding	No funding

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: TAMSULOSIN/ALFUZOSIN (UPPER) versus NSAIDS (UPPER)

Protocol outcome 1: Stone passage at Define
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: Stones passed at 4 weeks; Group 1: 13/22, Group 2: 1/4
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:

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: TAMSULOSIN/ALFUZOSIN (MID) versus NSAIDS (MID)

Protocol outcome 1: Stone passage at Define
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: Stones passed at 4 weeks; Group 1: 5/6, Group 2: 1/5
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:

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: TAMSULOSIN/ALDUZOSIN (LOWER) versus NSAIDS (LOWER)

Protocol outcome 1: Stone passage at Define
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: Stones passed at 4 weeks; Group 1: 46/52, Group 2: 12/23
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; Time to stone passage at Define; Adverse events at Define; Pain intensity at Define; Analgesic use at Define; Hospitalisation/ Use of healthcare services at Define

Study	Islam 2012[93]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=98)
Countries and setting	Conducted in Bangladesh; Setting: not reported
Line of therapy	1st line
Duration of study	Intervention time: 4 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: abdominal ultrasonography, x-ray of the kidneys ureters and bladder and excretory urography
Stratum	Adults (≥16 years), ureteric stone <1 cm
Subgroup analysis within study	Not applicable
Inclusion criteria	distal ureteral stones (juxtavesical tract and ureterovesical junction); ≤1cm in size
Exclusion criteria	urinary tract infection; severe hydronephrosis; solitary kidney; extra stone in the upper urinary system; previous surgery for a urinary system stone; nonopaque stone; disease such as diabetes or hypertension; pregnant; renal reserve reduced by >50%
Recruitment/selection of patients	not reported
Age, gender and ethnicity	Age - Other: Tamsulosin group mean: 46.6, Nifedipine group mean: 47.4, control group mean: 42.8. Gender (M:F): 58/33. Ethnicity: not reported
Further population details	1. Kidney pole: Not applicable 2. Neuropathic/ cerebral-palsy /immobility: Not applicable 3. Obesity /skin-to-stone distance: Not applicable 4. Pregnant women: Non-pregnant 5. Stone composition/hounsfield units: Not applicable 6. Ureteric stone: Lower ureteric stones
Indirectness of population	No indirectness
Interventions	(n=33) Intervention 1: Alpha blockers - Tamsulosin. Tamsulosin 0.4mg daily. Duration up to 4 weeks. Concurrent medication/care: prophylactic antibiotic therapy (Ciprofloxacin 500mg twice daily), 2.5 L hydration daily and Diclofenac recommended for routine use during pain episodes. Indirectness: No indirectness (n=33) Intervention 2: Calcium channel blockers - Nifedipine. Nifedipine 20mg (slow release) daily. Duration up to 4 weeks. Concurrent medication/care: prophylactic antibiotic therapy (Ciprofloxacin 500mg twice daily), 2.5 L hydration daily and Diclofenac recommended for routine use during pain episodes. Indirectness: No indirectness (n=32) Intervention 3: No treatment. No treatment. Duration up to 4 weeks. Concurrent medication/care: prophylactic antibiotic therapy (Ciprofloxacin 500mg twice daily), 2.5 L hydration daily and Diclofenac

	recommended for routine use during pain episodes. Indirectness: No indirectness
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: TAMSULOSIN versus NIFEDIPINE

Protocol outcome 1: Hospitalisation/ Use of healthcare services
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: hospitalisation for recurrent colic at 4 weeks ; Group 1: 0/32, Group 2: 0/31
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex or stone size; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 2: Stone passage
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: stone expulsion at 4 weeks ; Group 1: 27/32, Group 2: 22/31
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex or stone size; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 3: Adverse events
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: hypotension at 4 weeks ; Group 1: 0/32, Group 2: 1/31
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex or stone size; Group 1 Number missing: ; Group 2 Number missing:

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: TAMSULOSIN versus NO TREATMENT

Protocol outcome 1: Hospitalisation/ Use of healthcare services
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: hospitalisation for recurrent colic at 4 weeks ; Group 1: 0/32, Group 2: 0/28
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex or stone size; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 2: Stone passage
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: stone expulsion at 4 weeks ; Group 1: 27/32, Group 2: 13/28
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex or stone size; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 3: Adverse events - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: hypotension at 4 weeks ; Group 1: 0/32, Group 2: 0/28 Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex or stone size; Group 1 Number missing: ; Group 2 Number missing: RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: NIFEDIPINE versus NO TREATMENT Protocol outcome 1: Hospitalisation/ Use of healthcare services - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: hospitalisation for recurrent colic at 4 weeks ; Group 1: 0/31, Group 2: 0/28 Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex or stone size; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 2: Stone passage - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: stone expulsion at 4 weeks ; Group 1: 22/31, Group 2: 13/28 Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex or stone size; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 3: Adverse events - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: hypotension at 4 weeks ; Group 1: 1/31, Group 2: 0/28 Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex or stone size; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Quality of life; Pain intensity; Analgesic use; Time to stone passage

Study	Itoh 2011[95]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=187)
Countries and setting	Conducted in Japan; Setting: Department of Nephro-urology, single centre
Line of therapy	1st line
Duration of study	Intervention time: 8 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: unenhanced computed tomography
Stratum	Adults (≥16 years), ureteric stone <1 cm
Subgroup analysis within study	Not applicable
Inclusion criteria	symptomatic unilateral ureteral calculi <10mm in diameter
Exclusion criteria	urinary tract infection; severe hydronephrosis; diabetes; ulcers; hypotension; multiple stones; ureteral stricture
Recruitment/selection of patients	not reported
Age, gender and ethnicity	Age - Mean (SD): silodosin: 57.2 (12.7), control: 56.5 (10.1). Gender (M:F): 187 males. Ethnicity: not reported
Further population details	1. Kidney pole: Not applicable 2. Neuropathic/ cerebral-palsy /immobility: Not applicable 3. Obesity /skin-to-stone distance: Not applicable 4. Pregnant women: Not applicable 5. Stone composition/hounsfield units: Not applicable 6. Ureteric stone: Not stated / Unclear
Indirectness of population	No indirectness
Interventions	(n=95) Intervention 1: Alpha blockers - Silodosin. Silodosin 8mg daily. Duration up to 8 weeks. Concurrent medication/care: instruction to drink 2 L of water daily. Indirectness: No indirectness (n=92) Intervention 2: No treatment. No treatment. Duration up to 8 weeks. Concurrent medication/care: instruction to drink 2 L of water daily. Indirectness: No indirectness
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: SILODOSIN versus NO TREATMENT

Protocol outcome 1: Stone passage
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: stone expulsion rate (proximal stones) at 8 weeks ; Group 1: 15/26, Group 2: 15/28; Comments: numbers calculated form percentages

Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, stone size, stone location, or stone composition ; Group 1 Number missing: ; Group 2 Number missing:
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: stone expulsion rate (mid-ureteral stones) at 8 weeks ; Group 1: 4/8, Group 2: 1/8; Comments: numbers calculated from percentages
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, stone size, stone location, or stone composition ; Group 1 Number missing: ; Group 2 Number missing:
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: stone expulsion rate (distal stones) at 8 weeks ; Group 1: 40/55, Group 2: 31/56; Comments: numbers calculated from percentages
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, stone size, stone location, or stone composition ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 2: Time to stone passage
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: expulsion time (proximal stones) at 8 weeks ; Group 1: mean 13.45 days (SD 13.48); n=26,
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, stone size, stone location, or stone composition ; Group 1 Number missing: ; Group 2 Number missing:
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: expulsion time (mid-ureteral stones) at 8 weeks ; Group 1: mean 8.67 days (SD 5.03); n=8,
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, stone size, stone location, or stone composition ; Group 1 Number missing: ; Group 2 Number missing:
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: expulsion time (distal stones) at 8 weeks ; Group 1: mean 9.29 days (SD 5.91); n=55,
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, stone size, stone location, or stone composition ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 3: Adverse events
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: retrograde ejaculation at 8 weeks ; Group 1: 3/95, Group 2: 0/92
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, stone size, stone location, or stone composition ; Group 1 Number missing: ; Group 2 Number missing:
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: hypotension at 8 weeks ; Group 1: 1/95, Group 2: 0/92
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, stone size, stone location, or stone composition ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 4: Analgesic use - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: number of times analgesics were required (proximal stones) at 8 weeks ; Group 1: mean 2.3 (SD 6.6); n=26, Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, stone size, stone location, or stone composition ; Group 1 Number missing: ; Group 2 Number missing: - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: number of times analgesics were required (mid-ureteral stones) at 8 weeks ; Group 1: mean 0.1 (SD 0.3); n=8, Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, stone size, stone location, or stone composition ; Group 1 Number missing: ; Group 2 Number missing: - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: number of times analgesics were required (distal stones) at 8 weeks ; Group 1: mean 0.3 (SD 0.9); n=55, Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, stone size, stone location, or stone composition ; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Quality of life; Pain intensity; Hospitalisation/ Use of healthcare services

Study	Ketabchi 2014[103]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=142)
Countries and setting	Conducted in Iran; Setting: Urology department, single centre
Line of therapy	Adjunctive to current care
Duration of study	Intervention + follow up: 2 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: KUB x-ray, abdominal ultrasonography and intravenous urography
Stratum	Adults (≥16 years), ureteric stone <1 cm: NA
Subgroup analysis within study	Not applicable: NA
Inclusion criteria	single radio opaque lower ureteral stone with 5-10mm diameter
Exclusion criteria	urinary tract infections; high grade hydronephrosis; diabetes; history of hypersensitivity to alpha-blockers; ureteral stricture; pregnant women; history of spontaneous stone expulsion; previous ureteral surgery; hypotension or systolic blood pressure <110mmHg
Recruitment/selection of patients	consecutive patients meeting the inclusion criteria during the recruitment period
Age, gender and ethnicity	Age - Mean (SD): Tamsulosin group: 24 (6.5), control group: 27 (8.8). Gender (M:F): 77/25. Ethnicity: not reported
Further population details	1. Kidney pole: Not applicable 2. Neuropathic/ cerebral-palsy /immobility: Not applicable 3. Obesity /skin-to-stone distance: Not applicable 4. Pregnant women: Non-pregnant 5. Stone composition/hounsfield units: Not applicable 6. Ureteric stone: Lower ureteric stones
Indirectness of population	No indirectness: NA
Interventions	(n=52) Intervention 1: Alpha blockers and URS. Tamsulosin 0.4mg daily starting one day before URS. Duration up to 2 weeks. Concurrent medication/care: recommendation to drink 2 L of water daily, those with moderate to severe pain (>5 VAS) consumed Pethidine 25mg intravenously after the procedure in the recovery room and Indomethacin 500mg suppository daily. Indirectness: No indirectness; Indirectness comment: NA (n=50) Intervention 2: Surgery and placebo - URS and placebo. Placebo daily starting one day before URS. Duration up to 2 weeks. Concurrent medication/care: recommendation to drink 2 L of water daily, those with moderate to severe pain (>5 VAS) consumed Pethidine 25mg intravenously after the procedure in the recovery room and Indomethacin 500mg suppository daily. Indirectness: No indirectness; Indirectness comment: NA

Funding	Academic or government funding (physiology center of Kerman University of Medical Sciences)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: ALPHA BLOCKERS AND URS versus URS AND PLACEBO

Protocol outcome 1: Stone passage
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: expulsion rate at 2 weeks ; Group 1: 49/52, Group 2: 35/50
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: no significant difference in age, sex, stone location (left/right) or stone size; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 2: Pain intensity
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: colic episodes at 2 weeks ; Group 1: mean 1 (SD 0.7); n=52,
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: no significant difference in age, sex, stone location (left/right) or stone size; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 3: Analgesic use
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: need for analgesia at 2 weeks ; Group 1: 4/52, Group 2: 12/50
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: no significant difference in age, sex, stone location (left/right) or stone size; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcomes not reported by the study	Quality of life; Time to stone passage; Adverse events; Hospitalisation/ Use of healthcare services

Study	Kupeli 2004[114]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=78)
Countries and setting	Conducted in Turkey; Setting: Department of Urology, single centre
Line of therapy	1st line
Duration of study	Intervention time: 15 days
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: x-rays, intravenous pyelography, helical computed tomography etc.
Stratum	Adults (≥16 years), ureteric stone <1 cm
Subgroup analysis within study	Not applicable
Inclusion criteria	lower ureteral stones within the distal 5cm of the ureter that ranged between 3 and 15mm in size
Exclusion criteria	signs and symptoms of urinary tract infection; pregnancy; severely impacted stones; multiple stones; nonopaque stones; severe hydronephrosis; hepatic dysfunction; non-functioning kidney; treatment with calcium antagonists; morbid obesity
Recruitment/selection of patients	not reported
Age, gender and ethnicity	Age - Mean (range): 42.9 (21-67). Gender (M:F): 56/22. Ethnicity: not reported
Further population details	1. Kidney pole: Not applicable 2. Neuropathic/ cerebral-palsy /immobility: Not applicable 3. Obesity /skin-to-stone distance: Not applicable 4. Pregnant women: Non-pregnant 5. Stone composition/hounsfield units: Not applicable 6. Ureteric stone: Lower ureteric stones
Indirectness of population	No indirectness: adjunctive therapy groups included stones < and > 10mm
Interventions	(n=15) Intervention 1: Alpha blockers - Tamsulosin. Tamsulosin 0.4mg daily. Duration 15 days. Concurrent medication/care: conventional treatment - oral hydration and oral Diclofenac 100mg daily. Indirectness: No indirectness; Indirectness comment: NA (n=15) Intervention 2: Pain management only - NSAIDs. Oral Diclofenac 100mg daily. Duration 15 days. Concurrent medication/care: oral hydration. Indirectness: No indirectness; Indirectness comment: NA (n=24) Intervention 3: Alpha blockers and SWL. Tamsulosin 0.4mg daily after SWL. Duration 15 days. Concurrent medication/care: conventional treatment - oral hydration and oral Diclofenac 100mg daily. Indirectness: No indirectness; Indirectness comment: NA (n=24) Intervention 4: Surgery and pain management - SWL and pain management. SWL. Duration 15 days. Concurrent medication/care: conventional treatment - oral hydration and oral Diclofenac 100mg daily.

	Indirectness: No indirectness; Indirectness comment: NA
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: TAMSULOSIN versus NSAIDS

Protocol outcome 1: Stone passage
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: stone-free rate at 15 days ; Group 1: 8/15, Group 2: 3/15
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 ; Baseline details: no significant difference in age or stone diameter ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 2: Adverse events
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: dizziness at 15 days ; Group 1: 1/39, Group 2: 0/39
Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age or stone diameter ; Group 1 Number missing: ; Group 2 Number missing:

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: ALPHA BLOCKERS AND SWL versus SWL AND PAIN MANAGEMENT

Protocol outcome 1: Stone passage
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: stone-free rate at 15 days ; Group 1: 17/24, Group 2: 8/24
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 ; Baseline details: no significant difference in age or stone diameter ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcomes not reported by the study	Quality of life; Time to stone passage; Pain intensity; Analgesic use; Hospitalisation/ Use of healthcare services

Study	Lee 2014[116]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=108)
Countries and setting	Conducted in South Korea; Setting: Department of Urology, 2 university hospitals
Line of therapy	1st line
Duration of study	Intervention time: 4 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: plain abdominal radiography kidney ureter bladder and non-contrast CT
Stratum	Adults (≥16 years), ureteric stone <1 cm
Subgroup analysis within study	Not applicable
Inclusion criteria	≥18 years; presenting with renal colic; diagnosed with single, unilateral radiopaque, proximal (defined as segment between the ureteropelvic junction and the upper border of the sacroiliac joint) ureteral calculi ≤6mm in diameter; agreed to undergo conservative management
Exclusion criteria	ureteral calculi ≥7mm or multiple ureteral calculi; febrile urinary tract infection; single kidney; non-functioning kidney; pregnancy; azotaemia (creatinine >1.8mg/dl); ureteral stricture; severe hydronephrosis; current treatment with medications that could affect stone passage such as alpha-blockers, calcium channel blockers, steroids, or nitrates; patients wanting immediate stone removal because of colic
Recruitment/selection of patients	not reported
Age, gender and ethnicity	Age - Mean (SD): 45.8 (12.1). Gender (M:F): 68/40. Ethnicity: not reported
Further population details	1. Kidney pole: Not applicable 2. Neuropathic/ cerebral-palsy /immobility: Not applicable 3. Obesity /skin-to-stone distance: Not applicable 4. Pregnant women: Non-pregnant 5. Stone composition/hounsfield units: Not applicable 6. Ureteric stone: Upper ureteric stones
Indirectness of population	No indirectness
Interventions	(n=54) Intervention 1: Alpha blockers - Tamsulosin. Tamsulosin 0.2mg daily. Duration up to 4 weeks. Concurrent medication/care: instruction to drink 2 L of water daily and oral painkiller (Ultracet® combination of Tramadol and Acetaminophen) on demand. Indirectness: No indirectness (n=54) Intervention 2: No treatment. No treatment. Duration up to 4 weeks. Concurrent medication/care: instruction to drink 2 L of water daily and oral painkiller (Ultracet® combination of Tramadol and Acetaminophen) on demand. Indirectness: No indirectness
Funding	Study funded by industry (Korean Astellas Pharm, Co.)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: TAMSULOSIN versus NO TREATMENT

Protocol outcome 1: Quality of life
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: post-trial EuroQoL at 4 weeks ; Group 1: mean 5.4 (SD 0.6); n=44, Group 2: mean 5.5 (SD 0.8); n=35; EuroQoL 0-10 Top=High is good outcome
Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, past stone history, baseline pain and QoL scores, stone site or stone size; Group 1 Number missing: 10, Reason: 6 lost to follow-up, 4 converted to active treatment ; Group 2 Number missing: 19, Reason: 8 lost to follow-up, 11 converted to active treatment

Protocol outcome 2: Stone passage
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: stone passage at 4 weeks ; Group 1: 40/54, Group 2: 25/54
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, past stone history, baseline pain and QoL scores, stone site or stone size; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 3: Time to stone passage
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: time to stone passage at 4 weeks ; Group 1: mean 14.3 days (SD 7.9); n=44,
Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, past stone history, baseline pain and QoL scores, stone site or stone size; Group 1 Number missing: 10, Reason: 6 lost to follow-up, 4 converted to active treatment ; Group 2 Number missing: 19, Reason: 8 lost to follow-up, 11 converted to active treatment

Protocol outcome 4: Analgesic use
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: requirement for oral analgesics at 4 weeks ; Group 1: mean 3.5 unclear (SD 3.8); n=44,
Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, past stone history, baseline pain and QoL scores, stone site or stone size; Group 1 Number missing: 10, Reason: 6 lost to follow-up, 4 converted to active treatment ; Group 2 Number missing: 19, Reason: 8 lost to follow-up, 11 converted to active treatment

Protocol outcomes not reported by the study	Adverse events; Pain intensity; Hospitalisation/ Use of healthcare services

Study	Lojanapiwat 2008[125]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=75)
Countries and setting	Conducted in Thailand; Setting: Division of Urology, Department of Surgery, 2 hospitals
Line of therapy	1st line
Duration of study	Intervention time: 4 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: plain kidney, ureter and bladder radiographs
Stratum	Adults (≥16 years), ureteric stone <1 cm
Subgroup analysis within study	Not applicable
Inclusion criteria	distal ureteric stones of 4-10mm; measured by plain KUB; gave informed consent; interviewed prior to taking part
Exclusion criteria	urinary tract infection; severe hydronephrosis; history of ureteric surgery
Recruitment/selection of patients	not reported
Age, gender and ethnicity	Age - Mean (SD): control group: 46.52 (13.63), Tamsulosin 0.2mg: 48 (15.74), Tamsulosin 0.4mg: 46.71 (12.2). Gender (M:F): 55/20. Ethnicity: not reported
Further population details	1. Kidney pole: Not applicable 2. Neuropathic/ cerebral-palsy /immobility: Not applicable 3. Obesity /skin-to-stone distance: Not applicable 4. Pregnant women: Not stated / Unclear 5. Stone composition/hounsfield units: Not applicable 6. Ureteric stone: Lower ureteric stones
Indirectness of population	No indirectness
Interventions	(n=50) Intervention 1: Alpha blockers - Tamsulosin. Tamsulosin 0.2mg or 0.4mg daily. Duration up to 4 weeks. Concurrent medication/care: Diclofenac 50mg twice daily for 10 days and Diclofenac 75mg infection if renal colic developed during treatment . Indirectness: No indirectness (n=25) Intervention 2: Pain management only - NSAIDs. Diclofenac 50mg twice daily. Duration 10 days. Concurrent medication/care: Diclofenac 75mg injection if renal colic developed. Indirectness: No indirectness
Funding	Equipment / drugs provided by industry (Astellas Pharma)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: TAMSULOSIN versus NSAIDS Protocol outcome 1: Stone passage	

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: expulsion rate (0.2mg Tamsulosin) at 4 weeks ; Group 1: 10/25, Group 2: 1/25
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, weight or stone size ; Group 1 Number missing: ; Group 2 Number missing:
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: expulsion rate (0.4mg Tamsulosin) at 4 weeks ; Group 1: 17/25, Group 2: 1/25
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, weight or stone size ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 2: Time to stone passage
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: expulsion time (0.2mg Tamsulosin) at 4 weeks ; Group 1: mean 9.3 days (SD 6.06); n=25,
Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, weight or stone size ; Group 1 Number missing: ; Group 2 Number missing:
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: expulsion time (0.4mg Tamsulosin) at 4 weeks ; Group 1: mean 10.76 days (SD 7.52); n=25,
Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, weight or stone size ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 3: Adverse events
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: hypotension (0.2mg Tamsulosin) at 4 weeks ; Group 1: 0/25, Group 2: 0/25
Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, weight or stone size ; Group 1 Number missing: ; Group 2 Number missing:
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: hypotension (0.4mg Tamsulosin) at 4 weeks ; Group 1: 0/25, Group 2: 0/25
Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, weight or stone size ; Group 1 Number missing: ; Group 2 Number missing:
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: retrograde ejaculation (0.2mg Tamsulosin) at 4 weeks ; Group 1: 0/15, Group 2: 0/20
Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, weight or stone size ; Group 1 Number missing: ; Group 2 Number missing:
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: retrograde ejaculation (0.4mg Tamsulosin) at 4 weeks ; Group 1: 0/20, Group 2: 0/20
Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, weight or stone size ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 4: Analgesic use - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: Diclofenac injection (0.2mg Tamsulosin) at 4 weeks ; Group 1: 1/25, Group 2: 0/25 Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, weight or stone size ; Group 1 Number missing: ; Group 2 Number missing: - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: Diclofenac injection (0.4mg Tamsulosin) at 4 weeks ; Group 1: 0/25, Group 2: 0/25 Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, weight or stone size ; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Quality of life; Pain intensity; Hospitalisation/ Use of healthcare services

Study	**Lv 2014[130]**
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=105)
Countries and setting	Conducted in China; Setting: Department of Urology, single centre
Line of therapy	1st line
Duration of study	Intervention time: 2 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: abdominal ultrasound, plain abdominal x-ray for KUB, intravenous urogram or unenhanced CT when necessary
Stratum	Adults (≥16 years), ureteric stone <1 cm
Subgroup analysis within study	Not applicable
Inclusion criteria	distal ureteral stone 4-9mm
Exclusion criteria	multiple stones; history of distal ureteral surgery; renal colic for >24hours; urinary tract infection; severe hydronephrosis; voiding dysfunction; hypotension; cardiovascular and cerebrovascular diseases; hepatic and renal dysfunction; pregnancy; diabetes; ulcer disease; history of hypersensitivity to Naftopidil; subjects receiving treatment with cardiovascular drugs, other NSAIDs, alpha receptor antagonists or calcium antagonists
Recruitment/selection of patients	not reported
Age, gender and ethnicity	Age - Mean (SD): Naftopidil group: 31.4 (2.94), Naftopidil + Celecoxib group: 33.2 (5.28), Celecoxib group: 33.75 (5.24). Gender (M:F): 59/44. Ethnicity: not reported

Further population details	1. Kidney pole: Not applicable 2. Neuropathic/ cerebral-palsy /immobility: Not applicable 3. Obesity /skin-to-stone distance: Not applicable 4. Pregnant women: Non-pregnant 5. Stone composition/hounsfield units: Not applicable 6. Ureteric stone: Lower ureteric stones
Indirectness of population	No indirectness
Interventions	(n=35) Intervention 1: Alpha blockers - Naftopidil. Naftopidil 50mg daily. Duration up to 2 weeks. Concurrent medication/care: instruction to drink at least 2 L of fluids daily. Indirectness: No indirectness (n=35) Intervention 2: Alpha blockers - Naftopidil . Naftopidil 50mg daily and Celecoxib 400mg immediately then 200mg every 12 hours. Duration up to 2 weeks. Concurrent medication/care: instruction to drink at least 2 L of fluids daily. Indirectness: No indirectness (n=33) Intervention 3: Pain management only - NSAIDs. Celecoxib 400mg immediately then 200mg every 12 hours. Duration up to 2 weeks. Concurrent medication/care: instruction to drink at least 2 L of fluids daily. Indirectness: No indirectness
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: NAFTOPIDIL versus NSAIDS

Protocol outcome 1: Stone passage
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: expulsion rate (Naftopidil) at 2 weeks; Group 1: 29/35, Group 2: 20/33
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, stone size, stone location (left/right) or baseline VAS score ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 2: Time to stone passage
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: time to expulsion (Naftopidil) at 2 weeks; Group 1: mean 8 days (SD 2.07); n=35,
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, stone size, stone location (left/right) or baseline VAS score ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 3: Adverse events
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: dizziness (Naftopidil) at 2 weeks; Group 1: 4/35, Group 2: 8/33
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, stone size, stone location (left/right) or baseline VAS score ; Group 1 Number missing: ; Group 2 Number missing:
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: headache (Naftopidil) at 2 weeks; Group 1: 2/35, Group 2: 0/33

Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, stone size, stone location (left/right) or baseline VAS score ; Group 1 Number missing: ; Group 2 Number missing:
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: retrograde ejaculation (Naftopidil) at 2 weeks; Group 1: 0/20, Group 2: 0/18
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, stone size, stone location (left/right) or baseline VAS score ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 4: Pain intensity
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: pain episodes (Naftopidil) at 2 weeks; Group 1: mean 2.22 pain episodes (SD 0.94); n=35,
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, stone size, stone location (left/right) or baseline VAS score ; Group 1 Number missing: ; Group 2 Number missing:
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: VAS score (Naftopidil) at 3 days ; Group 1: mean 5.74 (SD 0.92); n=35, Group 2: mean 3.06 (SD 1.14); n=33; visual analogue scale 0-10 Top=High is poor outcome
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, stone size, stone location (left/right) or baseline VAS score ; Group 1 Number missing: ; Group 2 Number missing:
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: VAS score (Naftopidil) at 7 days ; Group 1: mean 4.8 (SD 0.53); n=35, Group 2: mean 1.57 (SD 0.5); n=33; visual analogue scale 0-10 Top=High is poor outcome
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, stone size, stone location (left/right) or baseline VAS score ; Group 1 Number missing: ; Group 2 Number missing:

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: NAFTOPIDIL versus NSAIDS

Protocol outcome 1: Stone passage
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: expulsion rate (Naftopidil + Celecoxib) at 2 weeks; Group 1: 33/35, Group 2: 20/33
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, stone size, stone location (left/right) or baseline VAS score ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 2: Time to stone passage
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: time to expulsion (Naftopidil + Celecoxib) at 2 weeks; Group 1: mean 7.7 days (SD 2.34); n=35,
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, stone size, stone location (left/right) or baseline VAS score ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 3: Adverse events
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: dizziness (Naftopidil + Celecoxib) at 2 weeks; Group 1: 6/35, Group 2: 8/33
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, stone size, stone location (left/right) or baseline VAS score ; Group 1 Number missing: ; Group 2 Number missing:
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: headache (Naftopidil + Celecoxib) at 2 weeks; Group 1: 2/35, Group 2: 0/33
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, stone size, stone location (left/right) or baseline VAS score ; Group 1 Number missing: ; Group 2 Number missing:
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: retrograde ejaculation (Naftopidil + Celecoxib) at 2 weeks; Group 1: 1/21, Group 2: 0/18
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, stone size, stone location (left/right) or baseline VAS score ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 4: Pain intensity
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: pain episodes (Naftopidil + Celecoxib) at 2 weeks; Group 1: mean 1.37 pain episodes (SD 1.33); n=35,
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, stone size, stone location (left/right) or baseline VAS score ; Group 1 Number missing: ; Group 2 Number missing:
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: VAS score (Naftopidil + Celecoxib) at 3 days ; Group 1: mean 3.11 (SD 0.63); n=35, Group 2: mean 3.06 (SD 1.14); n=33; visual analogue scale 0-10 Top=High is poor outcome
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, stone size, stone location (left/right) or baseline VAS score ; Group 1 Number missing: ; Group 2 Number missing:
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: VAS score (Naftopidil + Celecoxib) at 7 days ; Group 1: mean 1.6 (SD 0.6); n=35, Group 2: mean 1.57 (SD 0.5); n=33; visual analogue scale 0-10 Top=High is poor outcome
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, stone size, stone location (left/right) or baseline VAS score ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcomes not reported by the study	Quality of life; Analgesic use; Hospitalisation/ Use of healthcare services

Study	**Mokhless 2012[138]**
Study type	RCT (Patient randomised; Parallel)

Number of studies (number of participants)	1 (n=61)
Countries and setting	Conducted in Egypt; Setting: Section of Pediatric Urology and Endourology, Department of Urology, single centre
Line of therapy	1st line
Duration of study	Intervention time: 4 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: ultrasound of urinary tract, plain x-ray of abdomen and pelvis and renal function tests, non-contrast CT when indicated
Stratum	Children (<16 years)
Subgroup analysis within study	Not applicable
Inclusion criteria	radiopaque lower ureteral stones of ≤12mm
Exclusion criteria	anatomical abnormalities; non-radiopaque stones; voiding dysfunction; urinary tract infection; severe hydronephrosis; history of endoscopic or open ureteral surgery
Recruitment/selection of patients	not reported
Age, gender and ethnicity	Age - Mean (SD): 8.1 (6.8). Gender (M:F): 36/25. Ethnicity: not reported
Further population details	1. Kidney pole: Not applicable 2. Neuropathic/ cerebral-palsy /immobility: Not applicable 3. Obesity /skin-to-stone distance: Not applicable 4. Pregnant women: Not applicable 5. Stone composition/hounsfield units: Not applicable 6. Uteric stone: Lower ureteric stones
Indirectness of population	No indirectness
Interventions	(n=33) Intervention 1: Alpha blockers - Tamsulosin. Tamsulosin 0.4 mg for children older than 4 years and 0.2 mg for younger children at bed time in addition to standard analgesia (ibuprofen). Those who could swallow the whole capsule were allowed to do so otherwise the content of the capsule was evacuated in water or juice . Duration 4 weeks. Concurrent medication/care: Standard analgesia (ibuprofen) (n=28) Intervention 2: Placebo. Placebo. Duration 4 weeks. Concurrent medication/care: Standard analgesia (ibuprofen)
Funding	No funding
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: TAMSULOSIN versus PLACEBO	

Protocol outcome 1: Stone passage at Define - Actual outcome for Children (<16 years): Expulsion rate at 4 weeks; Group 1: 29/33, Group 2: 18/28 Risk of bias: All domain - Very high, Selection - Very 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: Time to stone passage at Define - Actual outcome for Children (<16 years): Time to expulsion at 4 weeks; Group 1: mean 8.2 days (SD 3.4); n=33, Group 2: mean 14.5 days (SD 4.5); n=28 Risk of bias: All domain - Very high, Selection - Very 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: Adverse events at Define - Actual outcome for Children (<16 years): Hypotension at 4 weeks; Group 1: 0/33, Group 2: 0/28 Risk of bias: All domain - Very high, Selection - Very 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: Pain intensity at Define - Actual outcome for Children (<16 years): Pain episodes at 4 weeks; Group 1: mean 1.4 (SD 1.2); n=33, Group 2: mean 2.2 (SD 1.4); n=28 Risk of bias: All domain - Very high, Selection - Very 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 5: Analgesic use at Define - Actual outcome for Children (<16 years): Need for analgesia at 4 weeks; Group 1: mean 0.7 (SD 0.9); n=33, Group 2: mean 1.4 (SD 1.1); n=28 Risk of bias: All domain - Very high, Selection - Very 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; Hospitalisation/ Use of healthcare services at Define

Study	Mohseni 2006[137]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=64)
Countries and setting	Conducted in Iran; Setting: Department of Urology, single centre
Line of therapy	1st line
Duration of study	Intervention time: 4 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: abdominal sonography or kidney, ureter, bladder
Stratum	Adults (≥16 years), ureteric stone <1 cm
Subgroup analysis within study	Not applicable
Inclusion criteria	lower ureteral stone
Exclusion criteria	urinary tract infection; severe hydronephrosis; elevated creatinine; hypertension; history of peptic ulcer disease; spontaneous stone passage; any previous intervention
Recruitment/selection of patients	consecutive
Age, gender and ethnicity	Age - Mean (SD): Terazosin group: 44.2 (12.9), control group: 39.3 (14.2). Gender (M:F): 44/20. Ethnicity: not reported
Further population details	1. Kidney pole: Not applicable 2. Neuropathic/ cerebral-palsy /immobility: Not applicable 3. Obesity /skin-to-stone distance: Not applicable 4. Pregnant women: Not stated / Unclear 5. Stone composition/hounsfield units: Not applicable 6. Ureteric stone: Lower ureteric stones
Indirectness of population	No indirectness
Interventions	(n=32) Intervention 1: Pain management only - NSAIDs. Indomethacin. Duration up to 4 weeks. Concurrent medication/care: intravenous Pethidine in cases of incomplete pain control. Indirectness: No indirectness (n=32) Intervention 2: Alpha blockers - Terazosin. Terazosin 10mg daily. Duration up to 4 weeks. Concurrent medication/care: Indomethacin and intravenous Pethidine in cases of incomplete pain control. Indirectness: No indirectness
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: TERAZOSIN versus NSAIDS

Protocol outcome 1: Stone passage
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: stone expulsion rate at 4 weeks ; Group 1: 29/32, Group 2: 20/32

Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age or stone size ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 2: Time to stone passage - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: time to expulsion at 4 weeks ; Group 1: mean 76.3 hours (SD 60); n=32, Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age or stone size ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 3: Adverse events - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: hypotension at 4 weeks ; Group 1: 3/32, Group 2: 0/32 Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age or stone size ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 4: Analgesic use - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: amount of Pethidine administered at 4 weeks ; Group 1: mean 34.4 mg (SD 12.7); n=32, Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age or stone size ; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Quality of life; Pain intensity; Hospitalisation/ Use of healthcare services

Study	Moursy 2010[140]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=88)
Countries and setting	Conducted in Egypt; Setting: Urology department, single centre
Line of therapy	Adjunctive to current care
Duration of study	Intervention + follow up: 4 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: KUB radiographs
Stratum	Adults (≥16 years), ureteric stone <1 cm: NA
Subgroup analysis within study	Not applicable: NA
Inclusion criteria	>18 years with unilateral steinstrasse
Exclusion criteria	clinical and laboratory signs of urinary tract infection, severe hydronephrosis, alterations in creatininaemia, diabetes, ulcer disease or hypotension; concomitant usage of calcium antagonists; distal ureteral surgery
Recruitment/selection of patients	not reported
Age, gender and ethnicity	Age - Mean (SD): Tamsulosin group: 35.6 (9.95), control group: 33.9 (9.71). Gender (M:F): 55/33. Ethnicity: not reported
Further population details	1. Kidney pole: Not applicable 2. Neuropathic/ cerebral-palsy /immobility: Not applicable 3. Obesity /skin-to-stone distance: Not applicable 4. Pregnant women: Not stated / Unclear 5. Stone composition/hounsfield units: Not applicable 6. Ureteric stone: Not stated / Unclear
Indirectness of population	No indirectness: NA
Interventions	(n=44) Intervention 1: Alpha blockers and SWL. Tamsulosin 0.4mg daily. Duration up to 4 weeks. Concurrent medication/care: Indomethacin 100mg suppository on demand and encouragement to drink a minimum 2.5 L of water daily. Indirectness: No indirectness; Indirectness comment: NA (n=44) Intervention 2: Surgery - SWL. Pain management only. Duration up to 4 weeks. Concurrent medication/care: Indomethacin 100mg suppository on demand and encouragement to drink a minimum 2.5 L of water daily. Indirectness: No indirectness; Indirectness comment: NA
Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: ALPHA BLOCKERS AND SWL versus SWL Protocol outcome 1: Hospitalisation/ Use of healthcare services	

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: Hospitalisation at 4 weeks ; Group 1: 12/44, Group 2: 19/44
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: no significant difference in age, sex, stone location, stone length or fragment size; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 2: Stone passage
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: stone expulsion rate at 4 weeks ; Group 1: 32/44, Group 2: 25/44
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: no significant difference in age, sex, stone location, stone length or fragment size; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 3: Time to stone passage
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: stone expulsion time at 4 weeks ; Group 1: mean 12.67 days (SD 2.29); n=44,
Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: no significant difference in age, sex, stone location, stone length or fragment size; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 4: Adverse events
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: anejaculation at 4 weeks ; Group 1: 6/28, Group 2: 0/27
Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: no significant difference in age, sex, stone location, stone length or fragment size; Group 1 Number missing: ; Group 2 Number missing:
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: headache at 4 weeks ; Group 1: 4/44, Group 2: 0/44
Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: no significant difference in age, sex, stone location, stone length or fragment size; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 5: Analgesic use
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: number of times analgesics used at 4 weeks ; Group 1: mean 4.39 (SD 2.42); n=44,
Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: no significant difference in age, sex, stone location, stone length or fragment size; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcomes not reported by the study	Quality of life; Pain intensity

Study	Mshemish 2012[141]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=105)
Countries and setting	Conducted in Iraq; Setting: Outpatient
Line of therapy	Unclear
Duration of study	Intervention + follow up: 45 days follow up
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Lower ureteral stones were diagnosed on the basis of plain abdominal X-rays, ultrasonography, and computed tomography when necessary
Stratum	Adults (≥16 years), ureteric stone <1 cm
Subgroup analysis within study	Not applicable
Inclusion criteria	Patients ≥18 years presenting with acute renal colic were evaluated for study participation. Patients with a single ureteral stone ≤10mm below the common iliac vessels were eligible for the study
Exclusion criteria	The presence of multiple ureteral stones; hydronephrosis; renal dysfunction; urinary tract infection; a solitary kidney; pregnancy; a history of ureteral surgery or previous endoscopic procedures; hypersensitivity to α-blocker; current α-blocker; calcium-antagonist or corticosteroid medication; and contraindications to NSAIDs
Recruitment/selection of patients	Not reported
Age, gender and ethnicity	Age - Other: Tamsulosin group mean age: 44.3 years (12.5); doxazosin group mean age: 45.1 years (11.6); pain management only group mean age: 43.8 (13.2) . Gender (M:F): 68/32. Ethnicity: Not reported
Further population details	1. Kidney pole: Not applicable 2. Neuropathic/ cerebral-palsy /immobility: Not applicable 3. Obesity /skin-to-stone distance: Not applicable 4. Pregnant women: Not applicable 5. Stone composition/hounsfield units: Not applicable 6. Uteric stone: Not applicable
Indirectness of population	No indirectness
Interventions	(n=35) Intervention 1: Alpha blockers - Tamsulosin. A daily oral dose of tamsulosin (0.4mg). Duration 45 days. Concurrent medication/care: Patients received a first treatment of meloxicam injection (15mg) by intramuscular injection, with a second dose after 30 minutes if necessary, to relieve acute renal colic. All patients received high fluid intake with meloxicam tablets (7.5mg) every 12 hours for 1 week and then meloxicam injection (15mg) as needed, up to a maximum of 2 times per day. Indirectness: No indirectness (n=35) Intervention 2: Alpha blockers - Doxazosin. A daily oral dose of doxazosin (4mg). Duration 45 days. Concurrent medication/care: Same as for the tamsulosin group. Indirectness: No indirectness (n=35) Intervention 3: Pain management only - NSAIDs. Patients received a first treatment of meloxicam

	injection (15mg) by intramuscular injection, with a second dose after 30 minutes if necessary, to relieve acute renal colic; then meloxicam tablets (7.5mg) every 12 hours for 1 week and then meloxicam injection (15mg) as needed, up to a maximum of 2 times per day. Duration 45 days. Concurrent medication/care: All patients received high fluid intake. Indirectness: No indirectness
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: TAMSULOSIN versus NSAIDS

Protocol outcome 1: Hospitalisation/ Use of healthcare services at Define
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: Hospitalisation/ Use of healthcare services (hospitalisation) at 45 days; Group 1: 2/33, Group 2: 3/34
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low; Indirectness of outcome: No indirectness ; Baseline details: There were no statistically significant differences between the 3 groups in terms of sex, age, stone side, size, and location (p>0.05); Group 1 Number missing: 2, Reason: Not reported; Group 2 Number missing: 1, Reason: Not reported
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: Hospitalisation/ Use of healthcare services (emergency room visits) at 45 days; Group 1: 0/33, Group 2: 0/34
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low; Indirectness of outcome: No indirectness ; Baseline details: There were no statistically significant differences between the 3 groups in terms of sex, age, stone side, size, and location (p>0.05); Group 1 Number missing: 2, Reason: Not reported; Group 2 Number missing: 1, Reason: Not reported

Protocol outcome 2: Stone passage rate at Define
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: Stone passage (expulsion rate) at 45 days; Group 1: 27/33, Group 2: 16/34
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low; Indirectness of outcome: No indirectness ; Baseline details: There were no statistically significant differences between the 3 groups in terms of sex, age, stone side, size, and location (p>0.05); Group 1 Number missing: 2, Reason: Not reported; Group 2 Number missing: 1, Reason: Not reported

Protocol outcome 3: Time to stone passage at Define
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: Time to stone passage at 45 days; Group 1: mean 7.87 days (SD 36.9); n=33, Group 2: mean 15.23 days (SD 42); n=34; Comments: SEM reported in the study, which has been converted to SD. Tamsulosin group SEM: 6.43; NSAID group SEM: 7.21
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low; Indirectness of outcome: No indirectness ; Baseline details: There were no statistically significant differences between the 3 groups in terms of sex, age, stone side, size, and location (p>0.05); Group 1 Number missing: 2, Reason: Not reported; Group 2 Number missing: 1, Reason: Not reported

Protocol outcome 4: Adverse events at Define
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: Adverse events (retrograde ejaculation) at 45 days; Group 1: 1/33, Group 2: 0/34
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low;

Indirectness of outcome: No indirectness ; Baseline details: There were no statistically significant differences between the 3 groups in terms of sex, age, stone side, size, and location (p>0.05); Group 1 Number missing: 2, Reason: Not reported; Group 2 Number missing: 1, Reason: Not reported
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: Adverse events (episode of hypotension) at 45 days; Group 1: 0/33, Group 2: 0/34
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low; Indirectness of outcome: No indirectness ; Baseline details: There were no statistically significant differences between the 3 groups in terms of sex, age, stone side, size, and location (p>0.05); Group 1 Number missing: 2, Reason: Not reported; Group 2 Number missing: 1, Reason: Not reported

Protocol outcome 5: Pain intensity at Define
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: Pain intensity (pain episodes) at 45 days; Group 1: mean 1.14 Not applicable (SD 1.84); n=34, Group 2: mean 2.16 Not applicable (SD 3.03); n=34; Comments: SEM reported in the study, which has been converted to SD. Tamsulosin group SEM: 0.32; NSAID group SEM: 0.52
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low; Indirectness of outcome: No indirectness ; Baseline details: There were no statistically significant differences between the 3 groups in terms of sex, age, stone side, size, and location (p>0.05); Group 1 Number missing: 2, Reason: Not reported; Group 2 Number missing: 1, Reason: Not reported

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: DOXAZOSIN versus NSAIDS

Protocol outcome 1: Hospitalisation/ Use of healthcare services at Define
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: Hospitalisation/ Use of healthcare services (hospitalisation) at 45 days; Group 1: 2/33, Group 2: 3/34
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low; Indirectness of outcome: No indirectness ; Baseline details: There were no statistically significant differences between the 3 groups in terms of sex, age, stone side, size, and location (p>0.05); Group 1 Number missing: 2, Reason: Not reported; Group 2 Number missing: 1, Reason: Not reported
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: Hospitalisation/ Use of healthcare services (emergency room visits) at 45 days; Group 1: 0/33, Group 2: 0/34
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low; Indirectness of outcome: No indirectness ; Baseline details: There were no statistically significant differences between the 3 groups in terms of sex, age, stone side, size, and location (p>0.05); Group 1 Number missing: 2, Reason: Not reported; Group 2 Number missing: 1, Reason: Not reported

Protocol outcome 2: Stone passage rate at Define
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: Stone passage (expulsion rate) at 45 days; Group 1: 25/33, Group 2: 16/34
Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low; Indirectness of outcome: No indirectness ; Baseline details: There were no statistically significant differences between the 3 groups in terms of sex, age, stone side, size, and location (p>0.05); Group 1 Number missing: 2, Reason: Not reported; Group 2 Number missing: 1, Reason: Not reported

Protocol outcome 3: Time to stone passage at Define
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: Time to stone passage at 45 days; Group 1: mean 8.12 days (SD 32.6); n=33, Group 2: mean 15.23 days (SD 42); n=34; Comments: SEM reported in the study, which has been converted to SD. Doxazosin group SEM: 5.67; NSAID group

SEM: 7.21 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low; Indirectness of outcome: No indirectness ; Baseline details: There were no statistically significant differences between the 3 groups in terms of sex, age, stone side, size, and location (p>0.05); Group 1 Number missing: 2, Reason: Not reported; Group 2 Number missing: 1, Reason: Not reported Protocol outcome 4: Adverse events at Define - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: Adverse events (retrograde ejaculation) at 45 days; Group 1: 0/33, Group 2: 0/34 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low; Indirectness of outcome: No indirectness ; Baseline details: There were no statistically significant differences between the 3 groups in terms of sex, age, stone side, size, and location (p>0.05); Group 1 Number missing: 2, Reason: Not reported; Group 2 Number missing: 1, Reason: Not reported - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: Adverse events (episode of hypotension) at 45 days; Group 1: 2/33, Group 2: 0/34 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low; Indirectness of outcome: No indirectness ; Baseline details: There were no statistically significant differences between the 3 groups in terms of sex, age, stone side, size, and location (p>0.05); Group 1 Number missing: 2, Reason: Not reported; Group 2 Number missing: 1, Reason: Not reported Protocol outcome 5: Pain intensity at Define - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: Pain intensity (pain episodes) at 45 days; Group 1: mean 1.32 Not applicable (SD 2.47); n=33, Group 2: mean 2.16 Not applicable (SD 3.03); n=34; Comments: SEM reported in the study, which has been converted to SD. Doxazosin group SEM: 0.43; NSAID group SEM: 0.52 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low; Indirectness of outcome: No indirectness ; Baseline details: There were no statistically significant differences between the 3 groups in terms of sex, age, stone side, size, and location (p>0.05); Group 1 Number missing: 2, Reason: Not reported; Group 2 Number missing: 1, Reason: Not reported	
Protocol outcomes not reported by the study	Quality of life at Define; Analgesic use at Define

Study	Mustafa 2016[143]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=128)
Countries and setting	Conducted in Bangladesh; Setting: Outpatient Department of Urology
Line of therapy	1st line
Duration of study	Intervention time: 4 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: history, physical examination and investigations (e.g. ultrasonography)
Stratum	Adults (≥16 years), ureteric stone <1 cm
Subgroup analysis within study	Not applicable
Inclusion criteria	>18 years; unilateral, juxtavesical ureteral stone; normal functioning kidney; absence of clinical and laboratory signs of urinary tract infection; stone size up to 8mm
Exclusion criteria	multiple stones; severe hydronephrosis; history of spontaneous stone expulsion; distal ureteral surgery; diabetes; peptic ulcer disease; hypotension;
Recruitment/selection of patients	not reported
Age, gender and ethnicity	Age - Mean (SD): Tamsulosin group: 37.7 (9.33), control group: 38.5 (10.05). Gender (M:F): not reported . Ethnicity: not reported
Further population details	1. Kidney pole: Not applicable 2. Neuropathic/ cerebral-palsy /immobility: Not applicable 3. Obesity /skin-to-stone distance: Not applicable 4. Pregnant women: Not stated / Unclear 5. Stone composition/hounsfield units: Not applicable 6. Ureteric stone: Lower ureteric stones
Indirectness of population	No indirectness
Interventions	(n=64) Intervention 1: Alpha blockers - Tamsulosin. Tamsulosin 0.4mg daily. Duration up to 4 weeks. Concurrent medication/care: conventional treatment - hydration with minimum 2 L of water daily, physical exertion and analgesics (Diclofenac 50mg suppository with H2 blocker) if required. Indirectness: No indirectness (n=64) Intervention 2: No treatment. No treatment. Duration up to 4 weeks. Concurrent medication/care: hydration with minimum 2 L of water daily, physical exertion and analgesics (Diclofenac 50mg suppository with H2 blocker) if required. Indirectness: No indirectness
Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: TAMSULOSIN versus NO TREATMENT	

Protocol outcome 1: Stone passage - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: stone expulsion at 4 weeks ; Group 1: 51/60, Group 2: 32/60 Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age or stone size ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 2: Pain intensity - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: pain episodes at 4 weeks ; Group 1: mean 2.58 (SD 1.519); n=60, Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age or stone size ; Group 1 Number missing: ; Group 2 Number missing: - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: number of people suffering pain at 4 weeks ; Group 1: 36/60, Group 2: 48/60 Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age or stone size ; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Quality of life; Time to stone passage; Adverse events; Analgesic use; Hospitalisation/ Use of healthcare services

Study	Ochoa-gomez 2011[147]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=65)
Countries and setting	Conducted in Mexico; Setting: Emergency room, single centre
Line of therapy	1st line
Duration of study	Intervention time: 4 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: plain abdominal film and kidney ultrasound
Stratum	Adults (≥16 years), ureteric stone <1 cm
Subgroup analysis within study	Not applicable
Inclusion criteria	>18 years; reno-ureteral stones 5-10mm determined by plain abdominal film and kidney ultrasound
Exclusion criteria	hydronephrosis; acute or chronic renal insufficiency, multiple ureteral lithiasis; history of surgery or endourologic procedures; large and impacted ureteral calculi; pregnancy; lactation; distal ureteral lithiasis in a single kidney; patients taking alpha- or beta-blockers, nitrates or calcium antagonists; patients who worked as airline pilots
Recruitment/selection of patients	not reported
Age, gender and ethnicity	Age - Mean (SD): Tamsulosin group: 38.5 (11.3), placebo group: 38.2 (12.4). Gender (M:F): 36/39. Ethnicity: not reported
Further population details	1. Kidney pole: Not applicable 2. Neuropathic/ cerebral-palsy /immobility: Not applicable 3. Obesity /skin-to-stone distance: Not applicable 4. Pregnant women: Non-pregnant 5. Stone composition/hounsfield units: Not applicable 6. Ureteric stone: Lower ureteric stones
Indirectness of population	No indirectness
Interventions	(n=32) Intervention 1: Alpha blockers - Tamsulosin. Tamsulosin 0.4mg daily. Duration up to 4 weeks. Concurrent medication/care: instruction to drink at least 2 L of water daily. Indirectness: No indirectness (n=33) Intervention 2: Placebo. Placebo. Duration up to 4 weeks. Concurrent medication/care: instruction to drink at least 2 L of water daily. Indirectness: No indirectness
Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: TAMSULOSIN versus PLACEBO Protocol outcome 1: Stone passage	

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: stone expulsion at 4 weeks ; Group 1: 22/32, Group 2: 23/33 Risk of bias: All domain - High, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, stone size or stone location (left/right); Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 2: Time to stone passage - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: expulsion time at 4 weeks ; Group 1: mean 22 days (SD 6.77); n=32, Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, stone size or stone location (left/right); Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 3: Adverse events - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: dizziness at 4 weeks ; Group 1: 2/32, Group 2: 0/33 Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, stone size or stone location (left/right); Group 1 Number missing: ; Group 2 Number missing: - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: retrograde ejaculation at 4 weeks ; Group 1: 2/15, Group 2: 0/21 Risk of bias: All domain - Very high, Selection - High, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, stone size or stone location (left/right); Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Quality of life; Pain intensity; Analgesic use; Hospitalisation/ Use of healthcare services

Study	Park 2013[150]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=96)
Countries and setting	Conducted in South Korea; Setting: outpatient setting
Line of therapy	Adjunctive to current care
Duration of study	Intervention + follow up: 3 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: plain abdominal KUB radiography and non-enhanced kidney CT
Stratum	Adults (≥16 years), ureteric stone <1 cm: NA
Subgroup analysis within study	Not applicable: NA
Inclusion criteria	18-70 years with symptomatic, unilateral, single, proximal ureteral stone 6-20mm in longest axis
Exclusion criteria	active urinary tract infection; severe hydronephrosis; pregnancy; inadequate renal function (serum creatinine >2mg/dL); concomitant treatment with alpha blockers, calcium channel blockers or steroids; hypotension; multiple urinary stones; morbid obesity; stone on non-functioning kidney; history of previous failed ESWL; history of urinary tract surgery; uncorrected urinary tract obstruction
Recruitment/selection of patients	not reported
Age, gender and ethnicity	Age - Median (IQR): Tamsulosin group: 49.5 (34.25-57.75), control group: 50.5 (39.25-55.75). Gender (M:F): 57/31. Ethnicity: not reported
Further population details	1. Kidney pole: Not applicable 2. Neuropathic/ cerebral-palsy /immobility: Not applicable 3. Obesity /skin-to-stone distance: Not applicable 4. Pregnant women: Non-pregnant 5. Stone composition/hounsfield units: Not applicable 6. Ureteric stone: Upper ureteric stones
Indirectness of population	No indirectness: NA
Interventions	(n=48) Intervention 1: Alpha blockers and SWL. Tamsulosin 0.2mg once daily, starting just before ESWL. Duration up to 3 weeks. Concurrent medication/care: Aceclofenac 100mg on demand and asked to drink 1.5-2L of water daily. Indirectness: No indirectness; Indirectness comment: NA (n=48) Intervention 2: Surgery - SWL. ESWL . Duration up to 3 weeks. Concurrent medication/care: Aceclofenac 100mg on demand and asked to drink 1.5-2L of water daily. Indirectness: No indirectness; Indirectness comment: NA
Funding	Study funded by industry (Astellas Pharma Korea)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: ALPHA BLOCKERS AND SWL versus SWL	

Protocol outcome 1: Stone passage - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: stone free rate at 3 weeks ; Group 1: 37/44, Group 2: 29/44 Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, BMI, stone location (left/right) or stone size; Group 1 Number missing: 4; Group 2 Number missing: 4 Protocol outcome 2: Adverse events - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: dizziness at 3 weeks ; Group 1: 1/44, Group 2: 0/44 Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, BMI, stone location (left/right) or stone size; Group 1 Number missing: 4; Group 2 Number missing: 4	
Protocol outcomes not reported by the study	Quality of life; Time to stone passage; Pain intensity; Analgesic use; Hospitalisation/ Use of healthcare services

Study	Pedro 2008[152]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=69)
Countries and setting	Conducted in USA; Setting: Department of Urology (patients recruited from emergency room), single centre
Line of therapy	1st line
Duration of study	Intervention time: 4 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: CT
Stratum	Adults (≥16 years), ureteric stone <1 cm
Subgroup analysis within study	Not applicable
Inclusion criteria	distal ureteral calculus
Exclusion criteria	stones >8mm; renal insufficiency (serum creatinine >1.8mg/dl); solitary kidney; urinary infection; current alpha-blocker use; pregnancy; history of ureteral stricture; allergic reaction to study medication
Recruitment/selection of patients	consecutive patients meeting the inclusion/exclusion criteria during the recruitment period
Age, gender and ethnicity	Age - Mean (SD): Alfluzosin group: 36.69 (13.06), placebo group: 42.03 (12.85). Gender (M:F): 55/14. Ethnicity: not reported
Further population details	1. Kidney pole: Not applicable 2. Neuropathic/ cerebral-palsy /immobility: Not applicable 3. Obesity /skin-to-stone distance: Not applicable 4. Pregnant women: Non-pregnant 5. Stone composition/hounsfield units: Not applicable 6. Ureteric stone: Lower ureteric stones
Indirectness of population	No indirectness
Interventions	(n=34) Intervention 1: Alpha blockers - Alfuzosin. Alfuzosin daily. Duration up to 4 weeks. Concurrent medication/care: not reported. Indirectness: No indirectness (n=35) Intervention 2: Placebo. Placebo. Duration up to 4 weeks. Concurrent medication/care: not reported. Indirectness: No indirectness
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: ALFUZOSIN versus PLACEBO

Protocol outcome 1: Stone passage
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: spontaneous stone passage at 4 weeks ; Group 1: 25/34, Group 2: 27/35; Comments: numbers calculated from percentages

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 ; Baseline details: no significant difference in age, sex, blood pressure, degree of hydronephrosis or stone size, higher baseline pain score in Alfuzosin group ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 2: Time to stone passage - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: time to stone passage at 4 weeks ; Group 1: mean 5.19 days (SD 4.82); n=34, Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, blood pressure, degree of hydronephrosis or stone size, higher baseline pain score in Alfuzosin group ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 3: Adverse events - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: side effects (dizziness and hypotension) at 4 weeks ; Group 1: 4/34, Group 2: 0/35 Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, blood pressure, degree of hydronephrosis or stone size, higher baseline pain score in Alfuzosin group ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 4: Analgesic use - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: number of opioid derived medications consumed at 4 weeks ; Group 1: mean 8.63 (SD 8.58); n=34, Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, blood pressure, degree of hydronephrosis or stone size, higher baseline pain score in Alfuzosin group ; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Quality of life; Pain intensity; Hospitalisation/ Use of healthcare services

Study	Rahim 2012[165]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=90)
Countries and setting	Conducted in Pakistan; Setting: Urology department, single centre
Line of therapy	1st line
Duration of study	Intervention time: 4 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: ultrasound
Stratum	Adults (≥16 years), ureteric stone <1 cm
Subgroup analysis within study	Not applicable
Inclusion criteria	4-7mm stones in the distal segment of the ureter confirmed on ultrasound
Exclusion criteria	urinary tract infection; severe hydronephrosis; pregnancy; ulcer disease; hypotension; patients on calcium channel blockers; serum creatinine >2mg/dl; multiple ureteral stones; bilateral distal ureteric stones; solitary kidney; ureteral stricture; patient desire for immediate stone retrieval
Recruitment/selection of patients	not reported
Age, gender and ethnicity	Age - Mean (SD): 33.12 (11.2). Gender (M:F): 63/27. Ethnicity: not reported
Further population details	1. Kidney pole: Not applicable 2. Neuropathic/ cerebral-palsy /immobility: Not applicable 3. Obesity /skin-to-stone distance: Not applicable 4. Pregnant women: Non-pregnant 5. Stone composition/hounsfield units: Not applicable 6. Ureteric stone: Lower ureteric stones
Indirectness of population	No indirectness
Interventions	(n=45) Intervention 1: Alpha blockers - Terazosin. Terazosin 2mg daily. Duration up to 4 weeks. Concurrent medication/care: Diclofenac 50mg twice daily. Indirectness: No indirectness (n=45) Intervention 2: Pain management only - NSAIDs. Diclofenac 50mg twice daily. Duration up to 4 weeks. Concurrent medication/care: NA. Indirectness: No indirectness
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: TERAZOSIN versus NSAIDS

Protocol outcome 1: Stone passage
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: stone expulsion at 4 weeks ; Group 1: 37/45, Group 2: 22/45
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low,

Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 2: Time to stone passage - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: expulsion time at 4 weeks ; Group 1: mean 13.3 days (SD 6.31); n=45, Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age ; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Quality of life; Adverse events; Pain intensity; Analgesic use; Hospitalisation/ Use of healthcare services

Study	Resim 2005[170]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=60)
Countries and setting	Conducted in Turkey; Setting: outpatient Division of Urology, single centre
Line of therapy	1st line
Duration of study	Intervention time: 6 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: plain abdominal radiography and urinary ultrasonography
Stratum	Adults (≥16 years), ureteric stone <1 cm
Subgroup analysis within study	Not applicable
Inclusion criteria	lower ureteral calculi
Exclusion criteria	solitary kidney; severe refractory pain; urinary tract infection; multiple stones; severe hydronephrosis
Recruitment/selection of patients	consecutive meeting the inclusion/exclusion criteria during the recruitment period
Age, gender and ethnicity	Age - Mean (SD): Tamsulosin group: 35.3 (10.9), control group 33.5 (9.7). Gender (M:F): 45/15. Ethnicity: not reported
Further population details	1. Kidney pole: Not applicable 2. Neuropathic/ cerebral-palsy /immobility: Not applicable 3. Obesity /skin-to-stone distance: Not applicable 4. Pregnant women: Not stated / Unclear 5. Stone composition/hounsfield units: Not applicable 6. Ureteric stone: Lower ureteric stones
Indirectness of population	Serious indirectness: included stones < and > 10mm
Interventions	(n=30) Intervention 1: Alpha blockers - Tamsulosin. Tamsulosin 0.4mg daily. Duration up to 6 weeks. Concurrent medication/care: conservative treatment - hydration and Tenoxicam 20mg daily. Indirectness: No indirectness (n=30) Intervention 2: Pain management only - NSAIDs. Conservative treatment - hydration and Tenoxicam 20mg daily. Duration up to 6 weeks. Concurrent medication/care: NA. Indirectness: No indirectness
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: TAMSULOSIN versus NSAIDS

Protocol outcome 1: Stone passage
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: spontaneous stone passage at 6 weeks ; Group 1: 26/30, Group 2: 22/30
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High,

Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex or stone size, higher pain scores in control group ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 2: Adverse events - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: headache at 6 weeks ; Group 1: 4/30, Group 2: 4/30 Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex or stone size, higher pain scores in control group ; Group 1 Number missing: ; Group 2 Number missing: - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: dizziness at 6 weeks ; Group 1: 5/30, Group 2: 3/30 Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex or stone size, higher pain scores in control group ; Group 1 Number missing: ; Group 2 Number missing: - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: abnormal ejaculation at 6 weeks ; Group 1: 0/22, Group 2: 1/23 Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex or stone size, higher pain scores in control group ; Group 1 Number missing: ; Group 2 Number missing: - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: orthostatic hypotension at 6 weeks ; Group 1: 0/30, Group 2: 0/30 Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex or stone size, higher pain scores in control group ; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Quality of life; Time to stone passage; Pain intensity; Analgesic use; Hospitalisation/ Use of healthcare services

Study	Resim 2005[171]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=67)
Countries and setting	Conducted in Turkey; Setting: Department of Urology, single centre
Line of therapy	Adjunctive to current care
Duration of study	Intervention + follow up: 6 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: plain abdominal radiography and urinary ultrasonography
Stratum	Adults (≥16 years), ureteric stone <1 cm: NA
Subgroup analysis within study	Not applicable: NA
Inclusion criteria	steinstrasse in the lower ureter (juxtavesical or intramural portion) after undergoing ESWL
Exclusion criteria	<18 years; weight <50kg or >100kg; history of drug or alcohol abuse; ipsilateral ureteral surgery; chronic use of drugs such as antidepressants, histamine blockers and anxiolytics; allergy to one of the study medications
Recruitment/selection of patients	consecutive patients meeting the inclusion criteria during the recruitment period
Age, gender and ethnicity	Age - Median (range): Tamsulosin group: 39 (21-55), control group: 37 (23-57). Gender (M:F): 43/24. Ethnicity: not reported
Further population details	1. Kidney pole: Not applicable 2. Neuropathic/ cerebral-palsy /immobility: Not applicable 3. Obesity /skin-to-stone distance: Not applicable 4. Pregnant women: Not stated / Unclear 5. Stone composition/hounsfield units: Not applicable 6. Uteric stone: Lower ureteric stones
Indirectness of population	No indirectness: NA
Interventions	(n=32) Intervention 1: Alpha blockers and SWL. Tamsulosin 0.4mg daily. Duration up to 6 weeks. Concurrent medication/care: hydration and Tenoxicam 20mg daily. Indirectness: No indirectness; Indirectness comment: NA (n=35) Intervention 2: Surgery and pain management - SWL and pain management. Pain management only. Duration up to 6 weeks. Concurrent medication/care: hydration and Tenoxicam 20mg daily. Indirectness: No indirectness; Indirectness comment: NA
Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: ALPHA BLOCKERS AND SWL versus SWL AND PAIN MANAGEMENT Protocol outcome 1: Stone passage	

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: spontaneous passage at 6 weeks ; Group 1: 24/32, Group 2: 23/35 Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: no significant difference in age, sex or stone burden before ESWL; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 2: Adverse events - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: headache at 6 weeks ; Group 1: 5/32, Group 2: 2/35 Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: no significant difference in age, sex or stone burden before ESWL; Group 1 Number missing: ; Group 2 Number missing: - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: dizziness at 6 weeks ; Group 1: 4/32, Group 2: 0/35 Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: no significant difference in age, sex or stone burden before ESWL; Group 1 Number missing: ; Group 2 Number missing: - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: abnormal ejaculation at 6 weeks ; Group 1: 1/21, Group 2: 0/22 Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: no significant difference in age, sex or stone burden before ESWL; Group 1 Number missing: ; Group 2 Number missing: - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: orthostatic hypotension at 6 weeks ; Group 1: 0/32, Group 2: 0/35 Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: no significant difference in age, sex or stone burden before ESWL; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Quality of life; Time to stone passage; Pain intensity; Analgesic use; Hospitalisation/ Use of healthcare services

Study	Sameer 2014[174]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=105)
Countries and setting	Conducted in India; Setting: single centre
Line of therapy	1st line
Duration of study	Intervention time: 4 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: history, physical examination, X-rays KUB, ultrasonography, etc.
Stratum	Adults (≥16 years), ureteric stone <1 cm
Subgroup analysis within study	Not applicable
Inclusion criteria	≥8 years; single, unilateral ureteral stone of ≤10mm; distal defined as the segment from the lower border of the sacroiliac joint to the vesico-ureteric junction
Exclusion criteria	previous surgery on the ipsilateral ureter; bilateral ureteric stones; multiple stones; solitary kidney; urinary tract infection; moderate or severe hydronephrosis; contraindications for non-steroidal anti-inflammatory drugs; known allergy to Tamsulosin or Alfuzosin; renal insufficiency; currently on alpha-blocker therapy; pregnant or lactating women
Recruitment/selection of patients	not reported
Age, gender and ethnicity	Age - Mean (SD): Nifedipine group: 32.74 (9.58), Alfuzosin group: 30.82 (7.85), control group: 33.06 (8.76). Gender (M:F): 68/37. Ethnicity: not reported
Further population details	1. Kidney pole: Not applicable 2. Neuropathic/ cerebral-palsy /immobility: Not applicable 3. Obesity /skin-to-stone distance: Not applicable 4. Pregnant women: Non-pregnant 5. Stone composition/hounsfield units: Not applicable 6. Ureteric stone: Lower ureteric stones
Indirectness of population	No indirectness
Interventions	(n=35) Intervention 1: Calcium channel blockers - Nifedipine. Nifedipine 30mg daily. Duration up to 4 weeks. Concurrent medication/care: Diclofenac 50mg every 12 hours for 1 week, Diclofenac 75mg injection as needed and Tramadol 100mg injection for persistent pain . Indirectness: No indirectness (n=35) Intervention 2: Alpha blockers - Alfuzosin. Alfuzosin 10mg daily. Duration up to 4 weeks. Concurrent medication/care: Diclofenac 50mg every 12 hours for 1 week, Diclofenac 75mg injection as needed and Tramadol 100mg injection for persistent pain. Indirectness: No indirectness (n=35) Intervention 3: Pain management only - NSAIDs. Diclofenac 50mg every 12 hours for 1 week. Duration up to 4 weeks. Concurrent medication/care: Diclofenac 75mg injection as needed and Tramadol

	100mg injection for persistent pain. Indirectness: No indirectness
Funding	No funding

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: NIFEDIPINE versus NSAIDS

Protocol outcome 1: Hospitalisation/ Use of healthcare services
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: hospital readmissions due to uncontrollable pain at 4 weeks ; Group 1: 11/35, Group 2: 27/35
Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, stone size or location (left/right) ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 2: Stone passage
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: stone expulsion rate at 4 weeks ; Group 1: 21/35, Group 2: 7/35
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 ; Baseline details: no significant difference in age, sex, stone size or location (left/right) ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 3: Time to stone passage
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: duration of stone expulsion at 4 weeks ; Group 1: mean 12 days (SD 6.69); n=35,
Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, stone size or location (left/right) ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 4: Pain intensity
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: episodes of pain at 4 weeks ; Group 1: mean 2.91 days (SD 1.01); n=35,
Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, stone size or location (left/right) ; Group 1 Number missing: ; Group 2 Number missing:

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: ALFUZOSIN versus NIFEDIPINE

Protocol outcome 1: Hospitalisation/ Use of healthcare services
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: hospital readmissions due to uncontrollable pain at 4 weeks ; Group 1: 5/35, Group 2: 11/35
Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, stone size or location (left/right) ; Group

1 Number missing: ; Group 2 Number missing:

Protocol outcome 2: Stone passage
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: stone expulsion rate at 4 weeks ; Group 1: 30/35, Group 2: 21/35
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 ; Baseline details: no significant difference in age, sex, stone size or location (left/right) ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 3: Time to stone passage
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: duration of stone expulsion at 4 weeks ; Group 1: mean 12 days (SD 6.67); n=35,
Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, stone size or location (left/right) ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 4: Pain intensity
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: episodes of pain at 4 weeks ; Group 1: mean 1.8 days (SD 0.83); n=35,
Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, stone size or location (left/right) ; Group 1 Number missing: ; Group 2 Number missing:

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: ALFUZOSIN versus NSAIDS

Protocol outcome 1: Hospitalisation/ Use of healthcare services
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: hospital readmissions due to uncontrollable pain at 4 weeks ; Group 1: 5/35, Group 2: 27/35
Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, stone size or location (left/right) ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 2: Stone passage
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: stone expulsion rate at 4 weeks ; Group 1: 30/35, Group 2: 7/35
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 ; Baseline details: no significant difference in age, sex, stone size or location (left/right) ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 3: Time to stone passage
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: duration of stone expulsion at 4 weeks ; Group 1: mean 12 days (SD 6.67); n=35,
Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High,

Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, stone size or location (left/right) ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 4: Pain intensity - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: episodes of pain at 4 weeks ; Group 1: mean 1.8 days (SD 0.83); n=35, Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, stone size or location (left/right) ; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Quality of life; Analgesic use; Adverse events

Study	**Sayed 2008[176]**
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=90)
Countries and setting	Conducted in Egypt; Setting: Urology department, single centre
Line of therapy	1st line
Duration of study	Intervention time: 4 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: physical evaluation, urinalysis, abdominal ultrasound, KUB X-ray etc.
Stratum	Adults (≥16 years), ureteric stone <1 cm
Subgroup analysis within study	Not applicable
Inclusion criteria	>18 years; radiopaque stones 5-10mm in diameter in the distal ureter
Exclusion criteria	urinary tract infection; severe hydronephrosis; multiple stones; pregnancy; lactation; hypotension; ureteral stricture or a history of spontaneous stone passage; concomitant treatment with anaphalytic drugs, beta-blockers or calcium antagonists; desire by patient for immediate stone removal
Recruitment/selection of patients	not reported
Age, gender and ethnicity	Age - Mean (SD): standard therapy group: 37.1 (9.8), Tamsulosin group: 39.3 (10.6). Gender (M:F): 69/21. Ethnicity: not reported
Further population details	1. Kidney pole: Not applicable 2. Neuropathic/ cerebral-palsy /immobility: Not applicable 3. Obesity /skin-to-stone distance: Not applicable 4. Pregnant women: Non-pregnant 5. Stone composition/hounsfield units: Not applicable 6. Ureteric stone: Lower ureteric stones

Indirectness of population	No indirectness
Interventions	(n=45) Intervention 1: Alpha blockers - Tamsulosin. Tamsulosin 0.4mg daily. Duration up to 4 weeks. Concurrent medication/care: hydration (at least 2 L of water daily) and Diclofenac 100mg injection on demand. Indirectness: No indirectness (n=45) Intervention 2: No treatment. no treatment . Duration up to 4 weeks. Concurrent medication/care: hydration (at least 2 L of water daily) and Diclofenac 100mg injection on demand. Indirectness: No indirectness
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: TAMSULOSIN versus NO TREATMENT

Protocol outcome 1: Stone passage
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: stone expulsion rate at 4 weeks ; Group 1: 40/45, Group 2: 23/45
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex or stone size ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 2: Time to stone passage
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: time to expulsion at 4 weeks ; Group 1: mean 7.32 days (SD 0.78); n=45,
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex or stone size ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 3: Adverse events
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: hypotension or other side effects requiring cessation of treatment at 4 weeks ; Group 1: 0/45, Group 2: 0/45
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex or stone size ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 4: Pain intensity
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: number of pain episodes at 4 weeks ; Group 1: mean 1.53 (SD 0.25); n=45,
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex or stone size ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 5: Analgesic use - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: number of analgesic vials at 4 weeks ; Group 1: mean 0.14 (SD 0.5); n=45, Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex or stone size ; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Quality of life; Hospitalisation/ Use of healthcare services

Study	**Sen 2017[179]**
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=66)
Countries and setting	Conducted in Turkey; Setting: Not reported
Line of therapy	Unclear
Duration of study	Follow up (post intervention): 3 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Direct urinary system graphy, urinary system ultrasonography, and intravenous pyelography or unenhanced computed tomography
Stratum	Adults (≥16 years), ureteric stone <1 cm:
Subgroup analysis within study	Not applicable
Inclusion criteria	People with distal ureteral stones that were radio-opaque and ≤10mm
Exclusion criteria	Study discontinuation criteria included hypersensitivity to the agents used, advanced hydronephrosis, persistent pain despite proper and adequate analgesic use, urinary tract infection, low blood pressure
Recruitment/selection of patients	Not reported
Age, gender and ethnicity	Age - Mean (SD): Alpha blockers group 33.7 (10.4); control group 33 (11.3). Gender (M:F): Define. Ethnicity: Not reported
Further population details	1. Kidney pole: Not applicable 2. Neuropathic/ cerebral-palsy /immobility: Not stated / Unclear 3. Obesity /skin-to-stone distance: Not stated / Unclear 4. Pregnant women: Not stated / Unclear 5. Stone composition/hounsfield units: Not stated / Unclear 6. Uteric stone: Lower ureteric stones
Indirectness of population	No indirectness

Interventions	(n=47) Intervention 1: Alpha blockers - Doxazosin. Doxazosin: 25 participants received 4mg and 22 participants received 8mg. Duration 3 weeks. Concurrent medication/care: Diclofenac 100mg oral and daily 1500-2000 cc hydration . Indirectness: No indirectness (n=19) Intervention 2: Pain management only - NSAIDs. No treatment. Duration 3 weeks. Concurrent medication/care: Diclofenac 100mg oral and daily 1500-2000 cc hydration . Indirectness: No indirectness
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: DOXAZOSIN versus NSAIDS

Protocol outcome 1: Stone passage at Define
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: Stone expulsion at 3 weeks; Group 1: 33/47, Group 2: 5/19
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: Time to stone passage at Define
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: Stone expulsion rate at 3 weeks; Group 1: mean 13.51 days (SD 4.09); n=47, Group 2: mean 19.6 days (SD 4.2); n=19
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: Adverse events at Define
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: Hypotension at 3 weeks; Group 1: 3/47, Group 2: 0/19
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: Pain intensity at Define
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: Number of pain episodes at 3 weeks; Group 1: mean 0.64 (SD 0.33); n=47, Group 2: mean 1.3 (SD 0.5); n=19
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; Analgesic use at Define; Hospitalisation/ Use of healthcare services at Define

Study	Singh 2011[187]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=120)
Countries and setting	Conducted in India; Setting: outpatient department , single centre
Line of therapy	Adjunctive to current care
Duration of study	Intervention + follow up: 3 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: KUB x-ray and ultrasonography of the KUB region
Stratum	Adults (≥16 years), ureteric stone <1 cm: NA
Subgroup analysis within study	Not applicable: NA
Inclusion criteria	18-70 years; symptomatic, unilateral and solitary upper (between the peli-ureteral junction and sacroiliac joint) ureteral calculi 6-15mm in major axis
Exclusion criteria	active urinary tract infection; fever; acute renal failure; chronic renal failure; history of urinary tract surgery or endoscopic treatment; uncorrected distal obstruction; severe hydronephrosis; pregnancy; concomitant treatment with alpha-blockers, calcium channel blockers or steroids; morbid obesity; history of previous failed SWL
Recruitment/selection of patients	not reported
Age, gender and ethnicity	Age - Mean (SD): Tamsulosin group: 32.2 (12.22), control group: 36 (13.78). Gender (M:F): Define. Ethnicity: not stated
Further population details	1. Kidney pole: Not applicable 2. Neuropathic/ cerebral-palsy /immobility: Not applicable 3. Obesity /skin-to-stone distance: Not applicable 4. Pregnant women: Non-pregnant 5. Stone composition/hounsfield units: Not applicable 6. Ureteric stone: Upper ureteric stones
Indirectness of population	Serious indirectness: included stones < and > 10mm, results reported separately for primary outcome (stone clearance)
Interventions	(n=59) Intervention 1: Alpha blockers and SWL. Tamsulosin 0.4mg daily beginning just before the session of SWL, SWL repeated every 3 weeks for incomplete fragmented calculus. Duration up to 3 months. Concurrent medication/care: advice to drink 2.5L of fluid daily and Diclofenac on demand. Indirectness: No indirectness; Indirectness comment: NA (n=58) Intervention 2: Surgery - SWL. SWL repeated every 3 weeks for incomplete fragmented calculus up to 3 sessions. Duration up to 3 months. Concurrent medication/care: advice to drink 2.5L of fluid daily and Diclofenac on demand. Indirectness: No indirectness; Indirectness comment: NA

Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: ALPHA BLOCKERS AND SWL versus SWL

Protocol outcome 1: Stone passage
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: stone clearance (6-10mm) at 3 months; Group 1: 28/30, Group 2: 27/30
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: no significant difference in age, sex or stone size ; Group 1 Number missing: ; Group 2 Number missing:
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: stone clearance (11-15mm) at 3 months; Group 1: 26/29, Group 2: 23/28
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: no significant difference in age, sex or stone size ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 2: Time to stone passage
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: expulsion time at 3 months; Group 1: mean 26.78 days (SD 11.96); n=59,
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: no significant difference in age, sex or stone size ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 3: Pain intensity
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: visual analogue pain scale at 3 months; Group 1: mean 24.92 days (SD 7.57); n=59, Group 2: mean 41.81 days (SD 17.24); n=58; visual analogue pain scale 0-100 Top=High is poor outcome
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: no significant difference in age, sex or stone size ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcomes not reported by the study	Quality of life; Adverse events; Analgesic use; Hospitalisation/ Use of healthcare services

Study	Singh 2011[186]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=120)
Countries and setting	Conducted in India; Setting: Department of urology, single centre
Line of therapy	Adjunctive to current care
Duration of study	Intervention + follow up: 4 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: plain abdominal radiograph and sonography of KUB
Stratum	Adults (≥16 years), ureteric stone <1 cm: NA
Subgroup analysis within study	Not applicable: NA
Inclusion criteria	>18 years; symptomatic unilateral solitary lower ureteric calculus 4-12mm in major axis
Exclusion criteria	active urinary tract infection; fever; acute renal failure; chronic renal failure; history of urinary tract surgery or endoscopic treatment; uncorrected distal obstruction; severe hydronephrosis; pregnancy; concomitant treatment with alpha-blockers, calcium channel blockers or steroids; morbid obesity; history of previous failed ESWL
Recruitment/selection of patients	consecutive patients meeting the inclusion criteria during the recruitment period
Age, gender and ethnicity	Age - Mean (SD): Tamsulosin group: 34.2 (13.9), placebo group: 36 (12.2). Gender (M:F): 84/35. Ethnicity: not reported
Further population details	1. Kidney pole: Not applicable 2. Neuropathic/ cerebral-palsy /immobility: Not applicable 3. Obesity /skin-to-stone distance: Not applicable 4. Pregnant women: Non-pregnant 5. Stone composition/hounsfield units: Not applicable 6. Ureteric stone: Lower ureteric stones
Indirectness of population	Serious indirectness: includes stones < and > 10mm
Interventions	(n=60) Intervention 1: Alpha blockers and SWL. Tamsulosin 0.4mg daily from the day of ESWL just before the session. Duration up to 4 weeks. Concurrent medication/care: advice to drink 2.5L of fluid daily, antibiotics and Diclofenac on demand. Indirectness: No indirectness; Indirectness comment: NA (n=59) Intervention 2: Surgery and placebo - SWL and placebo. ESWL and placebo. Duration up to 4 weeks. Concurrent medication/care: advice to drink 2.5L of fluid daily, antibiotics and Diclofenac on demand. Indirectness: No indirectness; Indirectness comment: NA
Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: ALPHA BLOCKERS AND SWL versus SWL AND PLACEBO	

Protocol outcome 1: Stone passage - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: stone clearance at 4 weeks ; Group 1: 52/60, Group 2: 42/59 Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: no significant difference in age, sex or stone size; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 2: Time to stone passage - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: expulsion time at 4 weeks ; Group 1: mean 12.9 days (SD 7.5); n=60, Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: no significant difference in age, sex or stone size; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 3: Analgesic use - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: dose of analgesic at 4 weeks ; Group 1: mean 65.83 mg (SD 48.26); n=60, Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: no significant difference in age, sex or stone size; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Quality of life; Adverse events; Pain intensity; Hospitalisation/ Use of healthcare services

Study (subsidiary papers)	**Spontaneous Urinary Stone Passage Enabled by Drugs (SUSPEND) trial: Pickard 2015[154] (Pickard 2015[153])**
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=1167)
Countries and setting	Conducted in United Kingdom; Setting: 24 hospitals
Line of therapy	1st line
Duration of study	Intervention + follow up: 12 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: non-contrast CT KUB
Stratum	Adults (≥16 years), ureteric stone <1 cm: upper middle and lower ureteral stones included, analysed as subgroups for primary outcome (stone passage)
Subgroup analysis within study	Not applicable

Inclusion criteria	presenting acutely with ureteric colic; ≥ 18 years to ≤ 65 years; stone confirmed by non-contrast CT KUB; stone within any segment of the ureter; unilateral ureteric stone; largest dimension of the stone ≤ 10 mm; female participants willing to use two of the listed methods of contraception prior to taking any trial medication until at least 28 days after receiving the last dose of trial medication, who were post-menopausal or who had undergone permanent sterilisation; capable of giving written informed consent, which includes compliance with the requirements of the trial
Exclusion criteria	those requiring immediate intervention; sepsis; estimated glomerular filtration rate less than 30mL/min; already taking or unable to take alpha-blocker or calcium channel stabiliser; pregnancy; breastfeeding; women intending to become pregnant during study period; asymptomatic incidentally found ureteric stone; stone not previously confirmed by CT KUB; kidney stone without presence of ureteric stone; multiple stones within one ureter
Recruitment/selection of patients	consecutive patients meeting inclusion/exclusion criteria at participating sites during the recruitment period
Age, gender and ethnicity	Age - Mean (SD): Tamsulosin group: 43.1 (11.5), Nifedipine group: 42.3 (11), placebo group: 42.8 (12.3) . Gender (M:F): 931/219. Ethnicity: not reported
Further population details	1. Kidney pole: Not applicable 2. Neuropathic/ cerebral-palsy /immobility: Not applicable 3. Obesity /skin-to-stone distance: Not applicable 4. Pregnant women: Non-pregnant 5. Stone composition/hounsfield units: Not applicable 6. Ureteric stone: Not stated / Unclear (mixed).
Indirectness of population	Serious indirectness: population includes upper, middle and lower ureteric stones
Interventions	(n=391) Intervention 1: Alpha blockers - Tamsulosin. Tamsulosin 0.4mg daily. Duration up to 4 weeks. Concurrent medication/care: standard care - analgesics, antiemetics, advice on adequate fluid intake and resumption of normal activity. Indirectness: No indirectness (n=387) Intervention 2: Calcium channel blockers - Nifedipine. Nifedipine 30mg daily . Duration up to 4 weeks. Concurrent medication/care: standard care - analgesics, antiemetics and advice on adequate fluid intake and resumption of normal activity. Indirectness: No indirectness (n=389) Intervention 3: Placebo. Placebo. Duration up to 4 weeks. Concurrent medication/care: standard care - analgesics, antiemetics and advice on adequate fluid intake and resumption of normal activity. Indirectness: No indirectness
Funding	Academic or government funding (UK National Institute for Health Research Health Technology Assessment Programme)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: TAMSULOSIN versus NIFEDIPINE	

Protocol outcome 1: Stone passage
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: spontaneous stone passage (upper ureteric stones) at 4 weeks ; Group 1: 62/88, Group 2: 58/92
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: ; Group 2 Number missing:
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: spontaneous stone passage (middle ureteric stones) at 4 weeks ; Group 1: 29/41, Group 2: 32/40
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: ; Group 2 Number missing:
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: spontaneous stone passage (lower ureteric stones) at 4 weeks ; Group 1: 216/249, Group 2: 214/247
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: ; Group 2 Number missing:
Protocol outcome 2: Time to stone passage
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: time to stone passage (upper ureteric stones) at 4 weeks ; Group 1: 16.42 days (SD 12.32); n=89, Group 2: 17.4 days (SD 8.67); n=94
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: ; Group 2 Number missing: ;
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: time to stone passage (middle ureteric stones) at 4 weeks ; Group 1: 25.88 days (SD 17.55); n=43, Group 2: 22.18 days (SD 7.90); n=40
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data – Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: ; Group 2 Number missing: ;
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: time to stone passage (lower ureteric stones) at 4 weeks ; Group 1: 15.29 days (SD 11.64); n=251, Group 2: 14.68 days (SD 16.18); n=249
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: ; Group 2 Number missing: ;

Protocol outcome 3: Quality of life
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: SF-36 physical component summary (upper ureteric stones) at 12 weeks ; Group 1: 51.73 (SD 8.78); n=51, Group 2: 50.89 (SD 8.80); n=37

Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: 38; Group 2 Number missing: 57

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: SF-36 physical component summary (mid ureteric stones) at 12 weeks ; Group 1: 50.89 (SD 9.78); n=26, Group 2: 48.79 (SD 12.54); n=24

Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: 17; Group 2 Number missing: 16

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: SF-36 physical component summary (lower ureteric stones) at 12 weeks ; Group 1: 51.09 (SD 10.2); n=100, Group 2: 52.13 (SD 8.48); n=116

Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: 151; Group 2 Number missing: 133

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: SF-36 mental component summary (upper ureteric stones) at 12 weeks ; Group 1: 49.78 (SD 10.84); n=51, Group 2: 49.25 (SD 9.93); n=37

Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: 38; Group 2 Number missing: 57

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: SF-36 mental component summary (mid ureteric stones) at 12 weeks ; Group 1: 47.41 (SD 13.61); n=26, Group 2: 50.10 (SD 10.79); n=24

Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: 17; Group 2 Number missing: 16

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: SF-36 mental component summary (lower ureteric stones) at 12 weeks ; Group 1: 49.60 (SD 11.66); n=100, Group 2: 50.90 (SD 10.30); n=116

Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: 151; Group 2 Number missing: 133

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: EQ-5D (upper ureteric stones) at 12 weeks ; Group 1: 0.870 (SD 0.155); n=51, Group 2: 0.894 (SD 0.183); n=40

Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: 38; Group 2 Number missing: 54

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: EQ-5D (mid ureteric stones) at 12 weeks ; Group 1: 0.817 (SD 0.283); n=28, Group 2: 0.789 (SD 0.336); n=24

Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: 17; Group 2 Number missing: 16

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: EQ-5D (lower ureteric stones) at 12 weeks ; Group 1: 0.864 (SD 0.264); n=103, Group 2: 0.876 (SD 0.233); n=123

Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: 148; Group 2 Number missing: 126

Protocol outcome 4: Pain

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: pain medication use (upper ureteric stones) at 4 weeks ; Group 1: 42; n=66, Group 2: 34; n=50

Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: 23; Group 2 Number missing: 44

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: pain medication use (mid ureteric stones) at 4 weeks ; Group 1: 22; n=32, Group 2: 18; n=28

Risk of bias: Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: 11; Group 2 Number missing: 12

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: pain medication use (lower ureteric stones) at 4 weeks ; Group 1: 75; n=147, Group 2: 81; n=161

Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: 104; Group 2 Number missing: 88

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: number of days of pain medication use (upper ureteric stones) at 4 weeks ; Group 1: 11.98 (SD 9.07); n=41, Group 2: 13.56 (SD 10.59); n=34

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 ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: ; Group 2 Number missing: ;

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: number of days of pain medication use (mid ureteric stones) at 4 weeks ; Group 1: 12.3 (SD 8.77); n=22, Group 2: 10.18 (SD 8.22); n=17

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 ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: ; Group 2 Number missing: ;

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: number of days of pain medication use (lower ureteric stones) at 4 weeks ; Group 1: 11.19 (SD 8.53); n=74, Group 2: 9.56 (SD 8.20); n=78

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 ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: ; Group 2 Number missing: ;

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: VAS pain score (upper ureteric stones) at 4 weeks ; Group 1: 0.85 (SD 1.53); n=65, Group 2: 1.86 (SD 2.60); n=49

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 ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: ; Group 2 Number missing: ;

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: VAS pain score (mid ureteric stones) at 4 weeks ; Group 1: 1.58 (SD 2.88); n=31, Group 2: 1.85 (SD 3.16); n=27

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 ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: ; Group 2 Number missing: ;

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: VAS pain score (lower ureteric stones) at 4 weeks ; Group 1: 1.01 (SD 1.90); n=137, Group 2: 1.06 (SD 1.97); n=155

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 ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: ; Group 2 Number missing: ;

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: EQ-5D no pain or discomfort (upper ureteric stones) at 12 weeks ; Group 1: 32; n=51; Group 2: 30; n=40

Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: 38; Group 2 Number missing: 54

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: EQ-5D no pain or discomfort (mid ureteric stones) at 12 weeks ; Group 1:17; n=28, Group 2: 14; n=25

Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: 15; Group 2 Number missing: 15

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: EQ-5D no pain or discomfort (lower ureteric stones) at 12 weeks ; Group 1: 77; n=104, Group 2: 92; n=123

Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: 147; Group 2 Number missing: 126

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: EQ-5D moderate pain or discomfort (upper ureteric stones) at 12 weeks ; Group 1: 19; n=51; Group 2: 9; n=40

Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: 38; Group 2 Number missing: 54

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: EQ-5D moderate pain or discomfort (mid ureteric stones) at 12 weeks ; Group 1: 9; n=28, Group 2: 9; n=25

Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: 15; Group 2 Number missing: 15

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: EQ-5D moderate pain or discomfort (lower ureteric stones) at 12 weeks ; Group 1: 22; n=104, Group 2: 28; n=123

Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: 147; Group 2 Number missing: 126

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: EQ-5D extreme pain or discomfort (upper ureteric stones) at 12 weeks ; Group 1: ; Group 2: 1; n=40

Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: ; Group 2 Number missing: 54

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: EQ-5D extreme pain or discomfort (mid ureteric stones) at 12 weeks ; Group 1: 2; n=28, Group 2: 2; n=25

Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing:15 ; Group 2 Number missing: 15

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: EQ-5D extreme pain or discomfort (lower ureteric stones) at 12 weeks ; Group 1: 5; n=104, Group 2: 3; n=123

Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: 147; Group 2 Number missing: 126

Protocol outcome 5: Adverse events

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: discontinuation due to adverse events (upper ureteric stones) at 4 weeks ; Group 1: 8; n=66, Group 2: 8; n=51

Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: 23; Group 2 Number missing: 43

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: discontinuation due to adverse events (mid ureteric stones) at 4 weeks ; Group 1: 2; n=32, Group 2: 3; n=28

Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: 11; Group 2 Number missing: 12

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: discontinuation due to adverse events (lower ureteric stones) at 4 weeks ; Group 1: 15; n=149, Group 2: 29; n=162

Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: 102; Group 2 Number missing: 87

Protocol outcome 6: Use of healthcare services

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: doctor visits (upper ureteric stones) at 4 weeks ; Group 1: 0.24 (SD 0.67); n=70, Group 2: 0.19 (SD 0.61); n=67

Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement – Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: 19; Group 2 Number missing: 27

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: doctor visits (mid ureteric stones) at 4 weeks ; Group 1: 0.40 (SD 0.91); n=35, Group 2: 0.18 (SD 0.69); n=38

Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: 8; Group 2 Number missing: 2

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: doctor visits (lower ureteric stones) at 4 weeks ; Group 1: 0.16 (SD 0.63); n=224, Group 2: 0.17 (SD; 0.71); n=226

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 ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: 27; Group 2 Number missing: 23

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: nurse visits (upper ureteric stones) at 4 weeks ; Group 1: 0.03 (SD 0.17); n=70, Group 2: 0.04 (SD 0.27); n=67

Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: 19; Group 2 Number missing: 27

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: nurse visits (mid ureteric stones) at 4 weeks ; Group 1: 0.22 (SD 0.84); n=35, Group 2: 0.03 (SD 0.16); n=38

Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: 8; Group 2 Number missing: 2

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: nurse visits (lower ureteric stones) at 4 weeks ; Group 1: 0.01 (SD 0.13); n=224, Group 2: 0.01 (SD; 0.09); n=226

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 ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: 27; Group 2 Number missing: 23

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: outpatient visits (upper ureteric stones) at 4 weeks ; Group 1: 0.83 (SD 0.80); n=87, Group 2: 0.63 (SD 0.67); n=92

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 ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: 2; Group 2 Number missing: 2

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: outpatient visits (mid ureteric stones) at 4 weeks ; Group 1: 0.82 (SD 0.86); n=41, Group 2: 0.03 (SD 0.16); n=37

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 ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: 2; Group 2 Number missing: 3

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: outpatient visits (lower ureteric stones) at 4 weeks ; Group 1: 0.66 (SD 0.69); n=289, Group 2: 0.62 (SD; 0.66); n=246

Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: unclear; Group 2 Number missing: 3

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: excess admission days (upper ureteric stones) at 4 weeks ; Group 1: 0.17 (SD 0.71); n=88, Group 2: 0.44 (SD 1.56); n=91

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 ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: 1; Group 2 Number missing: 3

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: excess admission days (mid ureteric stones) at 4 weeks ; Group 1: 0.26 (SD 0.75); n=40, Group 2: 0.13 (SD 0.52); n=40

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 ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: 3; Group 2 Number missing: 0

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: excess admission days (lower ureteric stones) at 4 weeks ; Group 1: 0.15 (SD 0.59); n=247, Group 2: 0.17 (SD; 0.87); n=247

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 ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: 4; Group 2 Number missing: 2

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: TAMSULOSIN versus PLACEBO

Protocol outcome 1: Stone passage

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: spontaneous stone passage (upper ureteric stones) at 4 weeks ; Group 1: 62/88, Group 2: 65/89

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 ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: ; Group 2 Number missing:
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: spontaneous stone passage (middle ureteric stones) at 4 weeks ; Group 1: 29/41, Group 2: 36/44
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 ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: ; Group 2 Number missing:
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: spontaneous stone passage (lower ureteric stones) at 4 weeks ; Group 1: 216/249, Group 2: 202/246
Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 2: Time to stone passage

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: time to stone passage (upper ureteric stones) at 4 weeks ; Group 1: 16.42 days (SD 12.32); n=89, Group 2: 20.73 days (SD 11.09); n=93

Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: ; Group 2 Number missing:

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: time to stone passage (middle ureteric stones) at 4 weeks ; Group 1: 25.88 days (SD 17.55); n=43, Group 2: 18.15 days (SD 7.48); n=44

Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: ; Group 2 Number missing:

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: time to stone passage (lower ureteric stones) at 4 weeks ; Group 1: 15.29 days (SD 11.64); n=251, Group 2: 14.68 days (SD 11.80); n=247

Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 3: Quality of life

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: SF-36 physical component summary (upper ureteric stones) at 12 weeks ; Group 1: 51.73 (SD 8.78); n=51, Group 2: 49.73 (SD 9.30); n=33

Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: similar age, sex, stone size, stone location, history of previous stone,

duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: 38; Group 2 Number missing: 60

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: SF-36 physical component summary (mid ureteric stones) at 12 weeks ; Group 1: 50.89 (SD 9.78); n=26, Group 2: 51.53 (SD 9.20); n=24

Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: 17; Group 2 Number missing: 20

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: SF-36 physical component summary (lower ureteric stones) at 12 weeks ; Group 1: 51.09 (SD 10.2); n=100, Group 2: 52.24 (SD 8.88); n=110

Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: 151; Group 2 Number missing: 137

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: SF-36 mental component summary (upper ureteric stones) at 12 weeks ; Group 1: 49.78 (SD 10.84); n=51, Group 2: 50.18 (SD 11.89); n=33

Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data -High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: 38; Group 2 Number missing: 60

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: SF-36 mental component summary (mid ureteric stones) at 12 weeks ; Group 1: 47.41 (SD 13.61); n=26, Group 2: 52.27 (SD 8.10); n=24

Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: 17; Group 2 Number missing: 20

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: SF-36 mental component summary (lower ureteric stones) at 12 weeks ; Group 1: 49.60 (SD 11.66); n=100, Group 2: 51.39 (SD 9.64); n=110

Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data -High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: 151; Group 2 Number missing: 137

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: EQ-5D (upper ureteric stones) at 12 weeks ; Group 1: 0.870 (SD 0.155); n=51, Group 2: 0.884 (SD 0.240); n=33

Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: 38; Group 2 Number missing: 60

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: EQ-5D (mid ureteric stones) at 12 weeks ; Group 1: 0.817 (SD 0.283); n=28, Group 2: 0.908 (SD 0.139); n=28

Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: 15; Group 2 Number missing: 16

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: EQ-5D (lower ureteric stones) at 12 weeks ; Group 1: 0.864 (SD 0.264); n=103, Group 2: 0.900 (SD 0.176); n=114

Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: 148; Group 2 Number missing: 133

Protocol outcome 4: Pain

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: pain medication use (upper ureteric stones) at 4 weeks ; Group 1: 42; n=66, Group 2: 35; n=47

Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: 23; Group 2 Number missing: 46

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: pain medication use (mid ureteric stones) at 4 weeks ; Group 1: 22; n=32, Group 2: 19; n=31

Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: 11; Group 2 Number missing: 13

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: pain medication use (lower ureteric stones) at 4 weeks ; Group 1: 75; n=147, Group 2: 82; n=153

Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: 104; Group 2 Number missing: 94

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: number of days of pain medication use (upper ureteric stones) at 4 weeks ; Group 1: 11.98 (SD 9.07); n=41, Group 2: 10.97 (SD 7.38); n=33

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 ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: ; Group 2 Number missing:

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: number of days of pain medication use (mid ureteric stones) at 4 weeks ; Group 1: 12.3 (SD 8.77); n=22, Group 2: 8.32 (SD 5.93); n=19

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 ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: ; Group 2 Number missing:

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: number of days of pain medication use (lower ureteric stones) at 4 weeks ; Group 1: 11.19 (SD 8.53); n=74, Group 2: 10.78 (SD 8.95); n=79

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 ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: ; Group 2 Number missing:

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: VAS pain score (upper ureteric stones) at 4 weeks ; Group 1: 0.85 (SD 1.53); n=65, Group 2: 1.37 (SD 2.29); n=46

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 ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: ; Group 2 Number missing:

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: VAS pain score (mid ureteric stones) at 4 weeks ; Group 1: 1.58 (SD 2.88); n=31, Group 2: 1.14 (SD 2.27); n=28

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 ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: ; Group 2 Number missing:

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: VAS pain score (lower ureteric stones) at 4 weeks ; Group 1: 1.01 (SD 1.90); n=137, Group 2: 1.11 (SD 2.17); n=142

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 ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: ; Group 2 Number missing:

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: EQ-5D no pain or discomfort (upper ureteric stones) at 12 weeks ; Group 1: 32; n=51; Group 2: 25; n=34

Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: 38; Group 2 Number missing: 59

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: EQ-5D no pain or discomfort (mid ureteric stones) at 12 weeks ; Group 1:17; n=28, Group 2: 19; n=28

Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: 15; Group 2 Number missing: 16

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: EQ-5D no pain or discomfort (lower ureteric stones) at 12 weeks ; Group 1: 77; n=104, Group 2: 89; n=115

Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: 147; Group 2 Number missing: 132

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: EQ-5D moderate pain or discomfort (upper ureteric stones) at 12 weeks ; Group 1: 19; n=51; Group 2: 7; n=34

Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: 38; Group 2 Number missing: 59

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: EQ-5D moderate pain or discomfort (mid ureteric stones) at 12 weeks ; Group 1: 9; n=28, Group 2: 9; n=28

Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: 15; Group 2 Number missing: 16

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: EQ-5D moderate pain or discomfort (lower ureteric stones) at 12 weeks ; Group 1: 22; n=104, Group 2: 25; n=115

Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing:147 ; Group 2 Number missing: 132

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: EQ-5D extreme pain or discomfort (upper ureteric stones) at 12 weeks ; Group 1: ; Group 2: 2; n=34

Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: ; Group 2 Number missing: 59

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: EQ-5D extreme pain or discomfort (mid ureteric stones) at 12 weeks ; Group 1: 2; n=28, Group 2: ;

Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: 15; Group 2 Number missing:

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: EQ-5D extreme pain or discomfort (lower ureteric stones) at 12 weeks ; Group 1: 5; n=104, Group 2: 1; n=115

Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: 147; Group 2 Number missing: 132

Protocol outcome 5: Adverse events

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: discontinuation due to adverse events (upper ureteric stones) at 4 weeks ; Group 1: 8; n=66, Group 2: 3; n=47

Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: 23; Group 2 Number missing: 46

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: discontinuation due to adverse events (mid ureteric stones) at 4 weeks ; Group 1: 2; n=32, Group 2: 3; n=31

Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: 11; Group 2 Number missing: 13

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: discontinuation due to adverse events (lower ureteric stones) at 4 weeks ; Group 1: 15; n=149, Group 2: 9; n=153

Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: 102; Group 2 Number missing: 94

Protocol outcome 6: Use of healthcare services

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: doctor visits (upper ureteric stones) at 4 weeks ; Group 1: 0.24 (SD 0.67); n=70, Group 2: 0.20 (SD 0.55); n=71

Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: similar age, sex, stone size, stone location, history of previous stone,

duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: 19; Group 2 Number missing: 22

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: doctor visits (mid ureteric stones) at 4 weeks ; Group 1: 0.40 (SD 0.91); n=35, Group 2: 0.31 (SD 0.57); n=39

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 ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: 8; Group 2 Number missing: 5

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: doctor visits (lower ureteric stones) at 4 weeks ; Group 1: 0.16 (SD; 0.63); n=224, Group 2: 0.09 (SD 0.52); n=215

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 ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: 27; Group 2 Number missing: 32

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: nurse visits (upper ureteric stones) at 4 weeks ; Group 1: 0.03 (SD 0.17); n=70, Group 2: 0.24 (SD 1.90); n=71

Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: 19; Group 2 Number missing: 22

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: nurse visits (mid ureteric stones) at 4 weeks ; Group 1: 0.22 (SD 0.84); n=35, Group 2: 0.05 (SD 0.22); n=39

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 ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: 8; Group 2 Number missing: 5

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: nurse visits (lower ureteric stones) at 4 weeks ; Group 1: 0.01 (SD; 0.13); n=224, Group 2: 0.02 (SD 0.18); n=215

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 ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: 27; Group 2 Number missing: 32

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: outpatient visits (upper ureteric stones) at 4 weeks ; Group 1: 0.83 (SD 0.80); n=87, Group 2: 0.01 (SD 0.11); n=89

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 ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: 2; Group 2 Number missing: 4

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: outpatient visits (mid ureteric stones) at 4 weeks ; Group 1: 0.82 (SD 0.86); n=41, Group 2: 0.77 (SD 0.60); n=44

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 ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: 2; Group 2 Number missing: 0

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: outpatient visits (lower ureteric stones) at 4 weeks ; Group 1: 0.66 (SD; 0.69); n=289, Group 2: 0.67 (SD 0.66); n=246

Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: unclear; Group 2 Number missing: 1

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: excess admission days (upper ureteric stones) at 4 weeks ; Group 1: 0.17 (SD 0.71); n=88, Group 2: 0.52 (SD 1.65); n=88

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 ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: 1; Group 2 Number missing: 5

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: excess admission days (mid ureteric stones) at 4 weeks ; Group 1: 0.26 (SD 0.75); n=40 , Group 2: 0.05 (SD 0.22); n=41

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 ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: 3; Group 2 Number missing: 3

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: excess admission days (lower ureteric stones) at 4 weeks ; Group 1: 0.15 (SD; 0.59); n=247, Group 2: 0.18 (SD 0.97); n=246

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 ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: 4; Group 2 Number missing: 1

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: NIFEDIPINE versus PLACEBO

Protocol outcome 1: Stone passage

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: spontaneous stone passage (upper ureteric stones) at 4 weeks ; Group 1: 58/92, Group 2: 65/89

Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: ; Group 2 Number missing:

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: spontaneous stone passage (middle ureteric stones) at 4 weeks ; Group 1: 32/40, Group 2: 36/44

Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: ; Group 2 Number missing:

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: spontaneous stone passage (lower ureteric stones) at 4 weeks ; Group 1: 214/247, Group 2: 202/246

Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 2: Time to stone passage

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: time to stone passage (upper ureteric stones) at 4 weeks ; Group 1: 17.40 days (SD 8.67); n=94, Group 2: 20.73 days (SD 11.09); n=93

Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: ; Group 2 Number missing:

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: time to stone passage (middle ureteric stones) at 4 weeks ; Group 1: 22.18 days (SD 7.90); n=40, Group 2: 18.15 days (SD 7.48); n=44

Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: ; Group 2 Number missing:

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: time to stone passage (lower ureteric stones) at 4 weeks ; Group 1: 14.68 days (SD 16.18); n=249, Group 2: 14.68 days (SD 11.80); n=247

Risk of bias: All domain - Low, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: ; Group 2 Number missing:

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: SF-36 physical component summary (upper ureteric stones) at 12 weeks ; Group 1:50.89 (SD 8.80); n=37, Group 2: 49.73 (SD 9.30); n=33

Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: 57; Group 2 Number missing: 60

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: SF-36 physical component summary (mid ureteric stones) at 12 weeks ; Group 1: 48.79 (SD 12.54); n=24, Group 2: 51.53 (SD 9.20); n=24

Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: similar age, sex, stone size, stone location, history of previous stone,

duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: 16; Group 2 Number missing: 20

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: SF-36 physical component summary (lower ureteric stones) at 12 weeks ; Group 1: 52.13 (SD 8.48); n=116, Group 2: 52.24 (SD 8.88); n=110

Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: 133; Group 2 Number missing: 137

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: SF-36 mental component summary (upper ureteric stones) at 12 weeks ; Group 1: 49.25 (SD 9.93); n=37, Group 2: 50.18 (SD 11.89); n=33

Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: 57; Group 2 Number missing: 60

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: SF-36 mental component summary (mid ureteric stones) at 12 weeks ; Group 1: 50.10 (SD 10.79); n=24, Group 2: 52.27 (SD 8.10); n=24

Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: 16; Group 2 Number missing: 20

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: SF-36 mental component summary (lower ureteric stones) at 12 weeks ; Group 1: 50.90 (SD 10.30); n=116, Group 2: 51.39 (SD 9.64); n=110

Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: 133; Group 2 Number missing: 137

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: EQ-5D (upper ureteric stones) at 12 weeks ; Group 1: 0.894 (SD 0.183); n=40, Group 2: 0.884 (SD 0.240); n=33

Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: 54; Group 2 Number missing: 60

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: EQ-5D (mid ureteric stones) at 12 weeks ; Group 1: 0.789 (SD 0.336); n=24, Group 2: 0.908 (SD 0.139); n=28

Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: similar age, sex, stone size, stone location, history of previous stone,

duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: 16; Group 2 Number missing: 16

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: EQ-5D (lower ureteric stones) at 12 weeks ; Group 1: 0.876 (SD 0.233); n=123, Group 2: 0.900 (SD 0.176); n=114

Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: 126; Group 2 Number missing: 133

Protocol outcome 4: Pain

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: pain medication use (upper ureteric stones) at 4 weeks ; Group 1: 34; n=50, Group 2: 35; n=47

Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: 44; Group 2 Number missing: 46

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: pain medication use (mid ureteric stones) at 4 weeks ; Group 1: 18; n=28, Group 2: 19; n=31

Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: 12; Group 2 Number missing: 13

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: pain medication use (lower ureteric stones) at 4 weeks ; Group 1: 81; n=161, Group 2: 82; n=153

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 ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: 88; Group 2 Number missing: 94

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: number of days of pain medication use (upper ureteric stones) at 4 weeks ; Group 1: 13.56 (SD 10.59); n=34, Group 2: 10.97 (SD 7.38); n=33

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 ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: ; Group 2 Number missing:

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: number of days of pain medication use (mid ureteric stones) at 4 weeks ; Group 1: 10.18 (SD 8.22); n=17, Group 2: 8.32 (SD 5.93); n=19

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 ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: ; Group 2 Number missing:

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: number of days of pain medication use (lower ureteric stones) at 4 weeks ; Group 1: 9.56 (SD 8.20); n=78, Group 2: 10.78 (SD 8.95); n=79

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 ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: ; Group 2 Number missing:

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: VAS pain score (upper ureteric stones) at 4 weeks ; Group 1: 1.86 (SD 2.60); n=49, Group 2: 1.37 (SD 2.29); n=46

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 ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: ; Group 2 Number missing:

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: VAS pain score (mid ureteric stones) at 4 weeks ; Group 1: 1.85 (SD 3.16); n=27, Group 2: 1.14 (SD 2.27); n=28

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 ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: ; Group 2 Number missing:

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: VAS pain score (lower ureteric stones) at 4 weeks ; Group 1: 1.06 (SD 1.97); n=155, Group 2: 1.11 (SD 2.17); n=142

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 ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: ; Group 2 Number missing:

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: EQ-5D no pain or discomfort (upper ureteric stones) at 12 weeks ; Group 1: 30; n=40; Group 2: 25; n=34

Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: 54; Group 2 Number missing: 59

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: EQ-5D no pain or discomfort (mid ureteric stones) at 12 weeks ; Group 1:14; n=25, Group 2: 19; n=28

Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: 15; Group 2 Number missing: 16

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: EQ-5D no pain or discomfort (lower ureteric stones) at 12 weeks ; Group 1: 92; n=123, Group 2: 89; n=115

Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: 126; Group 2 Number missing: 132

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: EQ-5D moderate pain or discomfort (upper ureteric stones) at 12 weeks ; Group 1: 9; n=40; Group 2: 7; n=34

Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: 54; Group 2 Number missing: 59

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: EQ-5D moderate pain or discomfort (mid ureteric stones) at 12 weeks ; Group 1: 9; n=25, Group 2: 9; n=28

Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: 15; Group 2 Number missing: 16

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: EQ-5D moderate pain or discomfort (lower ureteric stones) at 12 weeks ; Group 1: 28; n=123, Group 2: 25; n=115

Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: ; Group 2 Number missing:

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: EQ-5D extreme pain or discomfort (upper ureteric stones) at 12 weeks ; Group 1: 1; n=40, Group 2: 2; n=34

Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: 54; Group 2 Number missing: 59

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: EQ-5D extreme pain or discomfort (mid ureteric stones) at 12 weeks ; Group 1: 2; n=25, Group 2: ;

Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: 15; Group 2 Number missing:

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: EQ-5D extreme pain or discomfort (lower ureteric stones) at 12 weeks ; Group 1: 3; n=123, Group 2: 1; n=115

Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: 126; Group 2 Number missing: 132

Protocol outcome 5: Adverse events

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: discontinuation due to adverse events (upper ureteric stones) at 4 weeks ; Group 1: 8; n=51, Group 2: 3; n=47

Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: 43; Group 2 Number missing: 46

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: discontinuation due to adverse events (mid ureteric stones) at 4 weeks ; Group 1: 3; n=28, Group 2: 3; n=31

Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: 12; Group 2 Number missing: 13

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: discontinuation due to adverse events (lower ureteric stones) at 4 weeks ; Group 1: 29; n=162, Group 2: 9; n=153

Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: 87; Group 2 Number missing: 94

Protocol outcome 6: Use of healthcare services

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: doctor visits (upper ureteric stones) at 4 weeks ; Group 1: 0.19 (SD 0.61); n=67, Group 2: 0.20 (SD 0.55); n=71

Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: 27; Group 2 Number missing: 22

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: doctor visits (mid ureteric stones) at 4 weeks ; Group 1: 0.18 (SD 0.69); n=38, Group 2: 0.31 (SD 0.57); n=39

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 ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: 2; Group 2 Number missing: 5

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: doctor visits (lower ureteric stones) at 4 weeks ; Group 1: 0.17 (SD 0.71); n=226, Group 2: 0.09 (SD; 0.52); n=215

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 ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: 23; Group 2 Number missing: 32

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: nurse visits (upper ureteric stones) at 4 weeks ; Group 1: 0.04 (SD 0.27); n=67, Group 2: 0.24 (SD 1.90); n=71

Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: 27; Group 2 Number missing: 22

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: nurse visits (mid ureteric stones) at 4 weeks ; Group 1: 0.03 (SD 0.16); n=38, Group 2: 0.05 (SD 0.22); n=39

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 ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: 2; Group 2 Number missing: 5

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: nurse visits (lower ureteric stones) at 4 weeks ; Group 1: 0.01 (SD 0.09); n=226, Group 2: 0.02 (SD; 0.18); n=215

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 ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: 23; Group 2 Number missing: 32

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: outpatient visits (upper ureteric stones) at 4 weeks ; Group 1: 0.63 (SD 0.67); n=92, Group 2: 0.01 (SD 0.11); n=89

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 ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: 2; Group 2 Number missing: 4

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: outpatient visits (mid ureteric stones) at 4 weeks ; Group 1: 0.03 (SD 0.16); n=37, Group 2: 0.77 (SD 0.60); n=44

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 ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: 3; Group 2 Number missing: 0

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: outpatient visits (lower ureteric stones) at 4 weeks ; Group 1: 0.62 (SD 0.66); n=246, Group 2: 0.67 (SD; 0.66); n=246

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 ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: 3; Group 2 Number missing: 1 - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: excess admission days (upper ureteric stones) at 4 weeks ; Group 1: 0.44 (SD 1.56); n=91, Group 2: 0.52 (SD 1.65); n=88 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 ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: 3; Group 2 Number missing: 5 - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: excess admission days (mid ureteric stones) at 4 weeks ; Group 1: 0.13 (SD 0.52); n=40, Group 2: 0.05 (SD 0.22); n=41 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 ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: 0; Group 2 Number missing: 3 - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: excess admission days (lower ureteric stones) at 4 weeks ; Group 1: 0.17 (SD 0.87); n=247, Group 2: 0.18 (SD; 0.97); n=246 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 ; Baseline details: similar age, sex, stone size, stone location, history of previous stone, duration of pain, pain score, analgesic use, antibiotic use, SF-36 physical and mental score between groups; Group 1 Number missing: 2; Group 2 Number missing: 1	
Protocol outcomes not reported by the study	

Study	Su 2016[194]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=272)
Countries and setting	Conducted in Taiwan; Setting: single centre
Line of therapy	1st line
Duration of study	Intervention time: 2 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: non-enhanced computed tomography
Stratum	Adults (≥16 years), ureteric stone <1 cm
Subgroup analysis within study	Not applicable
Inclusion criteria	radiopaque distal ureteral stones <10mm
Exclusion criteria	urinary tract infections; high grade hydronephrosis; diabetes; peptic ulcers; history of hypersensitivity to alpha-blockers; pregnancy or nursing; history of spontaneous stone expulsion; hypotension; systolic blood pressure <110mmHg
Recruitment/selection of patients	not reported
Age, gender and ethnicity	Age - Mean (SD): Tamsulosin group: 50.74 (10.08), Silodosin group: 51.58 (8.27), placebo group: 52.16 (9.2). Gender (M:F): 122/82. Ethnicity: not reported
Further population details	1. Kidney pole: Not applicable 2. Neuropathic/ cerebral-palsy /immobility: Not applicable 3. Obesity /skin-to-stone distance: Not applicable 4. Pregnant women: Non-pregnant 5. Stone composition/hounsfield units: Not applicable 6. Ureteric stone: Lower ureteric stones
Indirectness of population	No indirectness
Interventions	(n=76) Intervention 1: Alpha blockers - Tamsulosin. Tamsulosin 0.4mg daily. Duration up to 2 weeks. Concurrent medication/care: Ketorolac 10mg three times daily, Buprenorphine 0.2mg on demand and encouragement to drink a minimum of 2 L of water daily. Indirectness: No indirectness (n=79) Intervention 2: Alpha blockers - Silodosin. Silodosin 8mg daily. Duration up to 2 weeks. Concurrent medication/care: Ketorolac 10mg three times daily, Buprenorphine 0.2mg on demand and encouragement to drink a minimum of 2 L of water daily. Indirectness: No indirectness (n=82) Intervention 3: Placebo. Placebo. Duration up to 2 weeks. Concurrent medication/care: Ketorolac 10mg three times daily, Buprenorphine 0.2mg on demand and encouragement to drink a minimum of 2 L of water daily . Indirectness: No indirectness

Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: TAMSULOSIN versus PLACEBO

Protocol outcome 1: Stone passage
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: expulsion rate at 2 weeks ; Group 1: 40/47, Group 2: 29/49
Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, BMI, stone location (right/left) or stone size ; Group 1 Number missing: 29; Group 2 Number missing: 33

Protocol outcome 2: Time to stone passage
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: expulsion time at 2 weeks ; Group 1: mean 6.28 days (SD 2.41); n=47,
Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, BMI, stone location (right/left) or stone size ; Group 1 Number missing: 29; Group 2 Number missing: 33

Protocol outcome 3: Adverse events
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: adverse effects at 2 weeks ; Group 1: 1/47, Group 2: 0/49; Comments: adverse effect not reported
Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: Serious indirectness, Comments: adverse effect not reported ; Baseline details: no significant difference in age, sex, BMI, stone location (right/left) or stone size ; Group 1 Number missing: 29; Group 2 Number missing: 33

Protocol outcome 4: Analgesic use
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: Buprenorphine consumption at 2 weeks ; Group 1: mean 0.36 mg (SD 0.19); n=47,
Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, BMI, stone location (right/left) or stone size ; Group 1 Number missing: 29; Group 2 Number missing: 33
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: Ketorolac consumption at 2 weeks ; Group 1: mean 230.87 mg (SD 114.69); n=47,
Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, BMI, stone location (right/left) or stone size ; Group 1 Number missing: 29; Group 2 Number missing: 33

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: SILODOSIN versus PLACEBO

Protocol outcome 1: Stone passage
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: expulsion rate at 2 weeks ; Group 1: 38/48, Group 2: 29/49
Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - Low,

Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, BMI, stone location (right/left) or stone size ; Group 1 Number missing: 29; Group 2 Number missing: 33 Protocol outcome 2: Time to stone passage - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: expulsion time at 2 weeks ; Group 1: mean 6.03 days (SD 2.72); n=47, Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, BMI, stone location (right/left) or stone size ; Group 1 Number missing: 29; Group 2 Number missing: 33 Protocol outcome 3: Adverse events - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: adverse effects at 2 weeks ; Group 1: 6/48, Group 2: 0/49; Comments: adverse effects: transient hypotension, asthenia, syncope and retrograde ejaculation Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, BMI, stone location (right/left) or stone size ; Group 1 Number missing: 29; Group 2 Number missing: 33 Protocol outcome 4: Analgesic use - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: Buprenorphine consumption at 2 weeks ; Group 1: mean 0.37 mg (SD 0.19); n=48, Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, BMI, stone location (right/left) or stone size ; Group 1 Number missing: 29; Group 2 Number missing: 33 - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: Ketorolac consumption at 2 weeks ; Group 1: mean 221.56 (SD 94.22); n=47, Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - High, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, BMI, stone location (right/left) or stone size ; Group 1 Number missing: 29; Group 2 Number missing: 33	
Protocol outcomes not reported by the study	Quality of life; Pain intensity; Hospitalisation/ Use of healthcare services

Study	Sun 2009[196]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=60)
Countries and setting	Conducted in China; Setting: Departments of Urology and Pharmacy, single centre
Line of therapy	1st line
Duration of study	Intervention time: 2 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: urinary system ultrasonography and KUB
Stratum	Adults (≥16 years), ureteric stone <1 cm
Subgroup analysis within study	Not applicable
Inclusion criteria	18-65 years; unilateral distal (below the lower border of the sacroiliac joint) ureteral stones
Exclusion criteria	multiple stones; severe incarcerated stones; history of distal ureteral surgery or spontaneous stone expulsion; renal colic more than 24 hours in duration; urinary tract infection; severe hydronephrosis; voiding dysfunction; hypotension; cardiovascular and cerebrovascular diseases; hepatic and renal dysfunction; pregnancy; diabetes; ulcer disease; hypersensitivity to Naftopidil; receiving treatment with cardiovascular drugs, alpha-adrenergic receptor antagonists or calcium antagonists
Recruitment/selection of patients	not reported
Age, gender and ethnicity	Age - Mean (SD): watchful waiting group: 37.8 (10.2), Naftopidil group: 38.2 (12.6). Gender (M:F): 50/10. Ethnicity: not reported
Further population details	1. Kidney pole: Not applicable 2. Neuropathic/ cerebral-palsy /immobility: Not applicable 3. Obesity /skin-to-stone distance: Not applicable 4. Pregnant women: Non-pregnant 5. Stone composition/hounsfield units: Not applicable 6. Ureteric stone: Lower ureteric stones
Indirectness of population	No indirectness
Interventions	(n=30) Intervention 1: Alpha blockers - Naftopidil. Naftopidil 50mg daily. Duration up to 2 weeks. Concurrent medication/care: instruction to drink a minimum of 2 L of water daily and Indomethacin suppository to control acute episodes of ureteral colic if present. Indirectness: No indirectness (n=30) Intervention 2: No treatment - Watch and wait. Watchful waiting. Duration up to 2 weeks. Concurrent medication/care: instruction to drink a minimum of 2 L of water daily and Indomethacin suppository used to control acute episodes of ureteral colic if present. Indirectness: No indirectness
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: NAFTOPIDIL versus WATCH AND WAIT

Protocol outcome 1: Hospitalisation/ Use of healthcare services
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: hospitalisation at 2 weeks ; Group 1: 0/30, Group 2: 0/30
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex or stone size ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 2: Stone passage
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: stone expulsion at 2 weeks ; Group 1: 27/30, Group 2: 8/30
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex or stone size ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 3: Adverse events
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: dizziness and fatigue at 2 weeks ; Group 1: 2/30, Group 2: 0/30
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex or stone size ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 4: Pain intensity
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: significant ureteral colic at 2 weeks ; Group 1: 0/30, Group 2: 0/30
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex or stone size ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcomes not reported by the study	Quality of life; Analgesic use; Time to stone passage

Study	Sur 2015[197]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=239)
Countries and setting	Conducted in USA; Setting: 27 centres
Line of therapy	1st line
Duration of study	Intervention time: 4 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: KUB radiograph and/or non-contrast helical computed tomography
Stratum	Adults (≥16 years), ureteric stone <1 cm
Subgroup analysis within study	Not stratified but pre-specified: stone location
Inclusion criteria	≥18 years; unilateral calculus ≥4mm and ≤10mm in any location of the ureter
Exclusion criteria	multiple ureteral calculi; solitary kidney; refractory renal colic; nonopaque calculus; severe hydronephrosis
Recruitment/selection of patients	not reported
Age, gender and ethnicity	Age - Mean (SD): Silodosin group: 47 (13), placebo 47 (15). Gender (M:F): 152/80. Ethnicity: white 210/232
Further population details	1. Kidney pole: Not applicable 2. Neuropathic/ cerebral-palsy /immobility: Not applicable 3. Obesity /skin-to-stone distance: Not applicable 4. Pregnant women: Not stated / Unclear 5. Stone composition/hounsfield units: Not applicable 6. Ureteric stone: Not stated / Unclear
Indirectness of population	No indirectness
Interventions	(n=119) Intervention 1: Alpha blockers - Silodosin. Silodosin 8mg. Duration up to 4 weeks. Concurrent medication/care: Oxycodone 5mg to provide analgesia for renal colic and us concomitant pre-enrolment medications that would not confound study results. Indirectness: No indirectness (n=120) Intervention 2: Placebo. Placebo. Duration up to 4 weeks. Concurrent medication/care: Oxycodone 5mg to provide analgesia for renal colic and use of other concomitant pre-enrolment medications that would not confound study results. Indirectness: No indirectness
Funding	Study funded by industry (Actavis Inc.)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: SILODOSIN versus PLACEBO

Protocol outcome 1: Stone passage
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: spontaneous stone passage (distal) at 4 weeks; Group 1: 36/52, Group 2: 27/59
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 ; Baseline details: no significant difference in age, sex, ethnicity, weight, height, BMI, stone size or location ; Group 1 Number missing: ; Group 2 Number missing: - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: spontaneous stone passage (middle) at 4 weeks; Group 1: 8/20, Group 2: 10/21 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 ; Baseline details: no significant difference in age, sex, ethnicity, weight, height, BMI, stone size or location ; Group 1 Number missing: ; Group 2 Number missing: - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: spontaneous stone passage (proximal) at 4 weeks; Group 1: 16/43, Group 2: 15/37 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 ; Baseline details: no significant difference in age, sex, ethnicity, weight, height, BMI, stone size or location ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 2: Adverse events - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: retrograde ejaculation at 4 weeks; Group 1: 11/72, Group 2: 1/80 Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, ethnicity, weight, height, BMI, stone size or location ; Group 1 Number missing: ; Group 2 Number missing: - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: dizziness at 4 weeks; Group 1: 8/119, Group 2: 2/120 Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, ethnicity, weight, height, BMI, stone size or location ; Group 1 Number missing: ; Group 2 Number missing: - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: headache at 4 weeks; Group 1: 4/119, Group 2: 0/120 Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, ethnicity, weight, height, BMI, stone size or location ; Group 1 Number missing: ; Group 2 Number missing:
Protocol outcomes not reported by the study	Quality of life; Time to stone passage; Pain intensity; Analgesic use; Hospitalisation/ Use of healthcare services

Study	**Thapa 2014[199]**
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=70)
Countries and setting	Conducted in Nepal; Setting: Surgery outpatient department and emergency department, single centre
Line of therapy	1st line
Duration of study	Intervention time: 3 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: plain X-ray or ultrasound of the KUB

Stratum	Adults (≥16 years), ureteric stone <1 cm
Subgroup analysis within study	Not applicable
Inclusion criteria	>15 years; symptomatic, unilateral, solitary lower ureteral stones (located below sacroiliac joint) of 5-10mm
Exclusion criteria	urinary tract infection; renal failure; history of urinary surgery or endoscopic treatment; uncorrected distal obstruction; moderate to severe hydronephrosis; deranged renal function or intractable pain that couldn't be managed on outpatient basis; refusal to participate
Recruitment/selection of patients	not reported
Age, gender and ethnicity	Age - Range: 15-63. Gender (M:F): 41/29. Ethnicity: not reported
Further population details	1. Kidney pole: Not applicable 2. Neuropathic/ cerebral-palsy /immobility: Not applicable 3. Obesity /skin-to-stone distance: Not applicable 4. Pregnant women: Not stated / Unclear 5. Stone composition/hounsfield units: Not applicable 6. Ureteric stone: Lower ureteric stones
Indirectness of population	No indirectness
Interventions	(n=35) Intervention 1: Alpha blockers - Tamsulosin. Tamsulosin 0.4mg daily. Duration up to 3 weeks. Concurrent medication/care: advice to have high fluid intake more than 3 L daily and Diclofenac 50mg 3 times daily for 5 days, then on demand . Indirectness: No indirectness (n=35) Intervention 2: Pain management only - NSAIDs. Diclofenac 50mg 3 times daily for 5 days, then on demand. Duration up to 3 weeks. Concurrent medication/care: advice to have high fluid intake more than 3 L daily. Indirectness: No indirectness
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: TAMSULOSIN versus NSAIDS

Protocol outcome 1: Stone passage
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: stone clearance at 3 weeks ; Group 1: 28/35, Group 2: 21/35
Risk of bias: All domain - Very 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; Time to stone passage; Adverse events; Pain intensity; Analgesic use; Hospitalisation/ Use of healthcare services

Study	Wang 2008[206]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=95)
Countries and setting	Conducted in China; Setting: Division of Urology, Department of Surgery, single centre
Line of therapy	1st line
Duration of study	Intervention time: 2 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: x-ray of KUB, abdominal ultrasonography and intravenous urography
Stratum	Adults (≥16 years), ureteric stone <1 cm
Subgroup analysis within study	Not applicable
Inclusion criteria	radiopaque lower ureteral stones
Exclusion criteria	urinary tract infections; high grade hydronephrosis; diabetes; ulcers; history of hypersensitivity to alpha-blockers; pregnant women; history of spontaneous stone expulsion; hypotension; systolic blood pressure <110mmHg
Recruitment/selection of patients	not reported
Age, gender and ethnicity	Age - Mean (SD): Tamsulosin group: 50.4 (9.7), Terazosin group: 51.4 (8.6), control group: 50.9 (9.6). Gender (M:F): 66/29. Ethnicity: not reported
Further population details	1. Kidney pole: Not applicable 2. Neuropathic/ cerebral-palsy /immobility: Not applicable 3. Obesity /skin-to-stone distance: Not applicable 4. Pregnant women: Non-pregnant 5. Stone composition/hounsfield units: Not applicable 6. Ureteric stone: Lower ureteric stones
Indirectness of population	No indirectness
Interventions	(n=32) Intervention 1: Alpha blockers - Tamsulosin. Tamsulosin 0.4mg daily. Duration up to 2 weeks. Concurrent medication/care: Ketorolac 10mg 3 times daily, sublingual Buprenorphine 0.2mg as needed and a minimum of 2 L of water daily. Indirectness: No indirectness (n=32) Intervention 2: Alpha blockers - Terazosin. Terazosin 2mg daily. Duration up to 2 weeks. Concurrent medication/care: Ketorolac 10mg 3 times daily, sublingual Buprenorphine 0.2mg on demand and a minimum of 2 L of water daily. Indirectness: No indirectness (n=31) Intervention 3: Pain management only - NSAIDs. Ketorolac 10mg 3 times daily. Duration up to 2 weeks. Concurrent medication/care: sublingual Buprenorphine 0.2mg as needed and a minimum of 2 L of water daily. Indirectness: No indirectness

Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: TAMSULOSIN versus NSAIDS

Protocol outcome 1: Stone passage
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: expulsion rate at 2 weeks ; Group 1: 26/32, Group 2: 17/31
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, stone size or stone location (left/right) ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 2: Time to stone passage
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: expulsion time at 2 weeks ; Group 1: mean 6.3 days (SD 2.4); n=32,
Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, stone size or stone location (left/right) ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 3: Adverse events
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: adverse events at 2 weeks ; Group 1: 1/32, Group 2: 0/31; Comments: adverse event not reported
Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: Serious indirectness, Comments: adverse effect not reported ; Baseline details: no significant difference in age, sex, stone size or stone location (left/right) ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 4: Pain intensity
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: colic episodes at 2 weeks ; Group 1: mean 1.97 (SD 1.45); n=32,
Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, stone size or stone location (left/right) ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 5: Analgesic use
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: Ketorolac consumption at 2 weeks ; Group 1: mean 231 mg (SD 112); n=32,
Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, stone size or stone location (left/right) ; Group 1 Number missing: ; Group 2 Number missing:
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: Buprenorphine consumption at 2 weeks ; Group 1: mean 0.39 mg (SD 0.29); n=32,
Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, stone size or stone location (left/right) ; Group 1 Number missing: ; Group 2 Number missing:

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: TERAZOSIN versus NSAIDS

Protocol outcome 1: Stone passage
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: expulsion rate at 2 weeks ; Group 1: 25/32, Group 2: 17/31
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, stone size or stone location (left/right) ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 2: Time to stone passage
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: expulsion time at 2 weeks ; Group 1: mean 6.3 days (SD 2.1); n=32,
Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, stone size or stone location (left/right) ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 3: Adverse events
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: adverse events at 2 weeks ; Group 1: 5/32, Group 2: 0/31; Comments: adverse effects: transient hypotension, asthenia, syncope and palpitations
Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: Serious indirectness, Comments: adverse effects: transient hypotension, asthenia, syncope and palpitations ; Baseline details: no significant difference in age, sex, stone size or stone location (left/right) ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 4: Pain intensity
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: colic episodes at 2 weeks ; Group 1: mean 1.84 (SD 1.51); n=32,
Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, stone size or stone location (left/right) ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 5: Analgesic use
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: Ketorolac consumption at 2 weeks ; Group 1: mean 256 mg (SD 112); n=32,
Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, stone size or stone location (left/right) ; Group 1 Number missing: ; Group 2 Number missing:
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: Buprenorphine consumption at 2 weeks ; Group 1: mean 0.36 mg (SD 0.3); n=32,
Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, stone size or stone location (left/right) ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcomes not reported by the study	Quality of life; Hospitalisation/ Use of healthcare services

Study	**Wang 2014[213]**
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=94)
Countries and setting	Conducted in China; Setting: Department of urology, single centre
Line of therapy	Adjunctive to current care
Duration of study	Intervention + follow up: 6 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: ultrasound and/or KUB x-ray
Stratum	Adults (≥16 years), ureteric stone 1-2 cm: NA
Subgroup analysis within study	Not applicable: NA
Inclusion criteria	symptomatic stone; 10-15mm in size; located in the proximal ureter (between the ureteropelvic junction and sacroiliac joint); associated with moderate hydroureteronephrosis
Exclusion criteria	fever; leukocytosis; presence of ureteral stricture distal to the stone; co-existence of a kidney stone on ultrasound; proximal stone migration during ureteroscopic Ho:YAG laser lithotripsy
Recruitment/selection of patients	not reported
Age, gender and ethnicity	Age - Other: not reported. Gender (M:F): not reported . Ethnicity: not reported
Further population details	1. Kidney pole: Not applicable 2. Neuropathic/ cerebral-palsy /immobility: Not applicable 3. Obesity /skin-to-stone distance: Not applicable 4. Pregnant women: Not stated / Unclear 5. Stone composition/hounsfield units: Not applicable 6. Ureteric stone: Upper ureteric stones
Indirectness of population	No indirectness: NA
Interventions	(n=48) Intervention 1: Alpha blockers and URS. Tamsulosin 0.4mg daily after URS. Duration up to 6 weeks. Concurrent medication/care: 2-3L hydration and Diclofenac 75mg on demand. Indirectness: No indirectness; Indirectness comment: NA (n=46) Intervention 2: Surgery - URS. URS only. Duration up to 6 weeks. Concurrent medication/care: 2-3L hydration and Diclofenac 75mg on demand. Indirectness: No indirectness; Indirectness comment: NA
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: ALPHA BLOCKERS AND URS versus URS

Protocol outcome 1: Stone passage
- Actual outcome for Adults (≥16 years), ureteric stone 1-2 cm: stone free rate at 6 weeks ; Group 1: 44/45, Group 2: 41/44; Comments: numbers calculated from percentages
Risk of bias: All domain - High, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: no significant difference in age, sex, stone size or operative time ; Group 1 Number missing: 3; Group 2 Number missing: 2

Protocol outcome 2: Time to stone passage
- Actual outcome for Adults (≥16 years), ureteric stone 1-2 cm: time of fragment expulsion at 6 weeks ; Group 1: mean 7.86 days (SD 4.99); n=45,
Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: no significant difference in age, sex, stone size or operative time ; Group 1 Number missing: 3; Group 2 Number missing: 2

Protocol outcome 3: Adverse events
- Actual outcome for Adults (≥16 years), ureteric stone 1-2 cm: dizziness at 6 weeks ; Group 1: 2/45, Group 2: 0/44
Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: no significant difference in age, sex, stone size or operative time ; Group 1 Number missing: 3; Group 2 Number missing: 2

Protocol outcome 4: Pain intensity
- Actual outcome for Adults (≥16 years), ureteric stone 1-2 cm: ureteral colic rate at 6 weeks ; Group 1: 2/45, Group 2: 10/44; Comments: numbers calculated from percentages
Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness, Comments: NA; Baseline details: no significant difference in age, sex, stone size or operative time ; Group 1 Number missing: 3; Group 2 Number missing: 2

Protocol outcomes not reported by the study	Quality of life; Analgesic use; Hospitalisation/ Use of healthcare services

Study	Wang 2016[208]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=141)
Countries and setting	Conducted in Taiwan; Setting: Department of Surgery, Division of Urology, single centre
Line of therapy	1st line
Duration of study	Intervention time: 2 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: non-enhanced computed tomography
Stratum	Adults (≥16 years), ureteric stone <1 cm
Subgroup analysis within study	Not applicable
Inclusion criteria	Radiopaque distal ureteral stones <10mm
Exclusion criteria	Urinary tract infections; high-grade hydronephrosis; diabetes; peptic ulcers; history of hypersensitivity to alpha-1 blockers; pregnancy or nursing; history of spontaneous stone expulsion; hypotension; systolic blood pressure <110mmHg
Recruitment/selection of patients	not reported
Age, gender and ethnicity	Age - Mean (SD): Silodosin group: 51.42 (8.68), control group: 51.51 (10.03). Gender (M:F): Define. Ethnicity: not reported
Further population details	1. Kidney pole: Not applicable 2. Neuropathic/ cerebral-palsy /immobility: Not applicable 3. Obesity /skin-to-stone distance: Not applicable 4. Pregnant women: Non-pregnant 5. Stone composition/hounsfield units: Not applicable 6. Ureteric stone: Lower ureteric stones
Indirectness of population	No indirectness
Interventions	(n=71) Intervention 1: Alpha blockers - Silodosin. Silodosin 8mg daily. Duration up to 2 weeks. Concurrent medication/care: Ketorolac three times daily, sublingual Buprenorphine 0.2mg on demand and encouragement to drink a minimum of 2 L of water daily. Indirectness: No indirectness (n=70) Intervention 2: Placebo. Placebo. Duration up to 2 weeks. Concurrent medication/care: Ketorolac 10mg three times daily, sublingual Buprenorphine 0.2mg on demand and encouragement to drink a minimum of 2 L of water daily. Indirectness: No indirectness
Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: SILODOSIN versus PLACEBO	

Protocol outcome 1: Stone passage
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: expulsion rate at 2 weeks; Group 1: 48/62, Group 2: 33/61
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 ; Baseline details: no significant difference in age, sex, BMI, stone location (right/left) or stone size ; Group 1 Number missing: 9, Reason: 5 missed primary outcome and 4 withdrew consent ; Group 2 Number missing: 9, Reason: 5 missed primary outcome and 4 withdrew consent

Protocol outcome 2: Time to stone passage
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: expulsion time at 2 weeks; Group 1: mean 6.31 days (SD 2.13); n=62,
Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, BMI, stone location (right/left) or stone size ; Group 1 Number missing: 9, Reason: 5 missed primary outcome and 4 withdrew consent ; Group 2 Number missing: 9, Reason: 5 missed primary outcome and 4 withdrew consent

Protocol outcome 3: Adverse events
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: adverse effects at 2 weeks; Group 1: 10/62, Group 2: 2/61
Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: Serious indirectness, Comments: control group adverse effects not reported, Silodosin group adverse effects: transient hypotension, asthenia, syncope and palpitations ; Baseline details: no significant difference in age, sex, BMI, stone location (right/left) or stone size ; Group 1 Number missing: 9, Reason: 5 missed primary outcome and 4 withdrew consent ; Group 2 Number missing: 9, Reason: 5 missed primary outcome and 4 withdrew consent

Protocol outcome 4: Pain intensity
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: Colic episodes at 2 weeks; Group 1: mean 2.39 (SD 1.3); n=62,
Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, BMI, stone location (right/left) or stone size ; Group 1 Number missing: 9, Reason: 5 missed primary outcome and 4 withdrew consent ; Group 2 Number missing: 9, Reason: 5 missed primary outcome and 4 withdrew consent

Protocol outcome 5: Analgesic use
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: Ketorolac consumption at 2 weeks; Group 1: mean 255.97 mg (SD 112.97); n=62,
Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, BMI, stone location (right/left) or stone size ; Group 1 Number missing: 9, Reason: 5 missed primary outcome and 4 withdrew consent ; Group 2 Number missing: 9, Reason: 5 missed primary outcome and 4 withdrew consent
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: Buprenorphine consumption at 2 weeks; Group 1: mean 0.47 mg (SD 0.27); n=62,
Risk of bias: All domain - High, Selection - Low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, BMI, stone location (right/left) or stone

size ; Group 1 Number missing: 9, Reason: 5 missed primary outcome and 4 withdrew consent ; Group 2 Number missing: 9, Reason: 5 missed primary outcome and 4 withdrew consent	
Protocol outcomes not reported by the study	Quality of life; Hospitalisation/ Use of healthcare services

Study	**Ye 2011[215]**
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=3189)
Countries and setting	Conducted in China; Setting: outpatient departments from 10 medical centres
Line of therapy	1st line
Duration of study	Intervention time: 4 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: plain abdominal radiography, urinary system ultrasonography, non-contrast CT and IVU
Stratum	Adults (≥16 years), ureteric stone <1 cm
Subgroup analysis within study	Not applicable
Inclusion criteria	18-50 years; emergency admission for renal colic; radiopaque or radiolucent single distal ureteric stone (juxtavesical or intramural portion) of 4-7mm
Exclusion criteria	fever; urinary tract infection; severe hydronephrosis; renal insufficiency (estimated GFR <60mL/min per 1.73m²); multiple ureteric stones; urethrostenosis; ureteric stricture; gastric ulcer; diabetes; hypotension; pregnancy; current use of alpha-adrenoceptor antagonists, calcium-channel blockers or corticosteroids; history of ipsilateral ureteric surgery, spontaneous stone expulsion or known or suspected allergy to one of the study medications
Recruitment/selection of patients	not reported
Age, gender and ethnicity	Age - Median (range): Tamsulosin group: 30.7 (18-48), Nifedipine group: 34.5 (22-50). Gender (M:F): 1987/1202. Ethnicity: not reported
Further population details	1. Kidney pole: Not applicable 2. Neuropathic/ cerebral-palsy /immobility: Not applicable 3. Obesity /skin-to-stone distance: Not applicable 4. Pregnant women: Non-pregnant 5. Stone composition/hounsfield units: Not applicable 6. Ureteric stone: Lower ureteric stones
Indirectness of population	No indirectness
Interventions	(n=1596) Intervention 1: Alpha blockers - Tamsulosin. Tamsulosin 0.4mg daily. Duration up to 4 weeks. Concurrent medication/care: encouragement to maintain a water intake of 2-2.5 L daily, Levofloxacin 0.2g

	twice daily and Diclofenac 50mg suppository on demand . Indirectness: No indirectness (n=1593) Intervention 2: Calcium channel blockers - Nifedipine. Nifedipine 10mg 3 times daily. Duration up to 4 weeks. Concurrent medication/care: encouragement to maintain a water intake of 2-2.5 L daily, Levofloxacin 0.2g twice daily and Diclofenac 50mg suppository on demand . Indirectness: No indirectness
Funding	Study funded by industry (Astellas Pharmaceutical)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: TAMSULOSIN versus NIFEDIPINE

Protocol outcome 1: Stone passage
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: expulsion rate at 4 weeks ; Group 1: 1530/1596, Group 2: 1171/1593
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 ; Baseline details: no significant difference in age, sex, stone size or stone location ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 2: Adverse events
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: side effect incidence at 4 weeks ; Group 1: 90/1596, Group 2: 98/1593
Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: Serious indirectness, Comments: side effects not specified ; Baseline details: no significant difference in age, sex, stone size or stone location ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 3: Analgesic use
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: rate of pain relief therapy at 4 weeks ; Group 1: 24/1596, Group 2: 77/1593; Comments: numbers calculated from percentages
Risk of bias: All domain - Very high, Selection - Low, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, stone size or stone location ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcomes not reported by the study	Quality of life; Time to stone passage; Pain intensity; Hospitalisation/ Use of healthcare services

Study	**Ye 2018[216]**
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=3390)

Countries and setting	Conducted in China; Setting: Not reported
Line of therapy	1st line
Duration of study	Intervention + follow up: 28 days
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: Confirmed by plain abdominal radiography (kidney–ureters–bladder), urinary ultrasonography, and/or non-contrast computed tomography (CT)
Stratum	Adults (≥16 years), ureteric stone <1 cm
Subgroup analysis within study	Not applicable
Inclusion criteria	Adults,18–60 yr; emergency admission for renal colic; presence of a single ureteral stone; a stone in the distal ureter, with a dimension of 4–7 mm; and a unilateral presentation
Exclusion criteria	Fever; urinary tract infections; severe hydronephrosis; renal insufficiency, defined by an estimated glomerular filtration rate of<60 ml/min per 1.73m2; abnormal anatomy, such as a solitary kidney, horseshoe kidney, or a duplex urinary system; urethrostenosis; a history of ureter strictures; diabetes mellitus; hypotension (systolic blood pressure<100 mmHg); known or suspected pregnancy; current use of a-adrenoceptor antagonists or corticosteroids; and a previous history of ipsilateral ureteral surgery, spontaneous stone expulsion, or known or suspected allergy to the study medications
Recruitment/selection of patients	Not reported
Age, gender and ethnicity	Age - Mean (SD): Tamsulosin 40.1 (11.6); placebo 40.7 (12.3). Gender (M:F): 2135/1161. Ethnicity: not reported
Further population details	1. Kidney pole: Not applicable 2. Neuropathic/ cerebral-palsy /immobility: Not stated / Unclear 3. Obesity /skin-to-stone distance: Not stated / Unclear 4. Pregnant women: Non-pregnant 5. Stone composition/hounsfield units: Not stated / Unclear 6. Uteric stone: Lower ureteric stones
Indirectness of population	No indirectness
Interventions	(n=1695) Intervention 1: Alpha blockers - Tamsulosin. Two capsules of tamsulosin 0.2 mg taken daily until spontaneous stone passage, up to a maximum of 28 d or the need for intervention . Duration 28 days. Concurrent medication/care: Participants were instructed to drink 2 l water per day and to collect the urine stone after urine filtration using a sieve. Additionally, the patients were authorized to use pain relief therapy with a 50mg sodium diclofenac suppository on demand. Participants were asked to stop taking their medication use if stones were passed over the course of treatment. Indirectness: No indirectness (n=1695) Intervention 2: Placebo. Placebo, taken daily until spontaneous stone passage, up to a maximum of 28 d or the need for intervention. Duration 28 days. Concurrent medication/care: Participants were instructed to drink 2 l water per day and to collect the urine stone after urine filtration using a sieve. Additionally, the patients were authorized to use pain relief therapy with a 50mg sodium diclofenac suppository on demand. Participants were asked to stop taking their

	medication use if stones were passed over the course of treatment. Indirectness: No indirectness
Funding	Academic or government funding (Supported by health industry special scientific research projects, Ministry of Health of China (201002010). Astellas Pharma supported this study and was involved with preparation of the manuscript.)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: TAMSULOSIN versus PLACEBO

Protocol outcome 1: Stone passage at Define
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: Stone expulsion at 28 days; Group 1: 1419/1642, Group 2: 1300/1654
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: 53; Group 2 Number missing: 41

Protocol outcome 2: Time to stone passage at Define
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: Time to stone passage at 28 days; Group 1: mean 148.3 hours (SD 63.2); n=1642, Group 2: mean 248.7 hours (SD 76.6); n=1654
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: 53; Group 2 Number missing: 41

Protocol outcome 3: Adverse events at Define
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: Retrograde ejaculation at 28 days; Group 1: 67/1642, Group 2: 48/1654
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: 53; Group 2 Number missing: 41
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: Dizziness at 28 days; Group 1: 52/1642, Group 2: 50/1654
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: 53; Group 2 Number missing: 41
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: Headache at 28 days; Group 1: 41/1642, Group 2: 46/1654
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: 53; Group 2 Number missing: 41

Protocol outcome 4: Analgesic use at Define
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: Rate of pain relief therapy at 28 days; Group 1: 31/1642, Group 2: 155/1654
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: 53; Group 2 Number missing: 41
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: Diclofenac dose at 28 days; Group 1: mean 86 mg (SD 32); n=1642, Group 2: mean 263 mg (SD 62); n=1654
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: 53; Group 2 Number missing: 41	
Protocol outcomes not reported by the study	Quality of life at Define; Pain intensity at Define; Hospitalisation/ Use of healthcare services at Define

Study	**Yilmaz 2005[218]**
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=114)
Countries and setting	Conducted in Turkey; Setting: Department of Urology, single centre
Line of therapy	1st line
Duration of study	Intervention time: 4 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: X-rays of KUB and urinary system ultrasonography
Stratum	Adults (≥16 years), ureteric stone <1 cm
Subgroup analysis within study	Not applicable
Inclusion criteria	18-65 years; radiopaque stones ≤10mm located in the distal tract of the ureter (juxtavesical tract and ureterovesical junction)
Exclusion criteria	urinary system infection; radiolucency stones; severe hydronephrosis; diabetes; ulcer disease; hypotension and having calcium antagonist medication; distal ureter surgery
Recruitment/selection of patients	not reported
Age, gender and ethnicity	Age - Mean (SD): control group: 41.6 (12.01), Tamsulosin group: 40.62 (10.27), Treazosin group: 41.67 (11.41), Doxazosin group: 42.13 (10.46). Gender (M:F): 46/68. Ethnicity: not reported
Further population details	1. Kidney pole: Not applicable 2. Neuropathic/ cerebral-palsy /immobility: Not applicable 3. Obesity /skin-to-stone distance: Not applicable 4. Pregnant women: Not stated / Unclear 5. Stone composition/hounsfield units: Not applicable 6. Ureteric stone: Lower ureteric stones
Indirectness of population	No indirectness
Interventions	(n=29) Intervention 1: Alpha blockers - Tamsulosin. Tamsulosin 0.4mg daily. Duration up to 4 weeks. Concurrent medication/care: symptomatic therapy with Diclofenac 75mg injections on demand and consumption of a minimum of 2 L of water daily. Indirectness: No indirectness (n=28) Intervention 2: Alpha blockers - Terazosin. Terazosin 5mg daily. Duration up to 4 weeks. Concurrent medication/care: symptomatic therapy with Diclofenac 75mg injections on demand and consumption of a

	minimum of 2 L of water daily. Indirectness: No indirectness (n=29) Intervention 3: Alpha blockers - Doxazosin. Doxazosin 4mg daily. Duration up to 4 weeks. Concurrent medication/care: symptomatic therapy with Diclofenac 75mg injections on demand and consumption of a minimum of 2 L of water daily. Indirectness: No indirectness (n=28) Intervention 4: Pain management only - NSAIDs. Symptomatic therapy with Diclofenac 75mg injections on demand. Duration up to 4 weeks. Concurrent medication/care: consumption of a minimum of 2 L of water daily. Indirectness: No indirectness
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: TAMSULOSIN versus NSAIDS

Protocol outcome 1: Stone passage
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: spontaneous stone passage at 4 weeks ; Group 1: 23/29, Group 2: 15/28
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, height, weight, stone size or stone location ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 2: Time to stone passage
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: time to expulsion at 4 weeks ; Group 1: mean 6.31 days (SD 0.88); n=29,
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, height, weight, stone size or stone location ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 3: Adverse events
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: hypotension or other side effects requiring cessation of medication at 4 weeks ; Group 1: 0/29, Group 2: 0/28
Risk of bias: All domain - ; Indirectness of outcome: No indirectness

Protocol outcome 4: Pain intensity
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: pain episodes at 4 weeks ; Group 1: mean 1.72 (SD 0.88); n=29,
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, height, weight, stone size or stone location ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 5: Analgesic use

- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: analgesic requirement at 4 weeks ; Group 1: mean 129.31 mg (SD 17.81); n=29,
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, height, weight, stone size or stone location ; Group 1 Number missing: ; Group 2 Number missing:

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: TERAZOSIN versus NSAIDS

Protocol outcome 1: Stone passage
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: spontaneous stone passage at 4 weeks ; Group 1: 22/28, Group 2: 15/28
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, height, weight, stone size or stone location ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 2: Time to stone passage
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: time to expulsion at 4 weeks ; Group 1: mean 5.75 days (SD 0.88); n=28,
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, height, weight, stone size or stone location ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 3: Adverse events
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: hypotension or other side effects requiring cessation of medication at 4 weeks ; Group 1: 0/28, Group 2: 0/28
Risk of bias: All domain - ; Indirectness of outcome: No indirectness

Protocol outcome 4: Pain intensity
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: pain episodes at 4 weeks ; Group 1: mean 1.57 (SD 0.23); n=28,
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, height, weight, stone size or stone location ; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 5: Analgesic use
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: analgesic requirement at 4 weeks ; Group 1: mean 117.85 mg (SD 17.85); n=28,
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, height, weight, stone size or stone location ; Group 1 Number missing: ; Group 2 Number missing:

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: DOXAZOSIN versus NSAIDS

Protocol outcome 1: Stone passage - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: spontaneous stone passage at 4 weeks ; Group 1: 22/29, Group 2: 15/28 Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, height, weight, stone size or stone location ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 2: Time to stone passage - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: time to expulsion at 4 weeks ; Group 1: mean 5.93 days (SD 0.59); n=29, Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, height, weight, stone size or stone location ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 3: Adverse events - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: hypotension or other side effects requiring cessation of medication at 4 weeks ; Group 1: 0/29, Group 2: 0/28 Risk of bias: All domain - ; Indirectness of outcome: No indirectness Protocol outcome 4: Pain intensity - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: pain episodes at 4 weeks ; Group 1: mean 1.67 (SD 0.17); n=29, Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, height, weight, stone size or stone location ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 5: Analgesic use - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: analgesic requirement at 4 weeks ; Group 1: mean 118.68 mg (SD 16.21); n=29, Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, height, weight, stone size or stone location ; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Quality of life; Hospitalisation/ Use of healthcare services

Study	Yuksel 2015[219]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=70)
Countries and setting	Conducted in Turkey; Setting: Department of Urology outpatient clinic, single centre
Line of therapy	1st line
Duration of study	Intervention time: 3 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: urinary system x-ray, urinary system ultrasonography and low-dose abdominal tomography if necessary
Stratum	Adults (≥16 years), ureteric stone <1 cm
Subgroup analysis within study	Not applicable
Inclusion criteria	detection of distal ureteral stone 4-10mm
Exclusion criteria	age <18 or >65 years; multiple stones; grade 3 or 4 hydronephrosis; solitary or transplanted kidney; urinary tract infection; recurrent and persistent renal colic in reaction to analgesic administration; renal failure; allergic reaction to NSAID or alpha-blocker; hypotension; current intake of alpha-blockers, calcium channel blockers or steroids
Recruitment/selection of patients	not reported
Age, gender and ethnicity	Age - Mean (SD): Silodosin group: 35.31 (11.55), control group: 35.23 (11.2). Gender (M:F): 39/31. Ethnicity: not reported
Further population details	1. Kidney pole: Not applicable 2. Neuropathic/ cerebral-palsy /immobility: Not applicable 3. Obesity /skin-to-stone distance: Not applicable 4. Pregnant women: Not stated / Unclear 5. Stone composition/hounsfield units: Not applicable 6. Ureteric stone: Lower ureteric stones
Indirectness of population	No indirectness
Interventions	(n=35) Intervention 1: Alpha blockers - Silodosin. Silodosin 4mg daily. Duration up to 3 weeks. Concurrent medication/care: Diclofenac 75mg daily as necessary, advice to remain active and drink at least 2 L of water daily. Indirectness: No indirectness (n=35) Intervention 2: Pain management only - NSAIDs. Diclofenac 75mg daily as necessary. Duration up to 3 weeks. Concurrent medication/care: advice to remain active and drink at least 2 L of water daily. Indirectness: No indirectness
Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: SILODOSIN versus NSAIDS	

Protocol outcome 1: Stone passage - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: stone expulsion at 3 weeks ; Group 1: 32/35, Group 2: 25/35 Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex or stone size ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 2: Time to stone passage - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: stone expulsion duration at 3 weeks ; Group 1: mean 8.03 days (SD 4.99); n=35, Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex or stone size ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 3: Pain intensity - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: renal colic episodes at 3 weeks ; Group 1: mean 1.17 (SD 1.44); n=35, Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex or stone size ; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 4: Analgesic use - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: analgesic dosage at 3 weeks ; Group 1: mean 113.57 mg (SD 130.38); n=35, Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex or stone size ; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Quality of life; Adverse events; Hospitalisation/ Use of healthcare services

Study	Zhang 2009[222]
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=314)
Countries and setting	Conducted in China; Setting: Department of Urology, single centre
Line of therapy	1st line
Duration of study	Intervention time: 4 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: plain abdominal X-rays, urinary ultrasonography and helical computed tomography
Stratum	Adults (≥16 years), ureteric stone <1 cm
Subgroup analysis within study	Not applicable
Inclusion criteria	distal ureteral stones
Exclusion criteria	history of urinary system stone; previous surgery on urinary tract; multiple stones; nonopaque stones; urinary tract infection; severe hydronephrosis; solitary kidney; diabetes; peptic ulcers; hypotension or hypertension treated with alpha-adrenoceptor blocker or calcium-antagonists; severe obesity; kidney failure; pregnancy
Recruitment/selection of patients	not reported
Age, gender and ethnicity	Age - Mean (SD): Tamsulosin group: 34.6 (11.4), Nifedipine group: 36.3 (9.7). Gender (M:F): 199/94. Ethnicity: not reported
Further population details	1. Kidney pole: Not applicable 2. Neuropathic/ cerebral-palsy /immobility: Not applicable 3. Obesity /skin-to-stone distance: Not applicable 4. Pregnant women: Non-pregnant 5. Stone composition/hounsfield units: Not applicable 6. Ureteric stone: Lower ureteric stones
Indirectness of population	No indirectness
Interventions	(n=102) Intervention 1: Alpha blockers - Tamsulosin. Tamsulosin 0.4mg daily. Duration up to 4 weeks. Concurrent medication/care: 2.5 L hydration daily, Levofloxacin 0.1g twice daily for the first 7 days and Diclofenac 75mg injection daily if needed. Indirectness: No indirectness (n=97) Intervention 2: Calcium channel blockers - Nifedipine. Nifedipine 30mg 3 times daily. Duration up to 4 weeks. Concurrent medication/care: 2.5 L hydration daily, Levofloxacin 0.1g twice daily for the first 7 days and Diclofenac 75mg injection daily if needed. Indirectness: No indirectness
Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: TAMSULOSIN versus NIFEDIPINE	

Protocol outcome 1: Stone passage - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: stone free rate at 4 weeks ; Group 1: 75/102, Group 2: 66/97 Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex or stone size ; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Quality of life; Time to stone passage; Adverse events; Pain intensity; Analgesic use; Hospitalisation/ Use of healthcare services

Study	**Zhou 2011[224]**
Study type	RCT (Patient randomised; Parallel)
Number of studies (number of participants)	1 (n=131)
Countries and setting	Conducted in China; Setting: Department of Urology, single centre
Line of therapy	1st line
Duration of study	Intervention time: 2 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: abdominal, ultrasonography and plain abdominal X-ray (kidney-ureter-bladder, IVU or unenhanced CT)
Stratum	Adults (≥16 years), ureteric stone <1 cm
Subgroup analysis within study	Not applicable
Inclusion criteria	distal ureteral stones ≤9mm to >4mm
Exclusion criteria	multiple stones; severe incarcerated stones; history of distal ureteral surgery; history of stone expulsion; renal colic for more than 24 hours; urinary tract infection; severe hydronephrosis; voiding dysfunction; hypotension; cardiovascular and cerebrovascular diseases; hepatic and renal dysfunction; pregnancy; diabetes; history of hypersensitivity to Naftopidil; subjects receiving treatment with cardiovascular drugs, alpha receptor antagonists or calcium antagonists
Recruitment/selection of patients	not reported
Age, gender and ethnicity	Age - Mean (SD): Naftopidil group: 33.73 (8.84), Tamsulosin group: 34.42 (8.64), control group: 34.79 (9.63). Gender (M:F): 79/52. Ethnicity: not reported
Further population details	1. Kidney pole: Not applicable 2. Neuropathic/ cerebral-palsy /immobility: Not applicable 3. Obesity /skin-to-stone distance: Not applicable 4. Pregnant women: Non-pregnant 5. Stone composition/hounsfield units: Not applicable 6. Ureteric stone: Lower ureteric stones

Indirectness of population	No indirectness
Interventions	(n=43) Intervention 1: Alpha blockers - Naftopidil . Naftopidil 10mg daily. Duration up to 2 weeks. Concurrent medication/care: instruction to drink at least 2 L of fluids daily and an Indomethacin suppository recommended for use during pain episodes. Indirectness: No indirectness (n=45) Intervention 2: Alpha blockers - Tamsulosin. Tamsulosin 0.4mg daily. Duration up to 2 weeks. Concurrent medication/care: instruction to drink at least 2 L of fluids daily and Indomethacin suppository recommended for routine use during pain episodes. Indirectness: No indirectness (n=43) Intervention 3: No treatment - Watch and wait. Watchful waiting. Duration up to 2 weeks. Concurrent medication/care: instruction to drink at least 2 L of fluids daily and Indomethacin suppository recommended for routine use during pain episodes. Indirectness: No indirectness
Funding	Funding not stated

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: NAFTOPIDIL versus WATCH AND WAIT

Protocol outcome 1: Stone passage
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: expulsion rate at 2 weeks ; Group 1: 31/43, Group 2: 13/43
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, stone location (left/right) or stone size; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 2: Time to stone passage
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: expulsion time at 2 weeks ; Group 1: mean 7.6 days (SD 2.26); n=43,
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, stone location (left/right) or stone size; Group 1 Number missing: ; Group 2 Number missing:

Protocol outcome 3: Pain intensity
- Actual outcome for Adults (≥16 years), ureteric stone <1 cm: pain episodes at 2 weeks ; Group 1: mean 1.3 (SD 1.18); n=43,
Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, stone location (left/right) or stone size; Group 1 Number missing: ; Group 2 Number missing:

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: TAMSULOSIN versus WATCH AND WAIT

Protocol outcome 1: Stone passage - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: expulsion rate at 2 weeks ; Group 1: 37/45, Group 2: 13/43 Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, stone location (left/right) or stone size; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 2: Time to stone passage - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: expulsion time at 2 weeks ; Group 1: mean 7.7 days (SD 1.94); n=45, Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, stone location (left/right) or stone size; Group 1 Number missing: ; Group 2 Number missing: Protocol outcome 3: Pain intensity - Actual outcome for Adults (≥16 years), ureteric stone <1 cm: pain episodes at 2 weeks ; Group 1: mean 1.2 (SD 1.65); n=45, Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - High, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no significant difference in age, sex, stone location (left/right) or stone size; Group 1 Number missing: ; Group 2 Number missing:	
Protocol outcomes not reported by the study	Quality of life; Adverse events; Analgesic use; Hospitalisation/ Use of healthcare services

Appendix E: Forest plots

E.1 Distal ureteric stones <10mm in adults

E.1.1 Alpha blockers versus placebo

Figure 2: Time to stone passage (days)

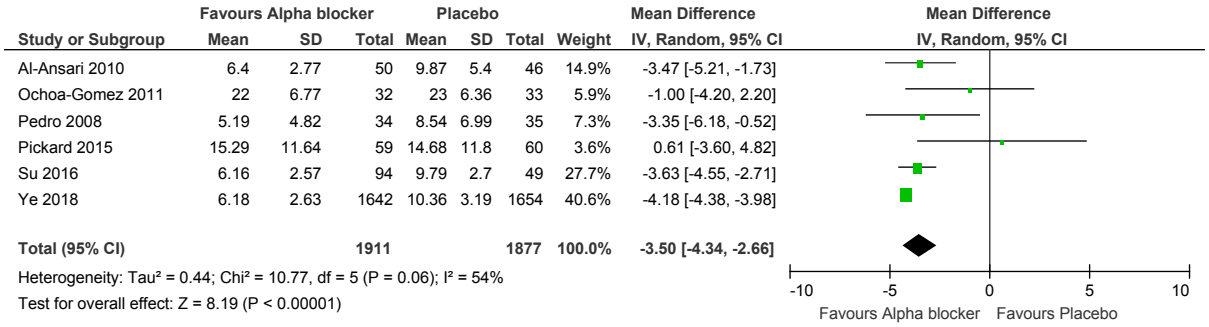


Figure 3: Time to stone passage

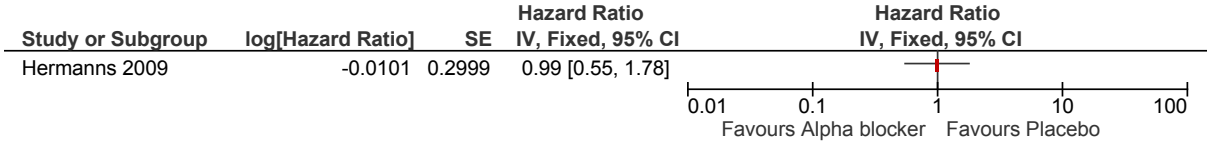


Figure 4: Stone passage

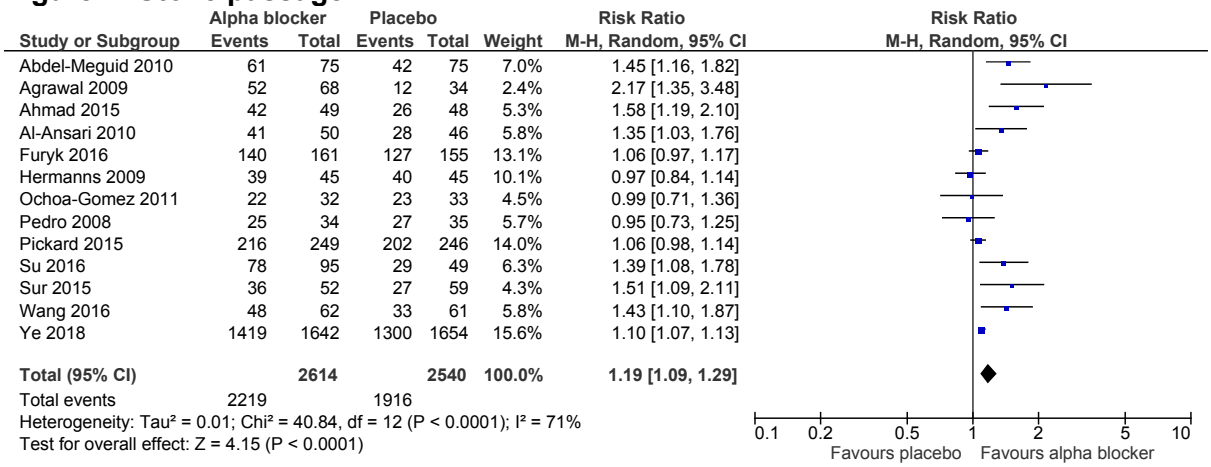


Figure 5: Hospitalisation

Study or Subgroup	Alpha blocker Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Ahmad 2015	0	49	1	48	5.7%	0.33 [0.01, 7.83]
Furyk 2016	20	198	23	195	86.8%	0.86 [0.49, 1.51]
Hermanns 2009	6	45	2	45	7.5%	3.00 [0.64, 14.08]
Total (95% CI)		**292**		**288**	**100.0%**	**0.99 [0.59, 1.64]**
Total events	26		26			

Heterogeneity: Chi² = 2.69, df = 2 (P = 0.26); I² = 26%
Test for overall effect: Z = 0.05 (P = 0.96)

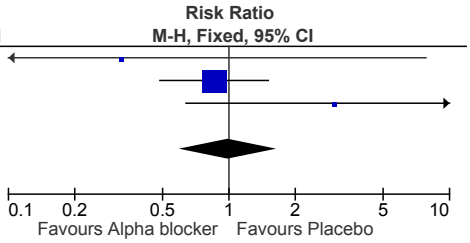


Figure 6: Hospitalisation (excess admission days)

Study or Subgroup	Alpha blocker Mean	SD	Total	Placebo Mean	SD	Total	Mean Difference IV, Fixed, 95% CI
Pickard 2015	0.15	0.59	247	0.18	0.97	246	-0.03 [-0.17, 0.11]

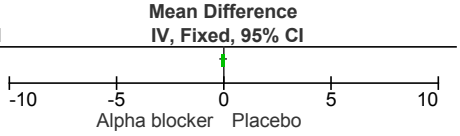


Figure 7: Use of healthcare services (representation to ED)

Study or Subgroup	Alpha blocker Events	Total	Placebo Events	Total	Risk Ratio M-H, Fixed, 95% CI
Furyk 2016	31	198	35	195	0.87 [0.56, 1.36]

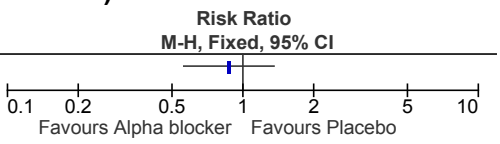


Figure 8: Use of healthcare services (visits)

Study or Subgroup	Alpha blocker Mean	SD	Total	Placebo Mean	SD	Total	Mean Difference IV, Fixed, 95% CI
1.2.1 Doctor visits							
Pickard 2015	0.16	0.63	224	0.09	0.52	215	0.07 [-0.04, 0.18]
1.2.2 Nurse visits							
Pickard 2015	0.01	0.13	224	0.02	0.18	215	-0.01 [-0.04, 0.02]
1.2.3 Outpatient visits							
Pickard 2015	0.66	0.69	289	0.67	0.66	246	-0.01 [-0.12, 0.10]

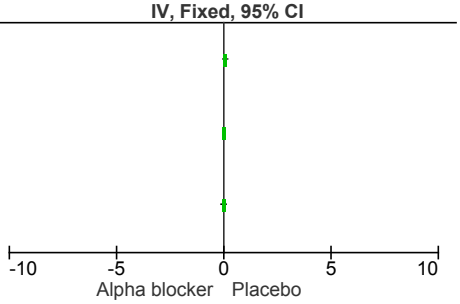


Figure 9: Quality of life (SF36)

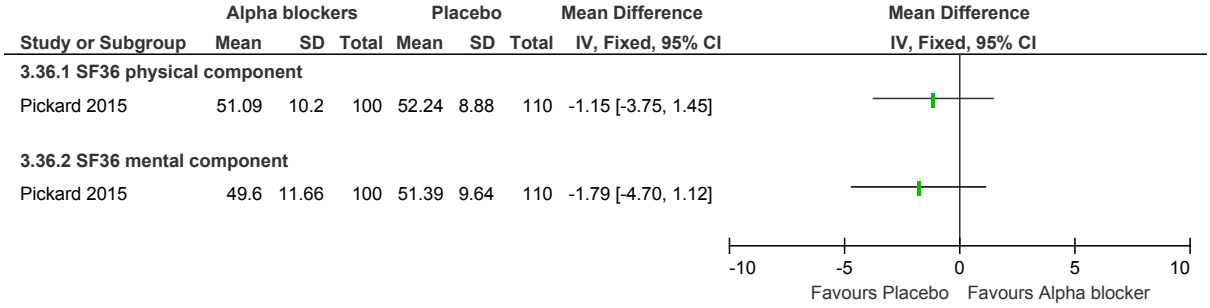


Figure 10: Quality of life (EQ5D)

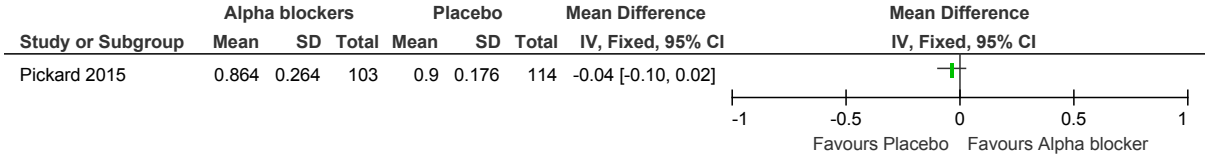


Figure 11: Adverse events (discontinuation due to adverse events)

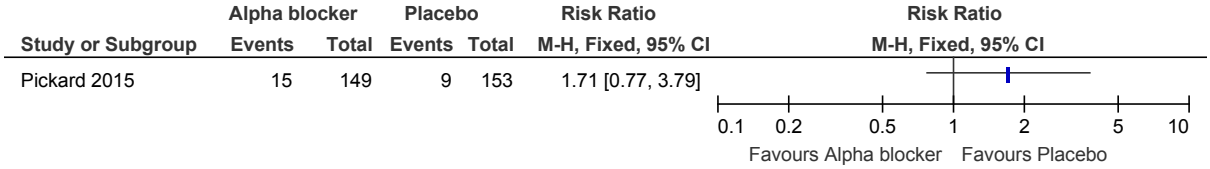


Figure 12: Adverse events (unspecified)

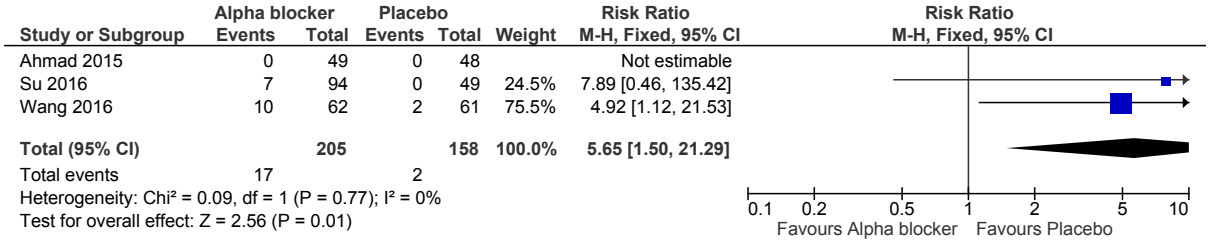


Figure 13: Adverse events (retrograde ejaculation)

Study or Subgroup	Alpha blocker Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Agrawal 2009	3	68	0	34	1.3%	3.55 [0.19, 66.84]
Al-Ansari 2010	1	32	0	35	0.9%	3.27 [0.14, 77.57]
Hermanns 2009	2	39	0	36	1.0%	4.63 [0.23, 93.20]
Ochoa-Gomez 2011	2	15	0	21	0.8%	6.88 [0.35, 133.64]
Sur 2015	11	72	1	80	1.9%	12.22 [1.62, 92.34]
Ye 2018	67	1642	48	1654	94.0%	1.41 [0.98, 2.02]
Total (95% CI)		**1868**		**1860**	**100.0%**	**1.73 [1.23, 2.43]**
Total events	86		49			

Heterogeneity: Chi² = 6.47, df = 5 (P = 0.26); I² = 23%
Test for overall effect: Z = 3.17 (P = 0.002)

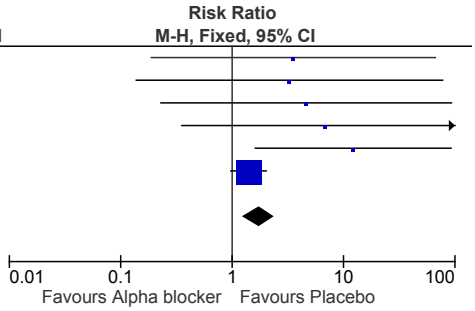


Figure 14: Adverse events (dizziness)

Study or Subgroup	Alpha blocker Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Agrawal 2009	9	68	2	34	4.5%	2.25 [0.51, 9.84]
Al-Ansari 2010	2	50	2	46	3.5%	0.92 [0.14, 6.27]
Hermanns 2009	0	45	1	45	2.5%	0.33 [0.01, 7.97]
Ochoa-Gomez 2011	2	32	0	33	0.8%	5.15 [0.26, 103.30]
Pedro 2008	4	34	0	35	0.8%	9.26 [0.52, 165.65]
Sur 2015	8	119	2	120	3.4%	4.03 [0.87, 18.60]
Ye 2018	52	1642	50	1654	84.4%	1.05 [0.71, 1.54]
Total (95% CI)		**1990**		**1967**	**100.0%**	**1.28 [0.92, 1.79]**
Total events	77		57			

Heterogeneity: Chi² = 7.23, df = 6 (P = 0.30); I² = 17%
Test for overall effect: Z = 1.45 (P = 0.15)

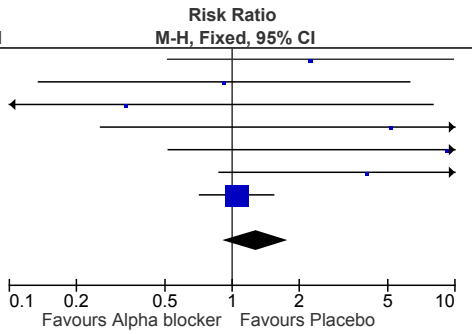


Figure 15: Adverse events (headache)

Study or Subgroup	Alpha blocker Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Agrawal 2009	8	68	1	34	2.7%	4.00 [0.52, 30.69]
Al-Ansari 2010	2	50	2	46	4.2%	0.92 [0.14, 6.27]
Sur 2015	4	119	0	120	1.0%	9.07 [0.49, 166.72]
Ye 2018	41	1642	46	1654	92.1%	0.90 [0.59, 1.36]
Total (95% CI)		**1879**		**1854**	**100.0%**	**1.06 [0.72, 1.56]**
Total events	55		49			

Heterogeneity: Chi² = 4.37, df = 3 (P = 0.22); I² = 31%
Test for overall effect: Z = 0.32 (P = 0.75)

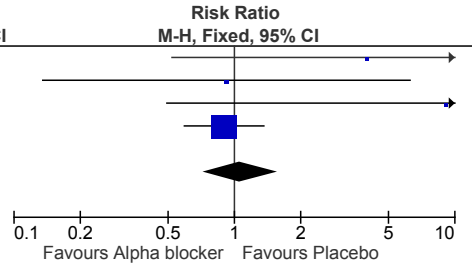


Figure 16: Adverse events (hypotension)

Study or Subgroup	Favours Alpha blocker Events	Total	Placebo Events	Total	Weight	Peto Odds Ratio Peto, Fixed, 95% CI
Agrawal 2009	0	68	0	34		Not estimable
Al-Ansari 2010	1	50	0	46	100.0%	6.82 [0.13, 344.93]
Total (95% CI)		**118**		**80**	**100.0%**	**6.82 [0.13, 344.93]**
Total events	1		0			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.96 (P = 0.34)

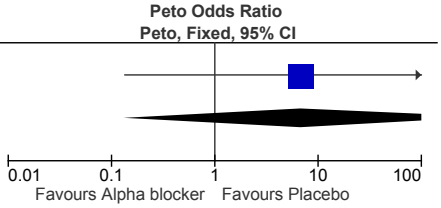


Figure 17: Pain intensity (VAS score)

Study or Subgroup	Alpha blocker Mean	SD	Total	Placebo Mean	SD	Total	Mean Difference IV, Fixed, 95% CI
Pickard 2015	1.01	1	137	1.11	2.17	142	-0.10 [-0.49, 0.29]

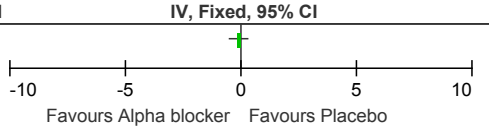


Figure 18: Pain intensity (EQ5D - no pain/discomfort)

Study or Subgroup	Alpha blockers Events	Total	Placebo Events	Total	Risk Ratio M-H, Fixed, 95% CI
Pickard 2015	77	104	89	115	0.96 [0.82, 1.11]

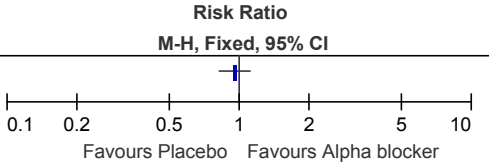


Figure 19: Pain intensity (EQ5D - moderate pain/discomfort)

Study or Subgroup	Alpha blockers Events	Total	Placebo Events	Total	Risk Ratio M-H, Fixed, 95% CI
Pickard 2015	22	104	25	115	0.97 [0.59, 1.62]

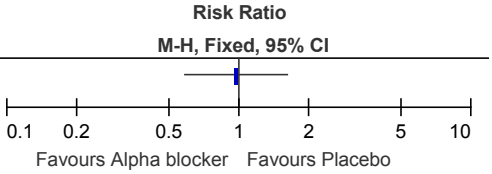


Figure 20: Pain intensity (EQ5D - extreme pain/discomfort)

Study or Subgroup	Alpha blockers Events	Total	Placebo Events	Total	Risk Ratio M-H, Fixed, 95% CI
Pickard 2015	5	104	1	115	5.53 [0.66, 46.55]

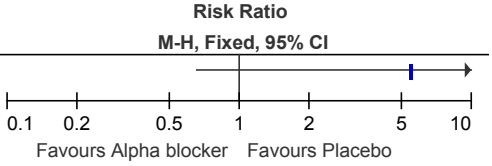


Figure 21: Pain intensity (people experiencing pain episodes)

Study or Subgroup	Alpha blockers Events	Total	Placebo Events	Total	Risk Ratio M-H, Fixed, 95% CI
Abdel-Meguid 2010	20	75	58	75	0.34 [0.23, 0.51]

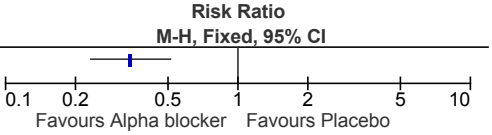


Figure 22: Pain intensity (pain episodes)

Study or Subgroup	Alpha blockers Mean	SD	Total	Placebo Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Al-Ansari 2010	1.6	1.3	50	2.3	1.4	46	43.4%	-0.70 [-1.24, -0.16]
Wang 2016	2.39	1.3	62	2.75	1.38	61	56.6%	-0.36 [-0.83, 0.11]
Total (95% CI)			**112**			**107**	**100.0%**	**-0.51 [-0.86, -0.15]**

Heterogeneity: Chi² = 0.86, df = 1 (P = 0.35); I² = 0%
Test for overall effect: Z = 2.79 (P = 0.005)

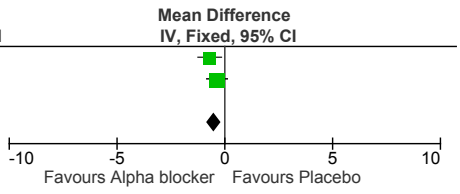


Figure 23: Pain intensity (pain score >0) at 1 week

Study or Subgroup	Alpha blocker Events	Total	Placebo Events	Total	Risk Ratio M-H, Fixed, 95% CI
Furyk 2016	142	185	143	182	0.98 [0.88, 1.09]

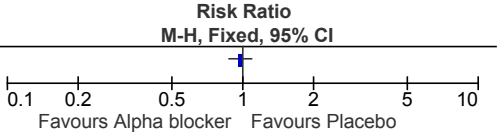


Figure 24: Pain intensity (pain score >0) at 2 weeks

Study or Subgroup	Alpha blocker Events	Total	Placebo Events	Total	Risk Ratio M-H, Fixed, 95% CI
Furyk 2016	60	176	58	177	1.04 [0.77, 1.40]

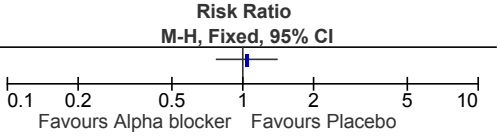


Figure 25: Pain intensity (pain score >0) at 3 weeks

Study or Subgroup	Alpha blockers Events	Total	Placebo Events	Total	Risk Ratio M-H, Fixed, 95% CI
Furyk 2016	34	170	37	173	0.94 [0.62, 1.42]

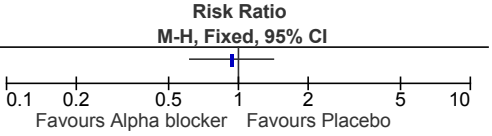


Figure 26: Pain intensity (pain score >0) at 4 weeks

Study or Subgroup	Alpha blockers Events	Total	Placebo Events	Total	Risk Ratio M-H, Fixed, 95% CI
Furyk 2016	26	173	28	174	0.93 [0.57, 1.53]

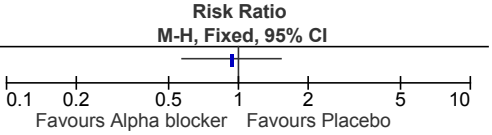


Figure 27: Analgesic use (number of people)

Study or Subgroup	Alpha blockers Events	Total	Placebo Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Ahmad 2015	9	49	19	48	31.6%	0.46 [0.23, 0.92]
Pickard 2015	75	147	82	153	34.6%	0.95 [0.77, 1.18]
Ye 2018	31	1642	155	1654	33.8%	0.20 [0.14, 0.29]
Total (95% CI)		**1838**		**1855**	**100.0%**	**0.45 [0.13, 1.54]**
Total events	115		256			

Heterogeneity: Tau² = 1.14; Chi² = 61.78, df = 2 (P < 0.00001); I² = 97%
Test for overall effect: Z = 1.27 (P = 0.20)

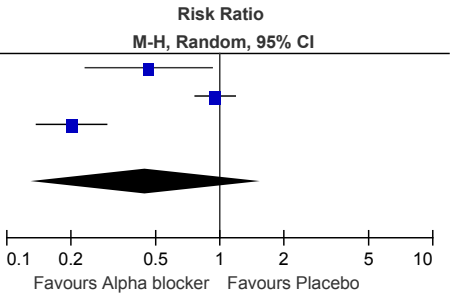


Figure 28: Analgesic use (number of times)

Study or Subgroup	Alpha blockers Mean	SD	Total	Placebo Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Al-Ansari 2010	0.9	0.93	50	1.8	1.3	46	98.8%	-0.90 [-1.36, -0.44]
Pedro 2008	8.63	8.58	34	9.41	9.08	35	1.2%	-0.78 [-4.95, 3.39]
Total (95% CI)			**84**			**81**	**100.0%**	**-0.90 [-1.35, -0.45]**

Heterogeneity: Chi² = 0.00, df = 1 (P = 0.96); I² = 0%
Test for overall effect: Z = 3.89 (P = 0.0001)

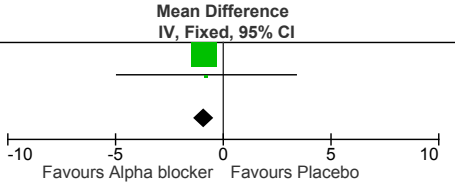


Figure 29: **Analgesic use (number of days of medication use)**

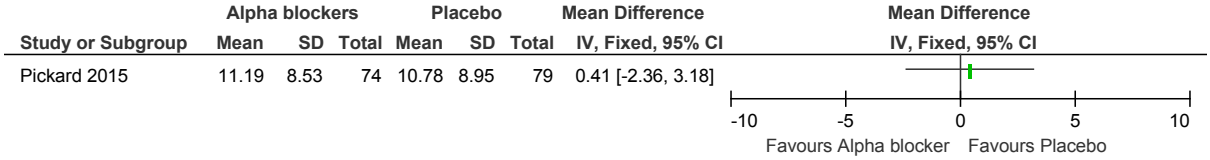
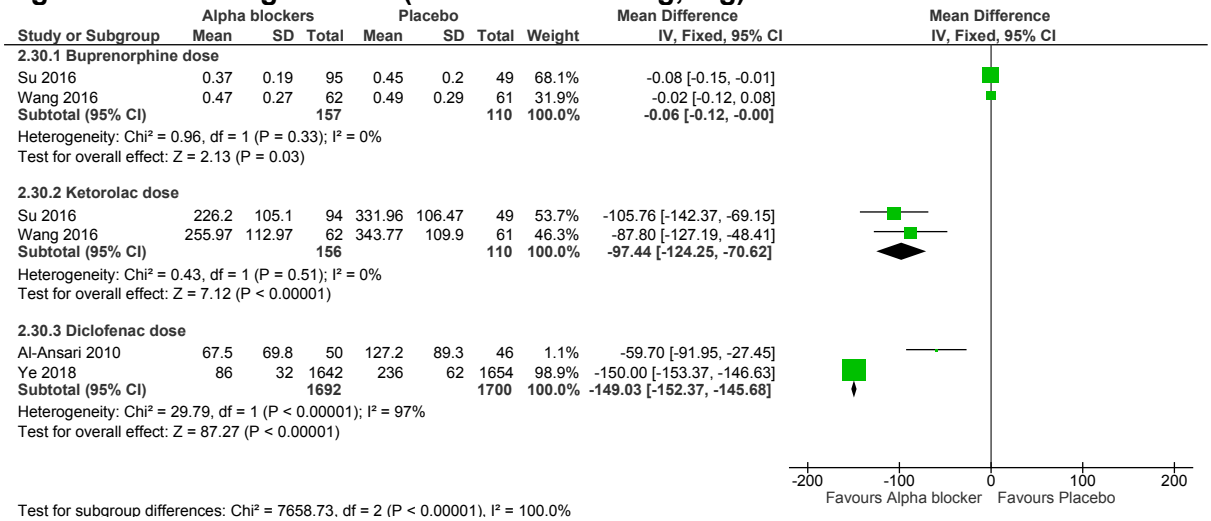


Figure 30: Analgesic use (mean dose of drug; mg)



E.1.2 Alpha blockers versus no treatment (pain management only)

Figure 31: Time to stone passage (days)

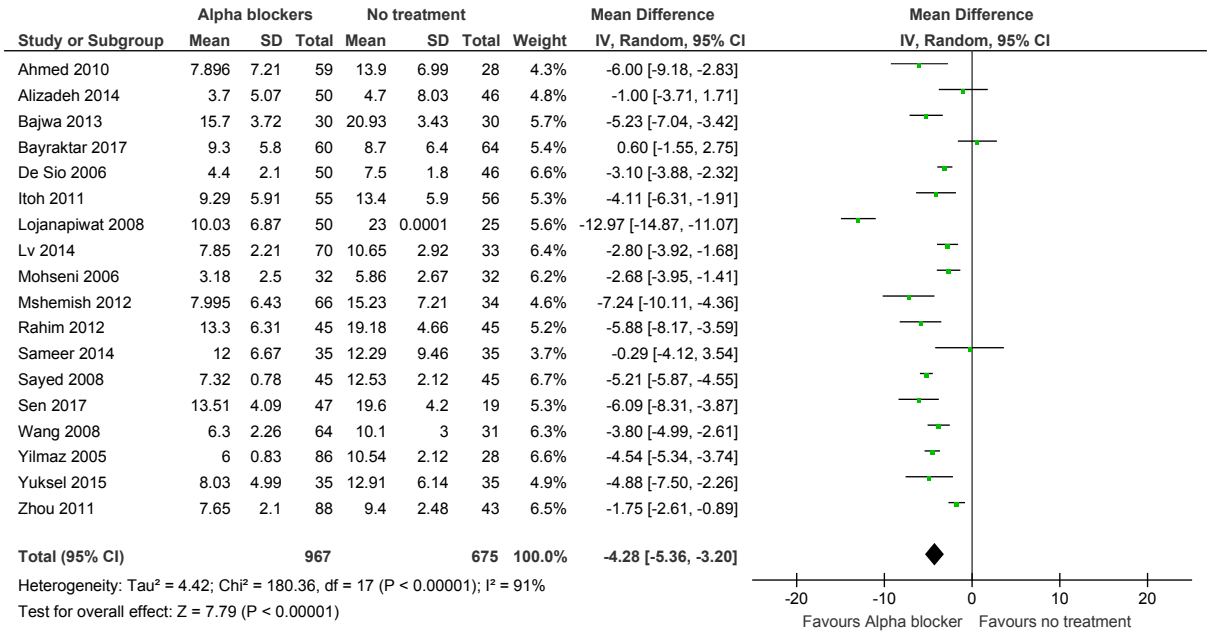


Figure 32: Stone passage

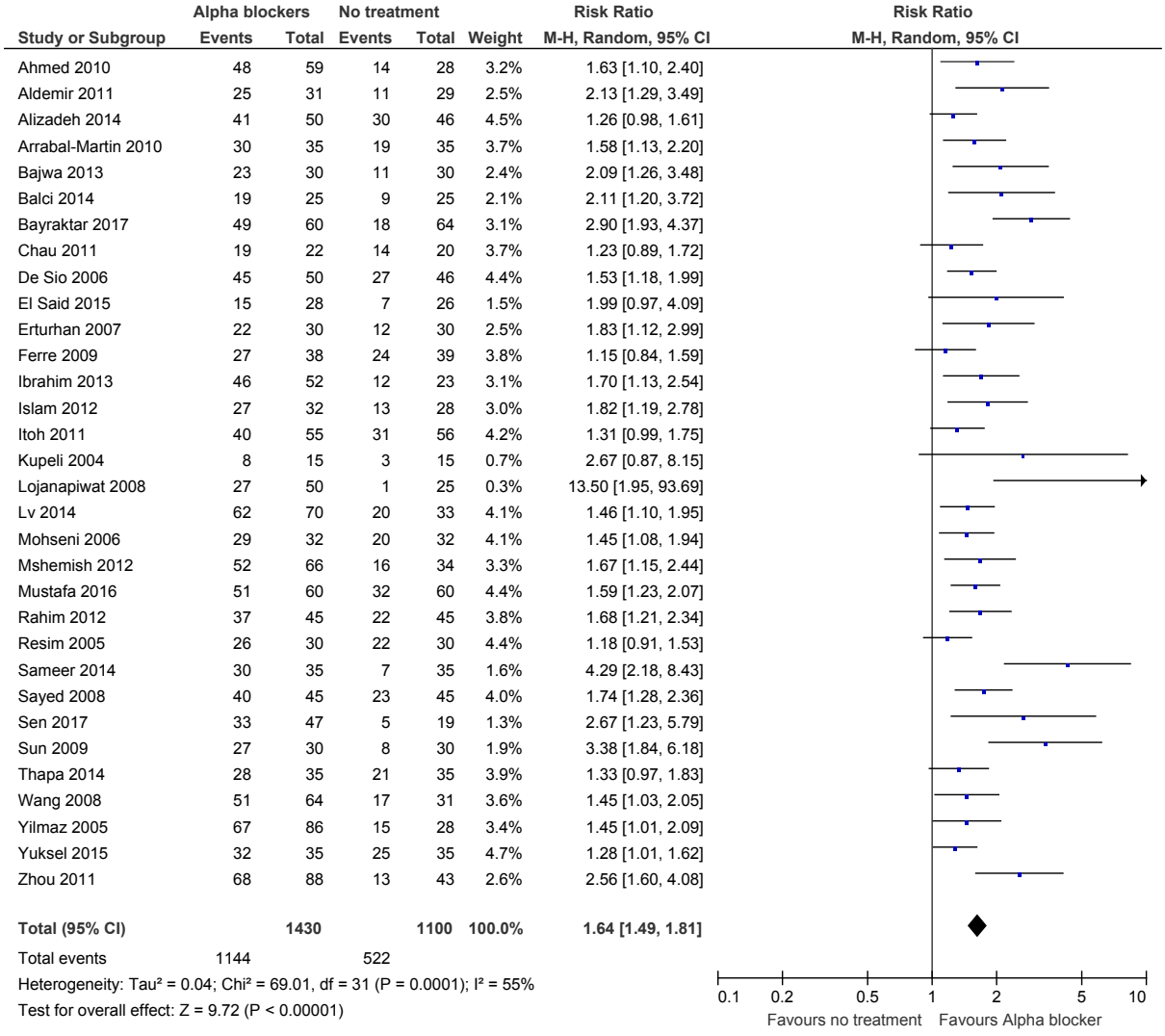


Figure 33: Hospitalisation

Study or Subgroup	Alpha blockers Events	Total	No treatment Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Ahmed 2010	3	59	4	28	10.1%	0.36 [0.09, 1.48]
De Sio 2006	5	50	11	46	21.4%	0.42 [0.16, 1.11]
El Said 2015	0	28	3	26	6.8%	0.13 [0.01, 2.46]
Erturhan 2007	1	30	2	30	3.7%	0.50 [0.05, 5.22]
Islam 2012	0	32	0	28		Not estimable
Mshemish 2012	4	66	3	34	7.4%	0.69 [0.16, 2.90]
Sameer 2014	5	35	27	35	50.5%	0.19 [0.08, 0.43]
Sun 2009	0	30	0	30		Not estimable
Total (95% CI)		**330**		**257**	**100.0%**	**0.30 [0.18, 0.49]**
Total events	18		50			

Heterogeneity: Chi² = 3.55, df = 5 (P = 0.62); I² = 0%
Test for overall effect: Z = 4.72 (P < 0.00001)

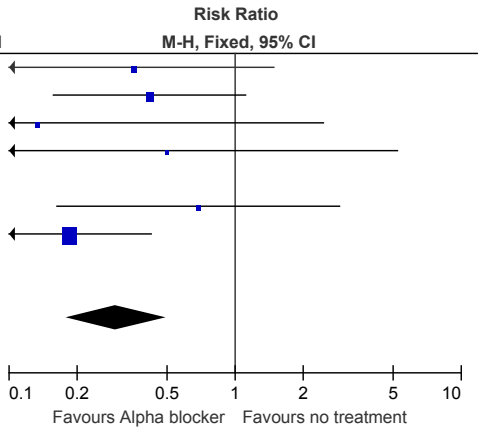


Figure 34: Use of healthcare services (return to ED/primary care visit)

Study or Subgroup	Alpha blockers Events	Total	No treatment Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Ferre 2009	6	38	8	39	100.0%	0.77 [0.29, 2.01]
Mshemish 2012	0	66	0	34		Not estimable
Total (95% CI)		**104**		**73**	**100.0%**	**0.77 [0.29, 2.01]**
Total events	6		8			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.53 (P = 0.59)

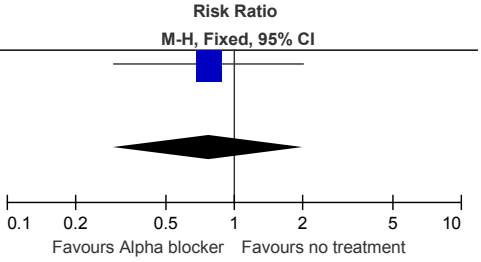


Figure 35: Adverse events (unspecified)

Study or Subgroup	Favours Alpha blocker Events	Total	No treatment Events	Total	Weight	Peto Odds Ratio Peto, Fixed, 95% CI
Aldemir 2011	0	31	0	29		Not estimable
Alizadeh 2014	0	50	0	46		Not estimable
Arrabal-Martin 2010	0	35	0	35		Not estimable
El Said 2015	4	28	0	26	43.0%	7.72 [1.03, 58.18]
Erturhan 2007	0	30	0	30		Not estimable
Ferre 2009	0	38	0	39		Not estimable
Sayed 2008	0	45	0	45		Not estimable
Wang 2008	6	64	0	31	57.0%	4.80 [0.83, 27.71]
Yilmaz 2005	0	86	0	28		Not estimable
Total (95% CI)		**407**		**309**	**100.0%**	**5.89 [1.57, 22.13]**
Total events	10		0			

Heterogeneity: Chi² = 0.12, df = 1 (P = 0.73); I² = 0%
Test for overall effect: Z = 2.62 (P = 0.009)

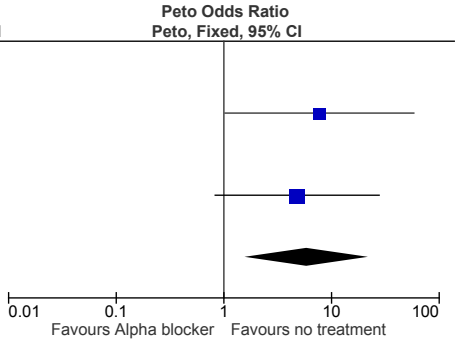


Figure 36: Adverse events (dizziness)

Study or Subgroup	Alpha blockers Events	Total	No treatment Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Balci 2014	2	25	0	25	3.1%	5.00 [0.25, 99.16]
Chau 2011	2	33	0	34	3.0%	5.15 [0.26, 103.33]
De Sio 2006	1	50	0	46	3.2%	2.76 [0.12, 66.22]
Kupeli 2004	1	39	0	39	3.1%	3.00 [0.13, 71.46]
Lv 2014	10	70	8	33	66.4%	0.59 [0.26, 1.35]
Resim 2005	5	30	3	30	18.3%	1.67 [0.44, 6.36]
Sun 2009	2	30	0	30	3.1%	5.00 [0.25, 99.95]
Total (95% CI)		**277**		**237**	**100.0%**	**1.34 [0.74, 2.40]**
Total events	23		11			

Heterogeneity: Chi² = 6.54, df = 6 (P = 0.37); I² = 8%
Test for overall effect: Z = 0.96 (P = 0.33)

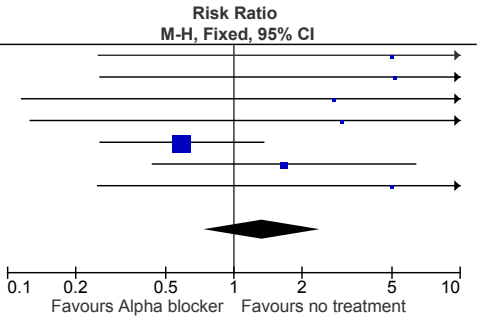


Figure 37: Adverse events (hypotension)

Study or Subgroup	Alpha blockers Events	Total	No treatment Events	Total	Weight	Peto Odds Ratio Peto, Fixed, 95% CI
Ahmed 2010	1	59	0	28	8.8%	4.37 [0.07, 290.00]
De Sio 2006	2	50	0	46	19.9%	6.96 [0.43, 113.22]
Islam 2012	0	32	0	28		Not estimable
Lojanapiwat 2008	0	50	0	25		Not estimable
Mohseni 2006	3	32	0	32	29.3%	7.89 [0.79, 78.69]
Mshemish 2012	2	66	0	34	17.9%	4.62 [0.24, 87.46]
Resim 2005	0	30	0	30		Not estimable
Sen 2017	3	47	0	19	24.0%	4.26 [0.34, 53.92]
Total (95% CI)		**366**		**242**	**100.0%**	**5.72 [1.65, 19.87]**
Total events	11		0			

Heterogeneity: Chi² = 0.18, df = 4 (P = 1.00); I² = 0%
Test for overall effect: Z = 2.75 (P = 0.006)

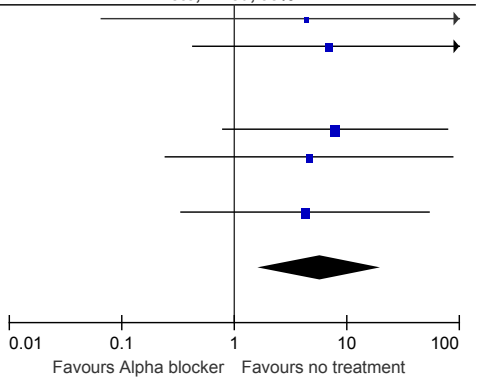


Figure 38: Adverse events (retrograde ejaculation)

Study or Subgroup	Alpha blockers Events	Total	No treatment Events	Total	Weight	Peto Odds Ratio Peto, Fixed, 95% CI
Ahmed 2010	2	59	0	28	38.6%	4.45 [0.22, 87.87]
Lojanapiwat 2008	0	35	0	20		Not estimable
Lv 2014	1	41	0	18	19.0%	4.22 [0.06, 297.59]
Mshemish 2012	1	66	0	34	20.1%	4.55 [0.07, 285.04]
Resim 2005	0	22	1	23	22.4%	0.14 [0.00, 7.13]
Total (95% CI)		**223**		**123**	**100.0%**	**2.05 [0.32, 13.06]**
Total events	4		1			

Heterogeneity: Chi² = 2.30, df = 3 (P = 0.51); I² = 0%
Test for overall effect: Z = 0.76 (P = 0.45)

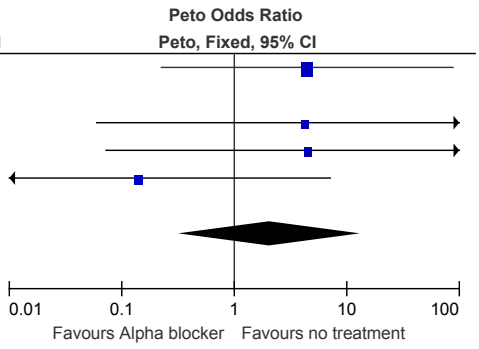


Figure 39: Adverse events (headache)

Study or Subgroup	Alpha blockers Events	Total	No treatment Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Lv 2014	4	70	0	33	14.5%	4.31 [0.24, 77.78]
Resim 2005	4	30	4	30	85.5%	1.00 [0.28, 3.63]
Total (95% CI)		**100**		**63**	**100.0%**	**1.48 [0.47, 4.69]**
Total events	8		4			

Heterogeneity: Chi² = 0.88, df = 1 (P = 0.35); I² = 0%
Test for overall effect: Z = 0.66 (P = 0.51)

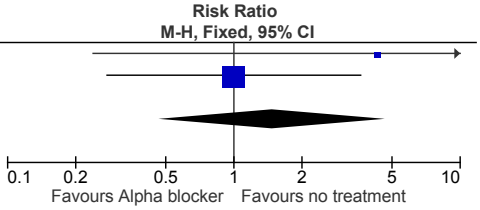


Figure 40: Pain intensity (people experiencing pain episodes)

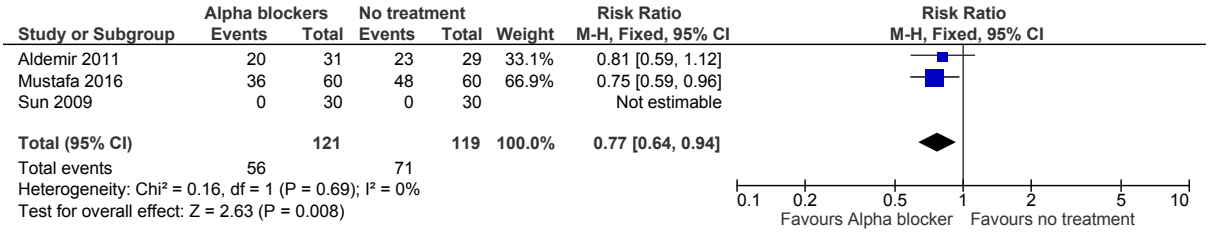


Figure 41: Pain intensity (colicky pain episodes)

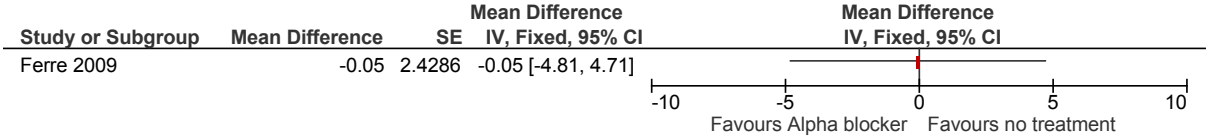


Figure 42: Pain intensity (pain episodes)

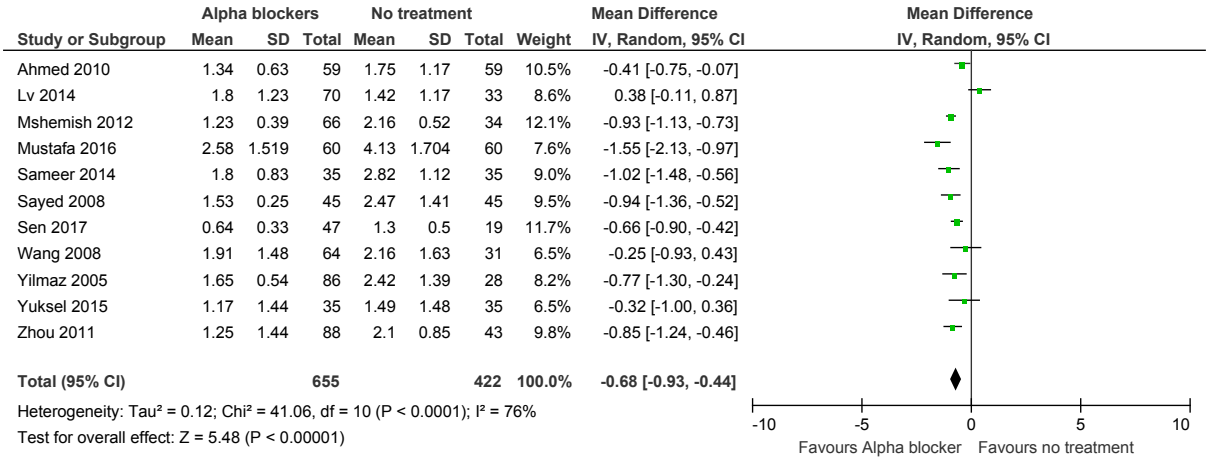


Figure 43: Pain intensity (VAS score) at 3 days

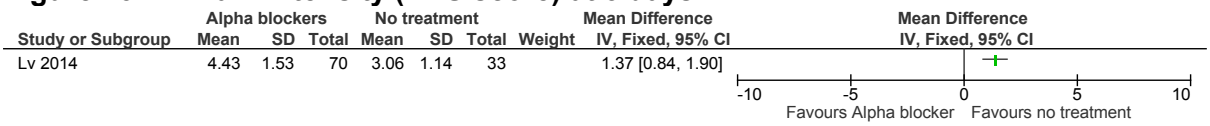


Figure 44: Pain intensity (VAS score) at 7 days

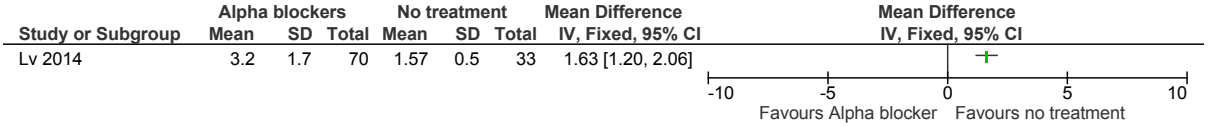


Figure 45: Analgesic use (number of people using analgesia)

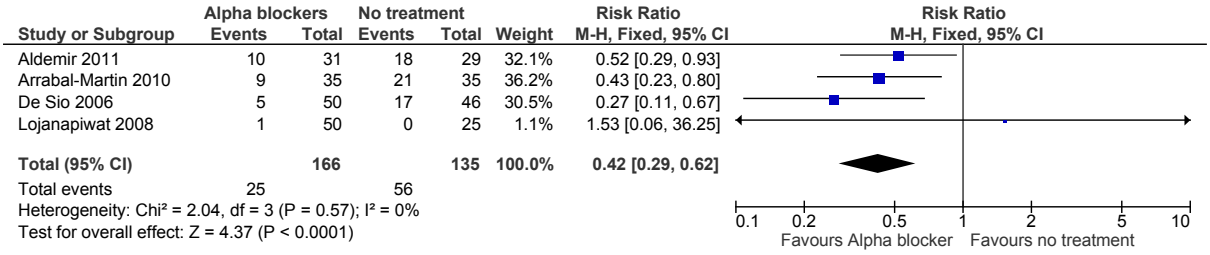


Figure 46: Analgesic use (number of times)

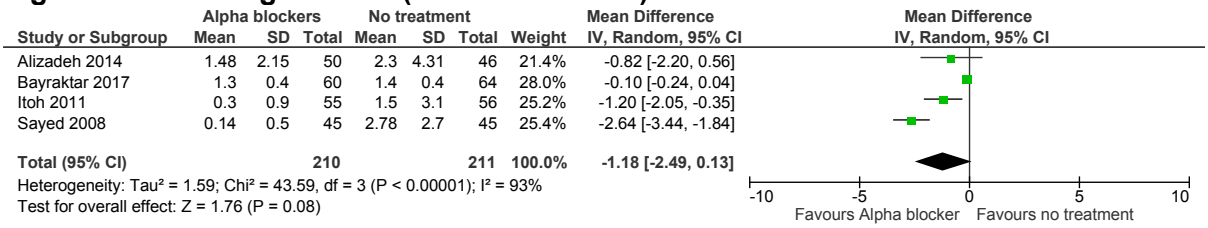


Figure 47: Analgesic use (Diclofenac dose, mg)

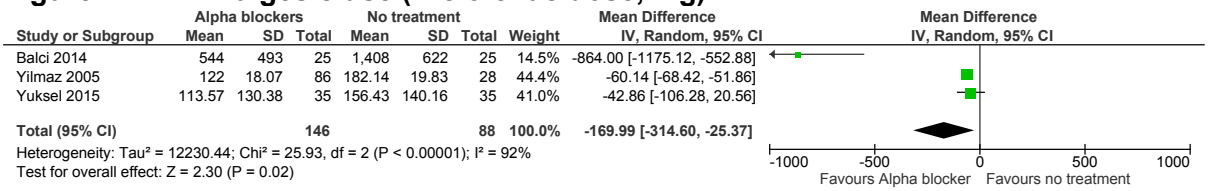


Figure 48: Analgesic use (days)

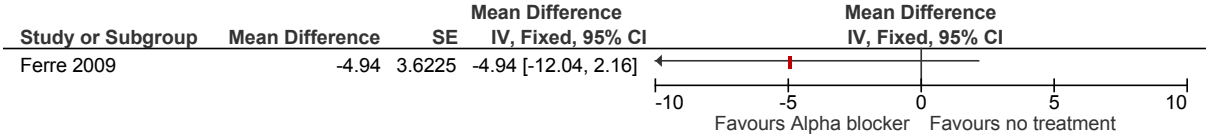


Figure 49: Analgesic use (Pethidine dose, mg)

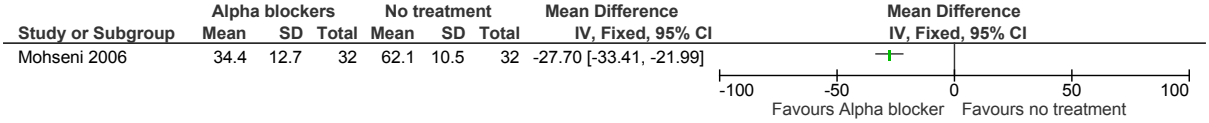


Figure 50: Analgesic use (Ketorolac dose, mg)

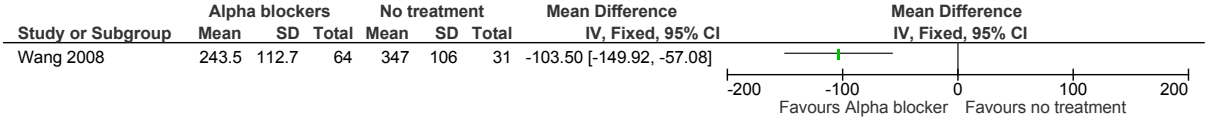
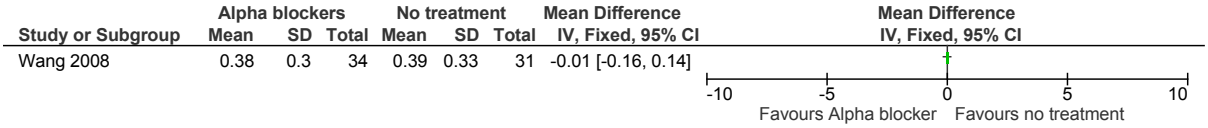


Figure 51: Analgesic use (Buprenorphine dose, mg)



E.1.3 Calcium channel blockers versus placebo

Figure 52: Stone passage

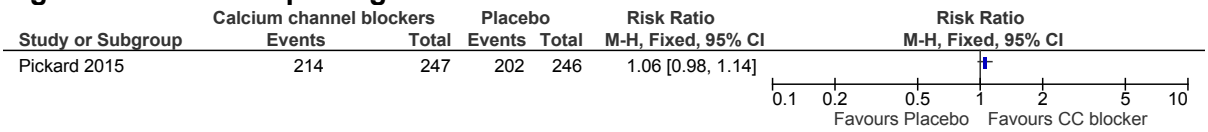


Figure 53: Time to stone passage

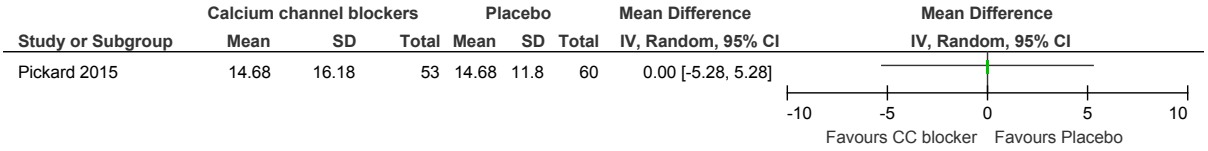


Figure 54: Use of healthcare services (visits)

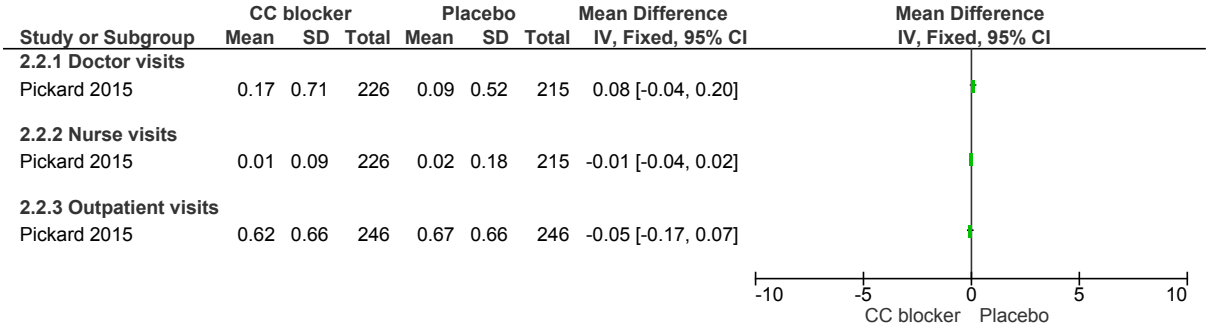


Figure 55: Use of healthcare services (excess admission days)

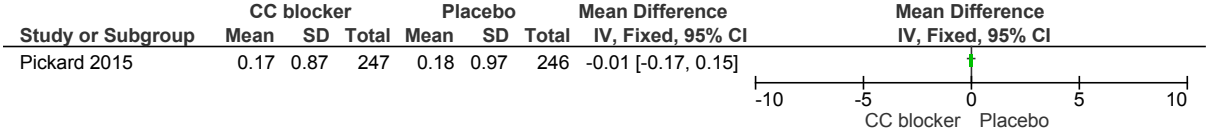


Figure 56: Quality of life (SF36)

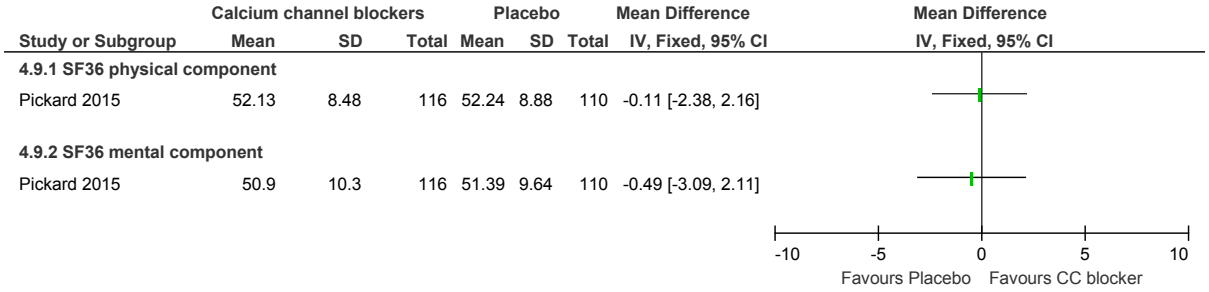


Figure 57: Quality of life (EQ5D)

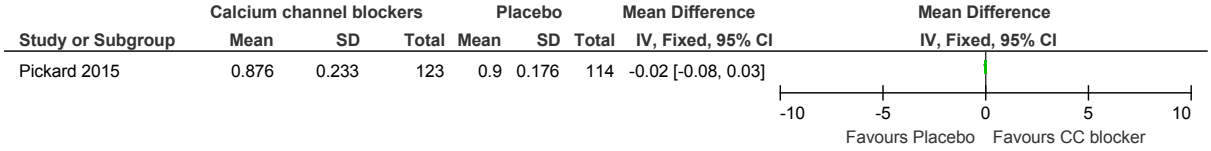


Figure 58: Adverse events (discontinuation due to adverse events)

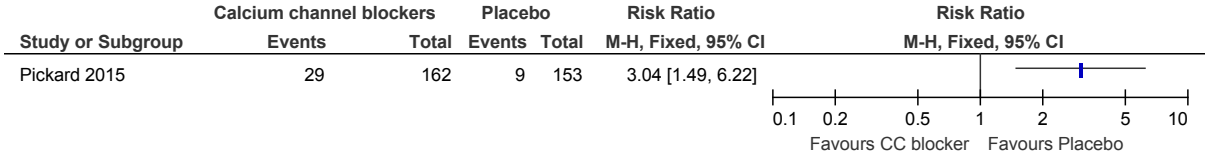


Figure 59: Pain intensity (VAS)

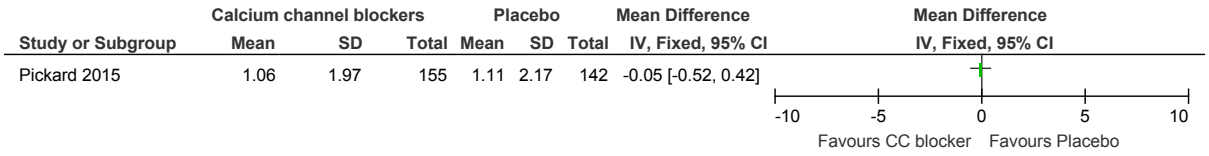


Figure 60: Pain intensity (EQ5D – no pain/discomfort)

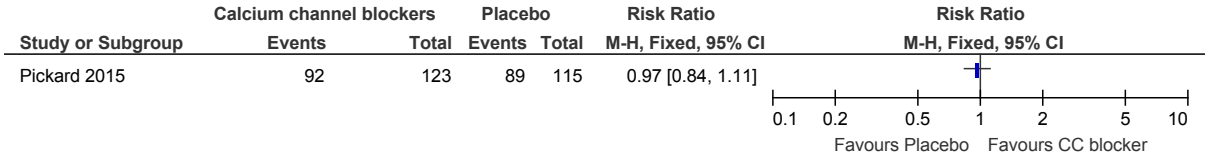


Figure 61: Pain intensity (EQ5D – moderate pain/discomfort)

Figure 62: Pain intensity (EQ5D – extreme pain/discomfort)

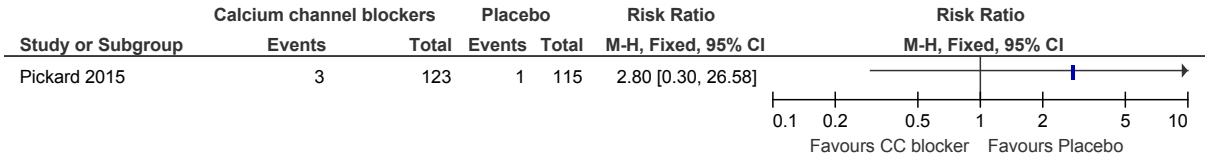


Figure 63: Analgesic use (pain medication use)

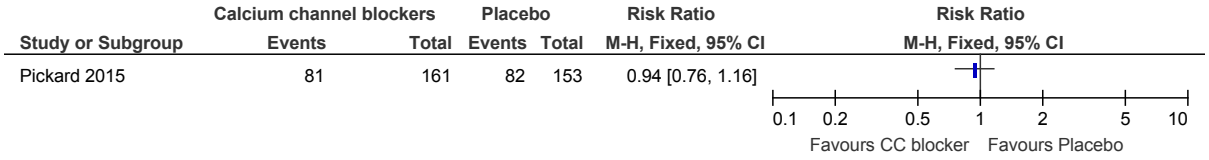
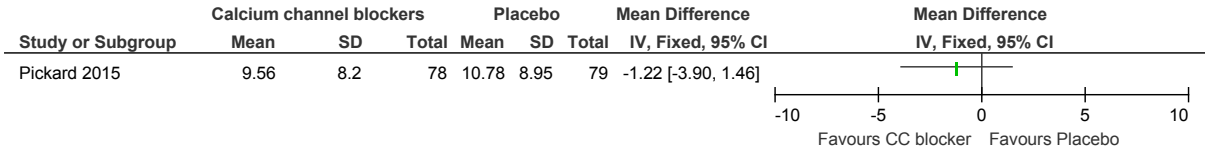


Figure 64: Analgesic use (number of days of pain medication use)



E.1.4 Calcium channel blockers versus no treatment (pain management only)

Figure 65: Time to stone passage (days)

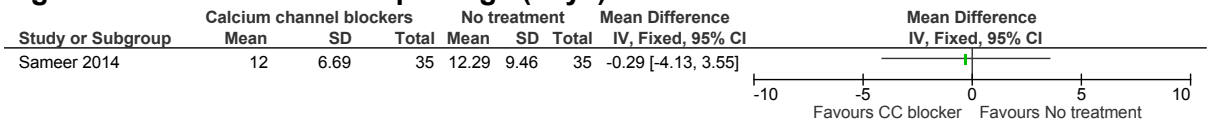


Figure 66: Stone passage

Study or Subgroup	Calcium channel blockers Events	Total	No treatment Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Balci 2014	16	25	9	25	30.3%	1.78 [0.98, 3.24]
Islam 2012	22	31	13	28	46.1%	1.53 [0.97, 2.41]
Sameer 2014	21	35	7	35	23.6%	3.00 [1.47, 6.14]
Total (95% CI)		**91**		**88**	**100.0%**	**1.95 [1.40, 2.71]**
Total events	59		29			

Heterogeneity: Chi² = 2.58, df = 2 (P = 0.28); I² = 22%
Test for overall effect: Z = 3.97 (P < 0.0001)

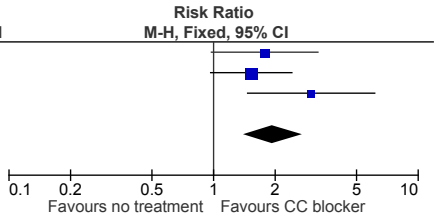


Figure 67: Hospitalisation

Study or Subgroup	Calcium channel blockers Events	Total	No treatment Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Islam 2012	0	31	0	28		Not estimable
Sameer 2014	11	35	27	35	100.0%	0.41 [0.24, 0.69]
Total (95% CI)		**66**		**63**	**100.0%**	**0.41 [0.24, 0.69]**
Total events	11		27			

Heterogeneity: Not applicable
Test for overall effect: Z = 3.37 (P = 0.0007)

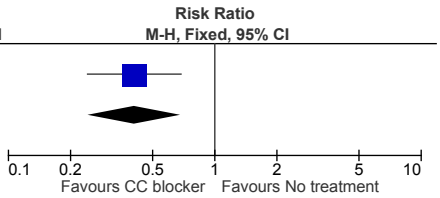


Figure 68: Adverse events (hypotension)

Study or Subgroup	Calcium channel blockers Events	Total	No treatment Events	Total	Peto Odds Ratio Peto, Fixed, 95% CI
Islam 2012	1	31	0	28	6.71 [0.13, 339.76]

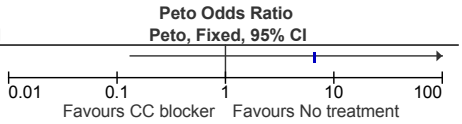


Figure 69: Adverse events (dizziness)

Study or Subgroup	Calcium channel blockers Events	Total	No treatment Events	Total	Risk Difference M-H, Fixed, 95% CI
Balci 2014	0	25	0	25	0.00 [-0.07, 0.07]

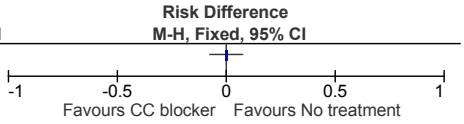


Figure 70: Pain intensity (pain episodes)

Study or Subgroup	Calcium channel blockers Mean	SD	Total	No treatment Mean	SD	Total	Mean Difference IV, Fixed, 95% CI
Sameer 2014	2.91	1.01	35	2.82	1.12	35	0.09 [-0.41, 0.59]

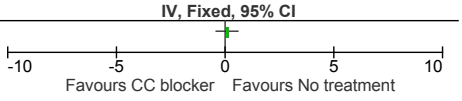
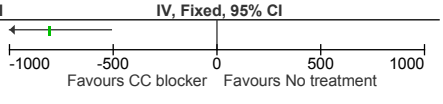


Figure 71: Analgesic use (Diclofenac dose, mg)

Study or Subgroup	Calcium channel blockers Mean	SD	Total	No treatment Mean	SD	Total	Mean Difference IV, Fixed, 95% CI
Balci 2014	602	434	25	1,408	622	25	-806.00 [-1103.31, -508.69]



E.1.5 Alpha blockers versus Calcium channel blockers

Figure 72: Time to stone passage (days)

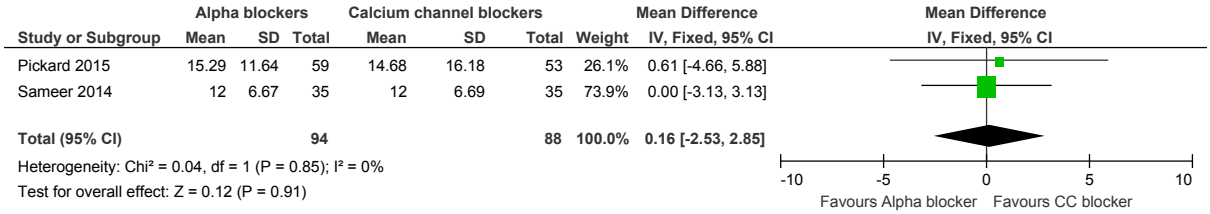


Figure 73: Stone passage

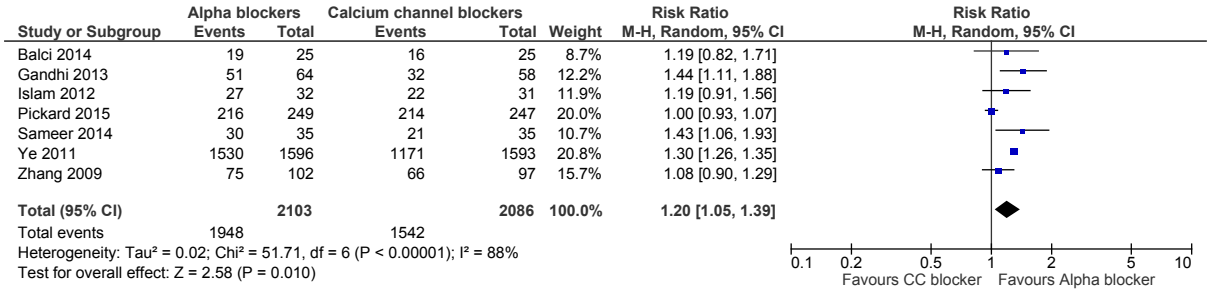


Figure 74: Hospitalisation

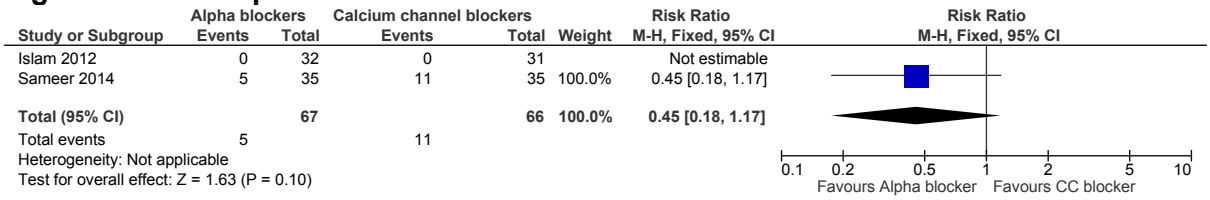


Figure 75: Hospitalisation (excess admission days)

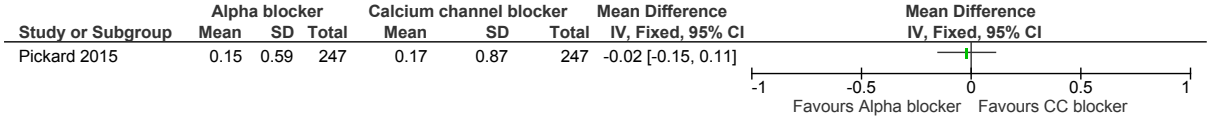


Figure 76: Use of healthcare services (visits)

Study or Subgroup	Alpha blocker Mean	SD	Total	Calcium channel blocker Mean	SD	Total	Mean Difference IV, Fixed, 95% CI
3.2.1 Doctor visits							
Pickard 2015	0.16	0.63	224	0.17	0.71	226	-0.01 [-0.13, 0.11]
3.2.2 Nurse visits							
Pickard 2015	0.01	0.13	224	0.01	0.09	226	0.00 [-0.02, 0.02]
3.2.4 Outpatient visits							
Pickard 2015	0.66	0.69	289	0.62	0.66	246	0.04 [-0.07, 0.15]

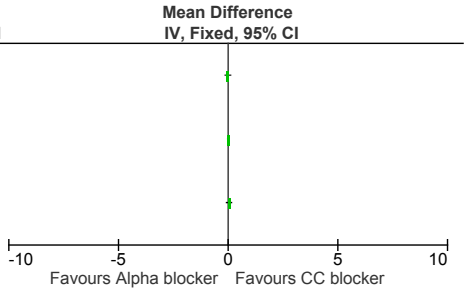


Figure 77: Quality of life (SF36)

Study or Subgroup	Alpha blockers Mean	SD	Total	Calcium channel blockers Mean	SD	Total	Mean Difference IV, Fixed, 95% CI
1.7.1 SF36 physical component							
Pickard 2015	51.98	10.2	100	52.13	8.48	116	-0.15 [-2.68, 2.38]
1.7.2 SF36 mental component							
Pickard 2015	49.6	11.66	100	50.9	10.3	116	-1.30 [-4.26, 1.66]

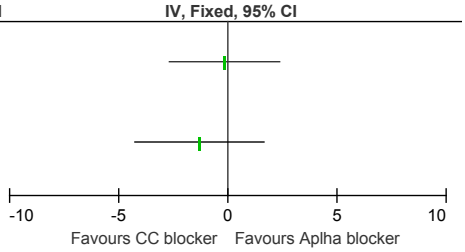


Figure 78: Quality of life (EQ5D)

Study or Subgroup	Alpha blockers Mean	SD	Total	Calcium channel blockers Mean	SD	Total	Mean Difference IV, Fixed, 95% CI
Pickard 2015	0.864	0.264	103	0.876	0.233	123	-0.01 [-0.08, 0.05]

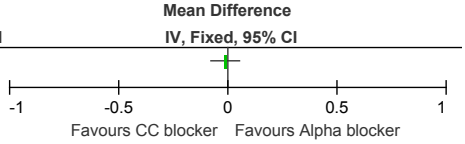


Figure 79: Adverse events (discontinuation due to adverse events)

Study or Subgroup	Favours Alpha blocker Events	Total	Calcium channel blockers Events	Total	Risk Ratio M-H, Fixed, 95% CI
Pickard 2015	15	149	29	162	0.56 [0.31, 1.01]

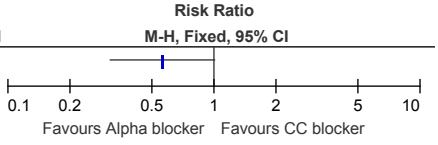


Figure 80: Adverse events (headache)

Study or Subgroup	Alpha blockers Events	Total	Calcium channel blockers Events	Total	Risk Ratio M-H, Fixed, 95% CI
Gandhi 2013	32	64	25	58	1.16 [0.79, 1.70]

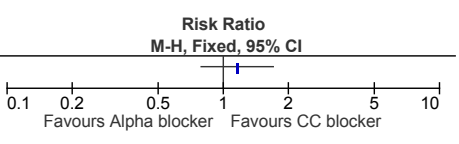


Figure 81: Adverse events (dizziness)

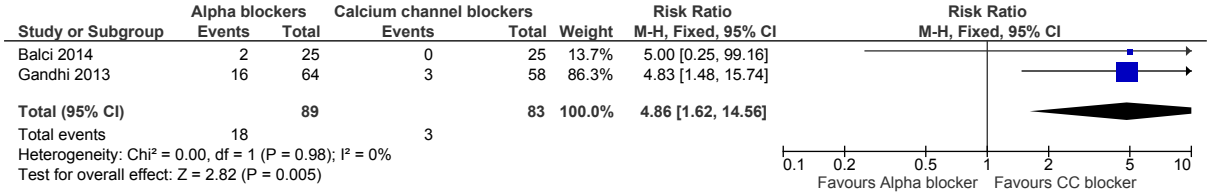


Figure 82: Adverse events (hypotension)

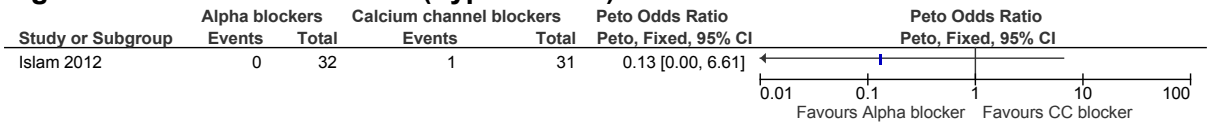


Figure 83: Adverse events (unspecified)

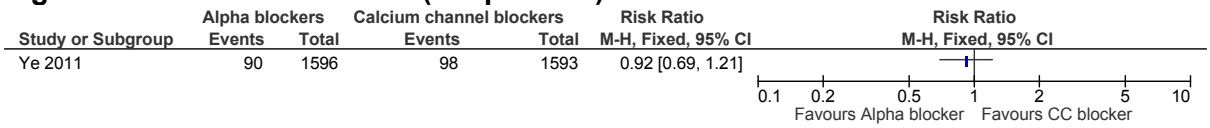


Figure 84: Adverse events (flushing)

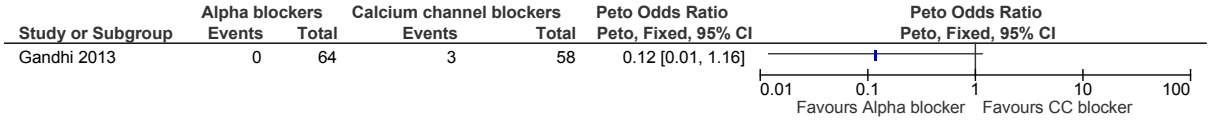


Figure 85: Pain intensity (VAS)

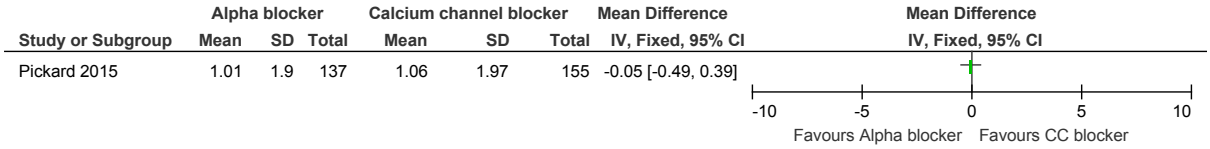


Figure 86: Pain intensity (EQ5D – no pain/discomfort)

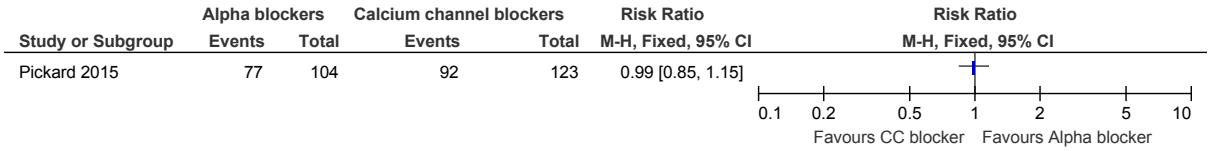


Figure 87: Pain intensity (EQ5D – moderate pain/discomfort)

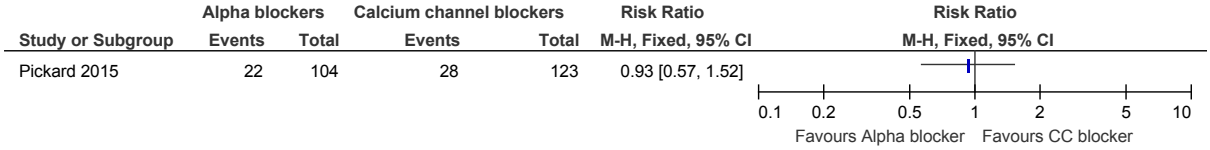


Figure 88: Pain intensity (EQ5D – extreme pain/discomfort)

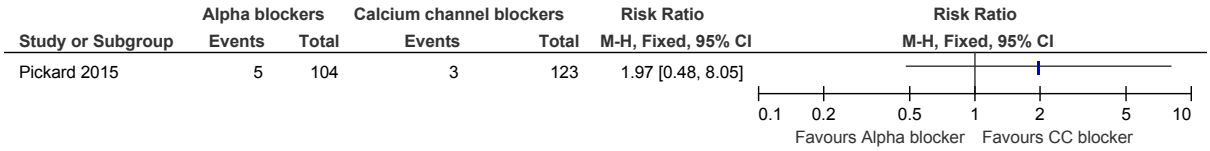


Figure 89: Pain intensity (pain episodes)

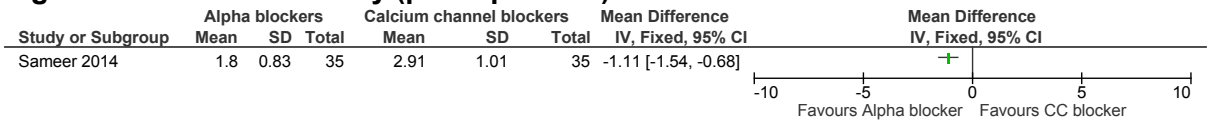


Figure 90: Analgesic use (number of people using analgesics)

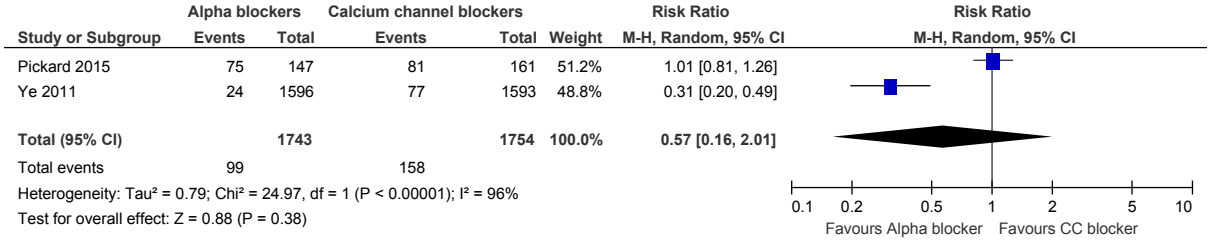


Figure 91: Analgesic use (days of medication use)

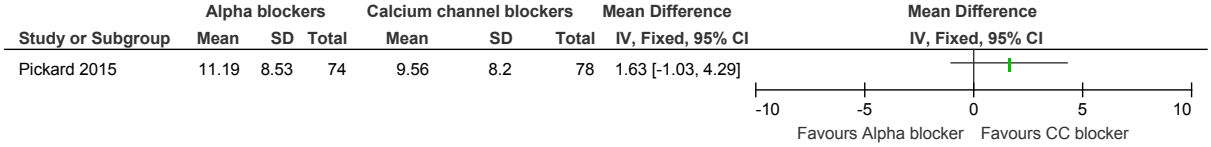


Figure 92: Analgesic use (mg)

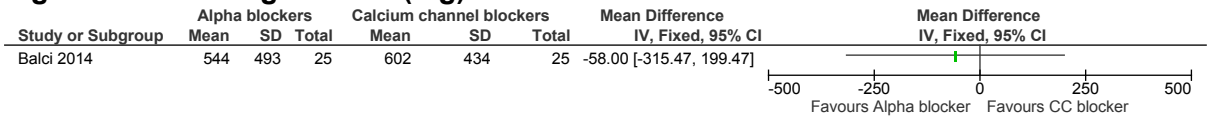
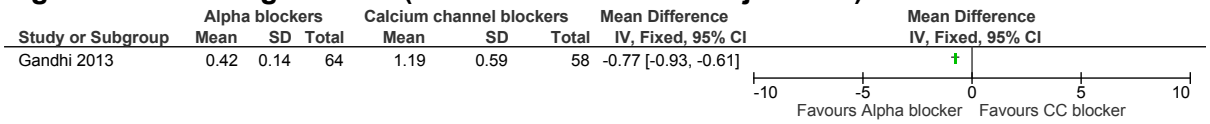


Figure 93: Analgesic use (number of diclofenac injections)



E.2 Mid ureteric stones <10mm in adults

E.2.1 Alpha blockers versus placebo

Figure 94: Time to stone passage (days)

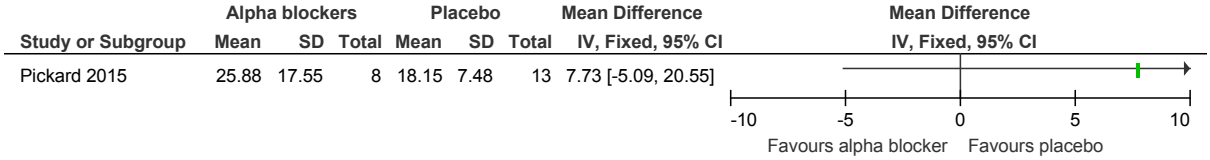


Figure 95: Stone passage

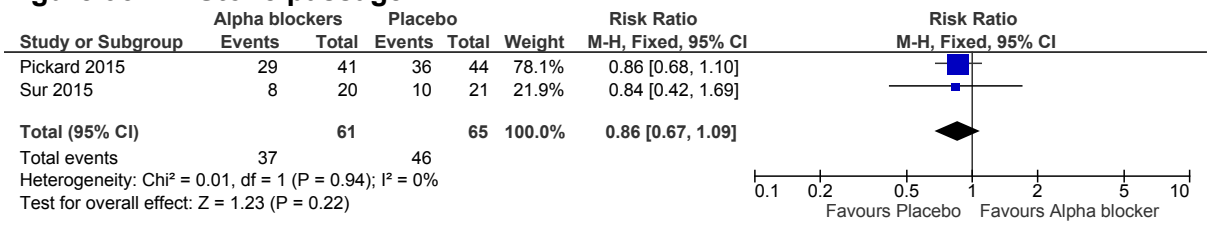


Figure 96: Hospitalisation (excess admission days)

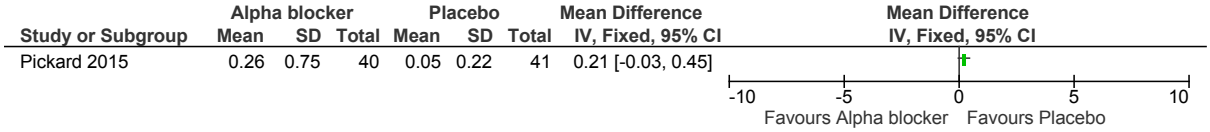


Figure 97: Use of healthcare services (visits)

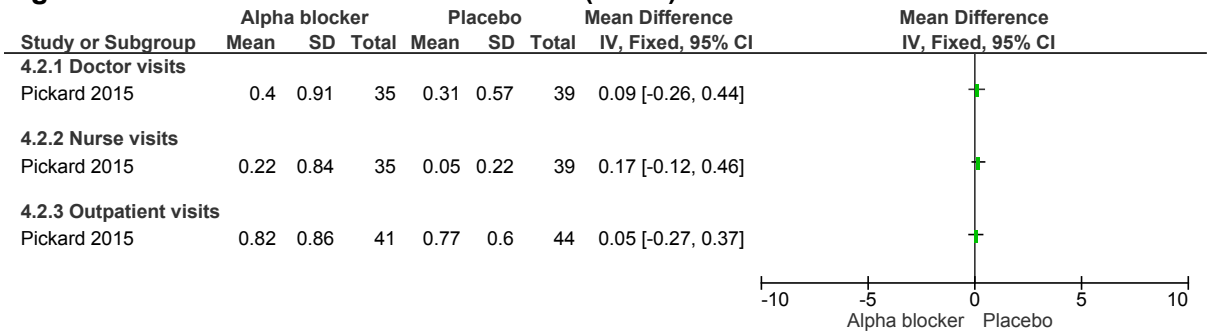


Figure 98: Quality of life (SF36)

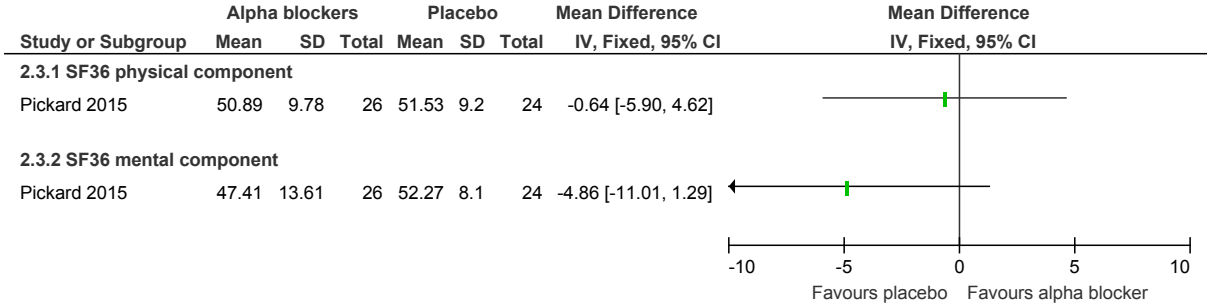


Figure 99: Quality of life (EQ5D)

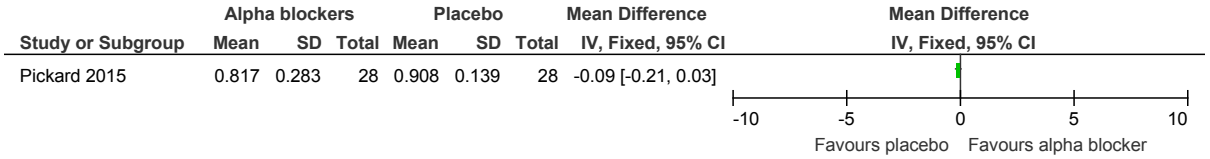


Figure 100: Adverse events (discontinuation due to adverse events)

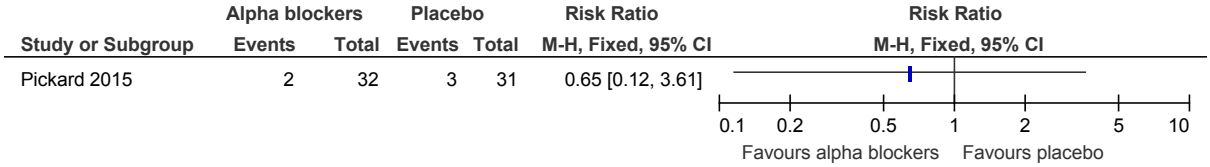


Figure 101: Pain intensity (VAS)

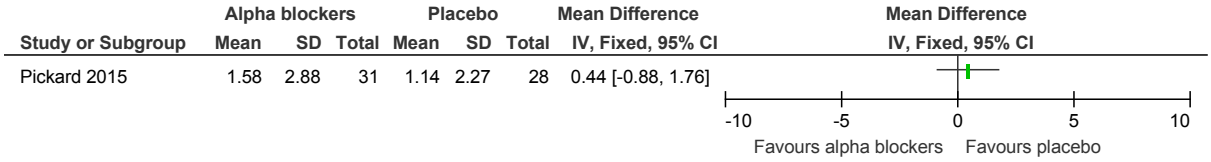


Figure 102: Pain intensity (EQ5D no pain/discomfort)

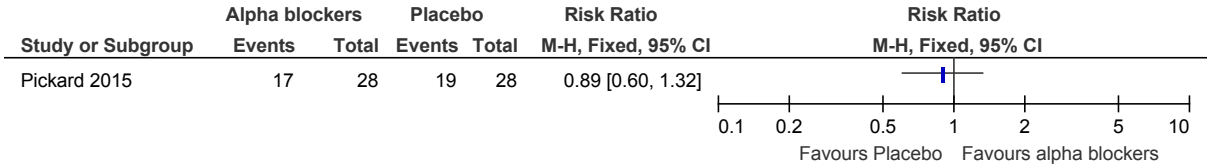


Figure 103: Pain intensity (EQ5D moderate pain/discomfort)

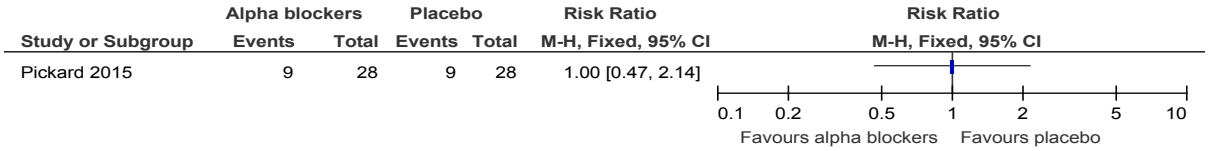


Figure 104: Pain intensity (EQ5D extreme pain/discomfort)

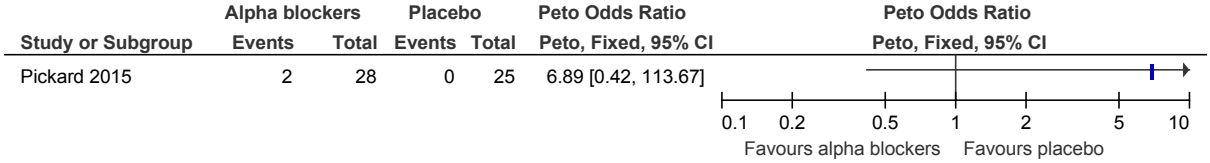


Figure 105: Analgesic use (pain medication use)

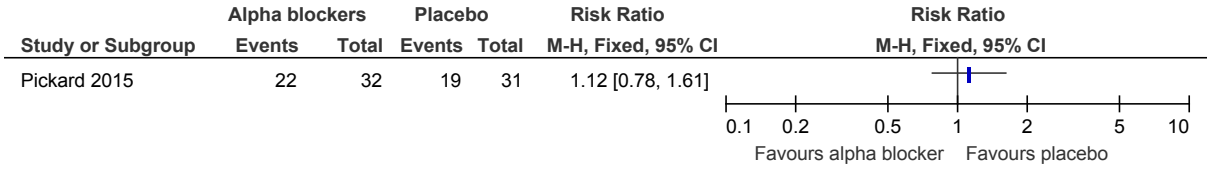
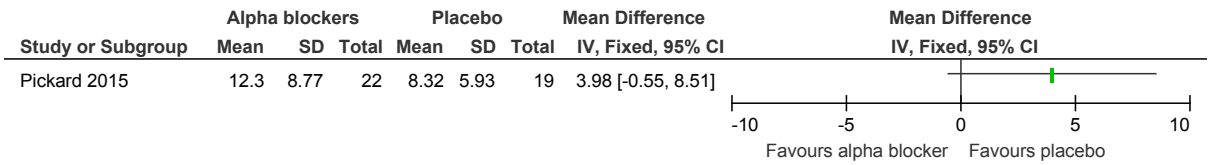


Figure 106: Analgesic use (number of days of pain medication use)



E.2.2 Alpha blockers versus no treatment (pain management only)

Figure 107: Time to stone passage

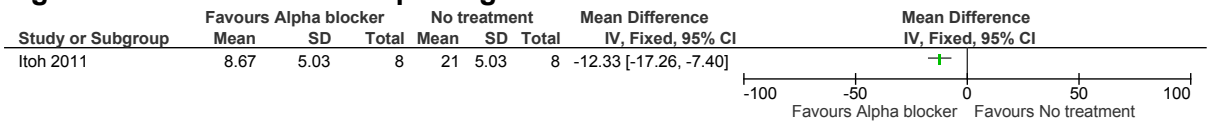


Figure 108: Stone passage

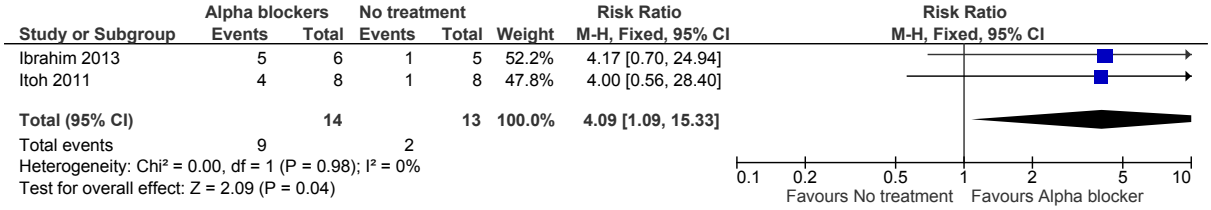
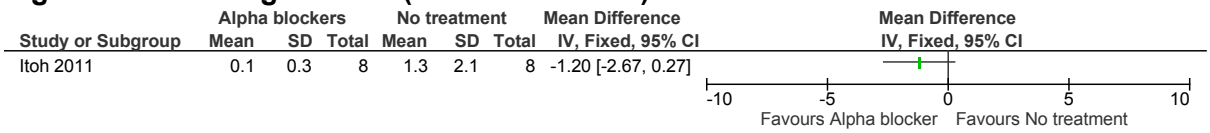


Figure 109: Analgesic use (number of times)



E.2.3 Calcium channel blockers versus placebo

Figure 110: Time to stone passage (days)

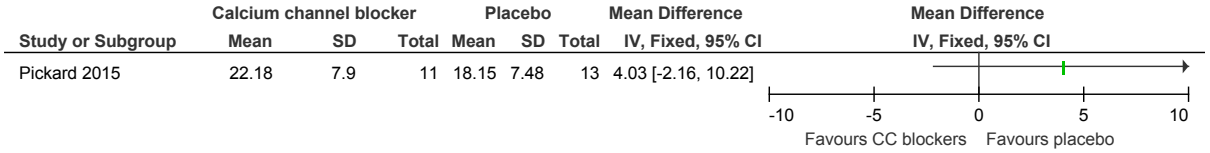


Figure 111: Stone passage

Figure 112: Hospitalisation (excess admission days)

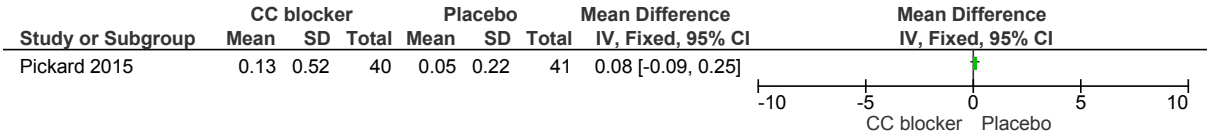


Figure 113: Use of healthcare services (visits)

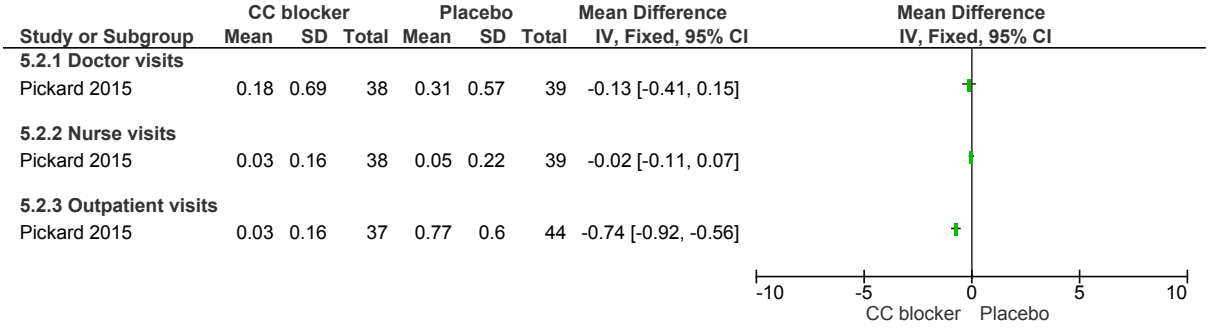


Figure 114: Quality of life (SF36)

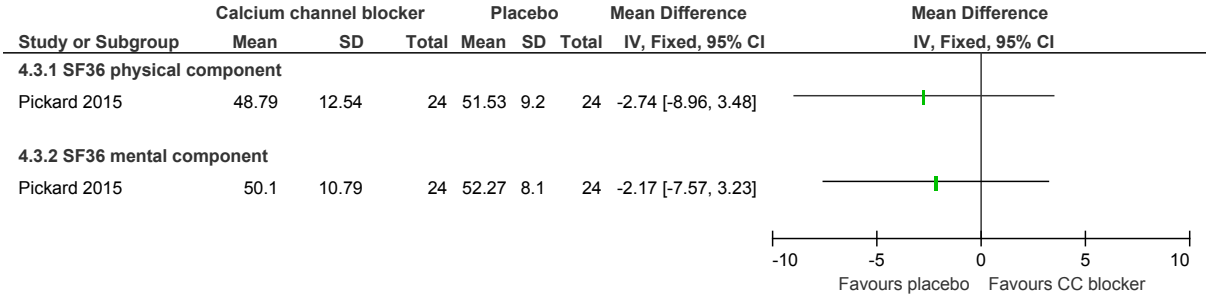


Figure 115: Quality of life (EQ5D)

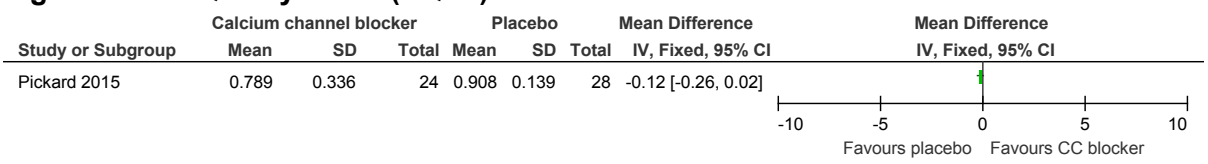


Figure 116: Adverse events (discontinuation due to adverse events)

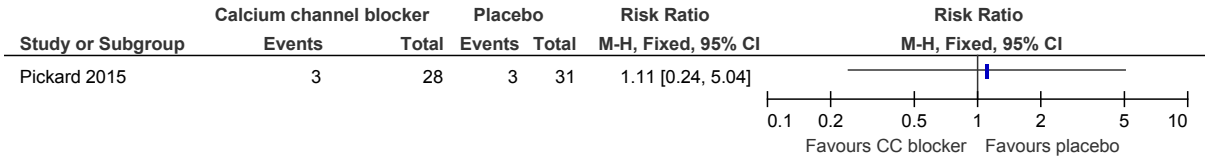


Figure 117: Pain intensity (VAS)

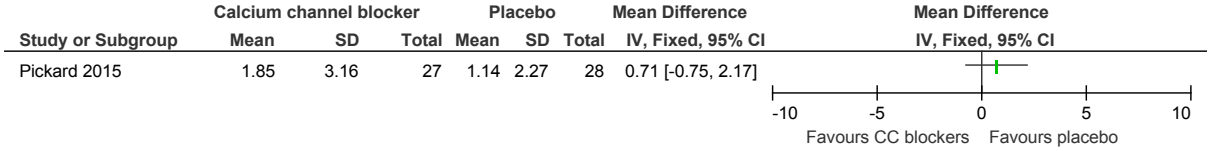


Figure 118: Pain intensity (EQ5D no pain/discomfort)

Figure 119: Pain intensity (EQ5D moderate pain/discomfort)

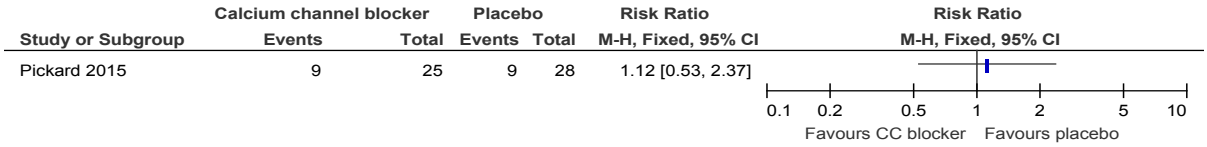


Figure 120: Pain intensity (EQ5D extreme pain/discomfort)

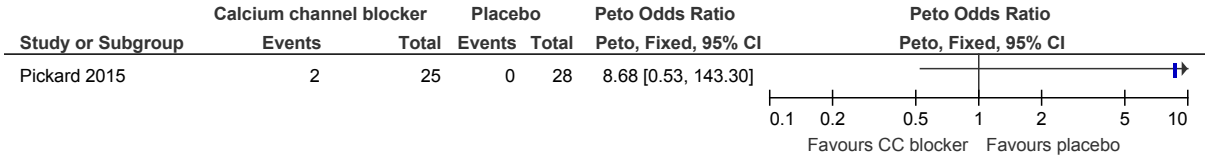


Figure 121: Analgesic use (pain medication use)

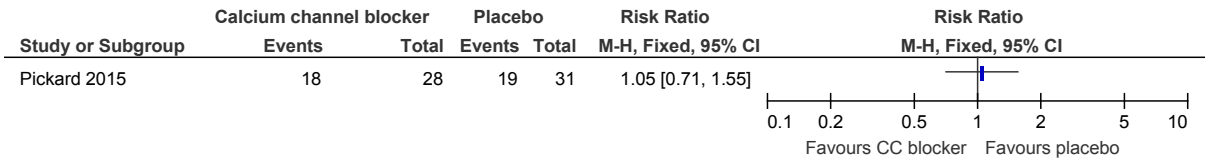
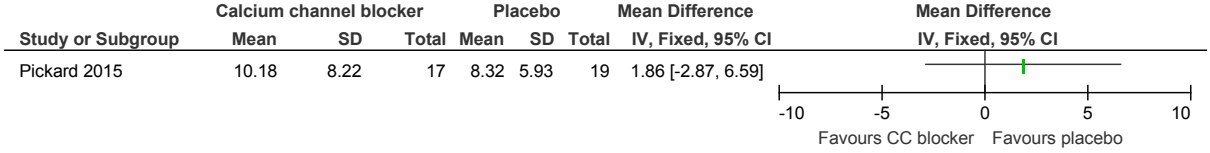


Figure 122: Analgesic use (days of pain medication use)



E.2.4 Alpha blockers versus Calcium channel blockers

Figure 123: Time to stone passage (days)

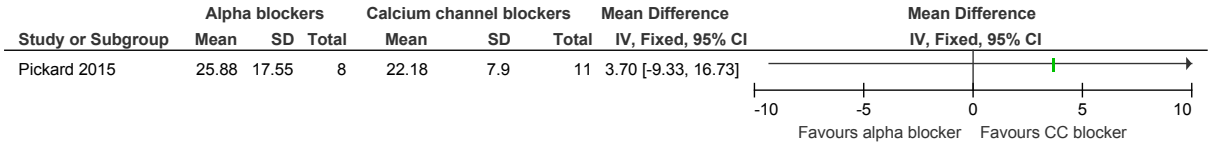


Figure 124: Stone passage

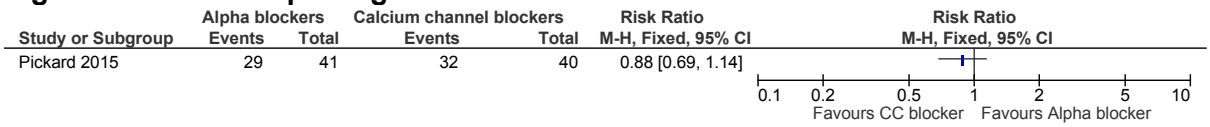


Figure 125: Hospitalisation (excess admission days)

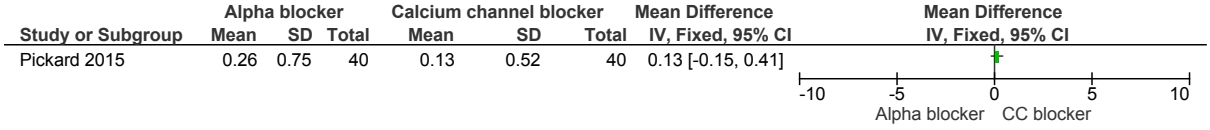


Figure 126: Use of healthcare services (visits)

Study or Subgroup	Alpha blocker Mean	SD	Total	Calcium channel blocker Mean	SD	Total	Mean Difference IV, Fixed, 95% CI
6.2.1 Doctor visits							
Pickard 2015	0.4	0.91	35	0.18	0.69	38	0.22 [-0.15, 0.59]
6.2.2 Nurse visits							
Pickard 2015	0.22	0.84	35	0.03	0.16	38	0.19 [-0.09, 0.47]
6.2.3 Outpatient visits							
Pickard 2015	0.82	0.86	41	0.03	0.16	37	0.79 [0.52, 1.06]

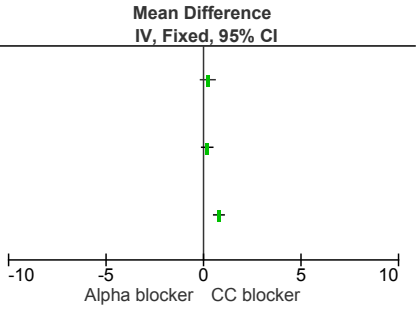


Figure 127: Quality of life (SF36)

Study or Subgroup	Alpha blockers Mean	SD	Total	Calcium channel blockers Mean	SD	Total	Mean Difference IV, Fixed, 95% CI
1.3.1 SF36 physical component							
Pickard 2015	50.89	9.78	26	48.79	12.54	24	2.10 [-4.17, 8.37]
1.3.2 SF36 mental component							
Pickard 2015	47.41	13.61	26	50.1	10.79	24	-2.69 [-9.47, 4.09]

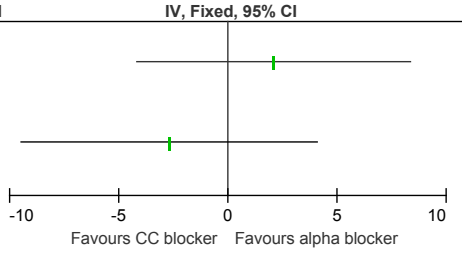


Figure 128: Quality of life (EQ5D)

Study or Subgroup	Alpha blockers Mean	SD	Total	Calcium channel blockers Mean	SD	Total	Mean Difference IV, Fixed, 95% CI
Pickard 2015	0.817	0.283	28	0.789	0.336	24	0.03 [-0.14, 0.20]

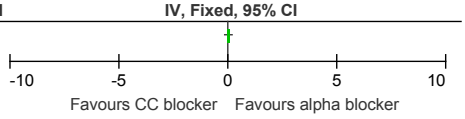


Figure 129: Adverse events (discontinuation due to adverse events)

Study or Subgroup	Alpha blockers Events	Total	Control Events	Total	Risk Ratio M-H, Fixed, 95% CI
Pickard 2015	2	32	3	28	0.58 [0.10, 3.24]

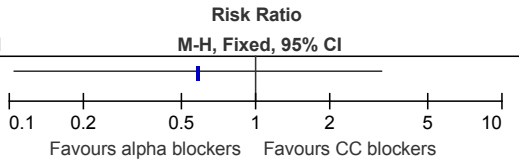


Figure 130: Pain intensity (VAS)

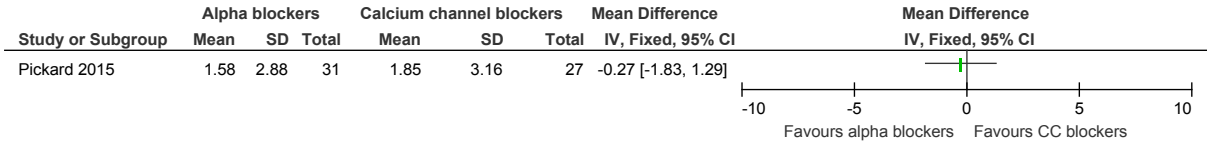


Figure 131: Pain intensity (EQ5D no pain/discomfort)

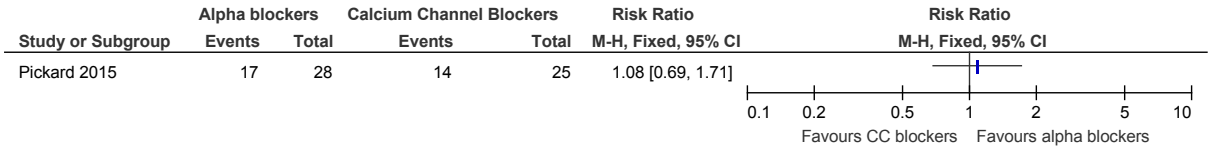


Figure 132: Pain intensity (EQ5D moderate pain/discomfort)

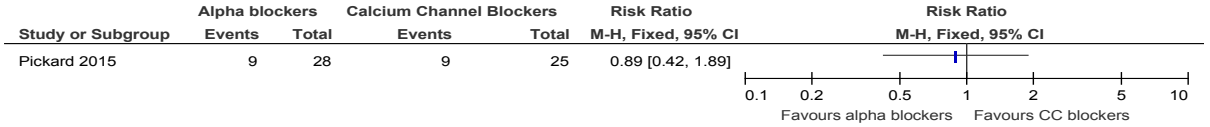


Figure 133: Pain intensity (EQ5D extreme pain/discomfort)

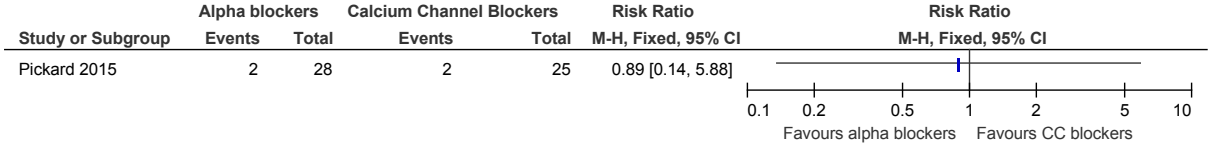


Figure 134: Analgesic use (pain medication use)

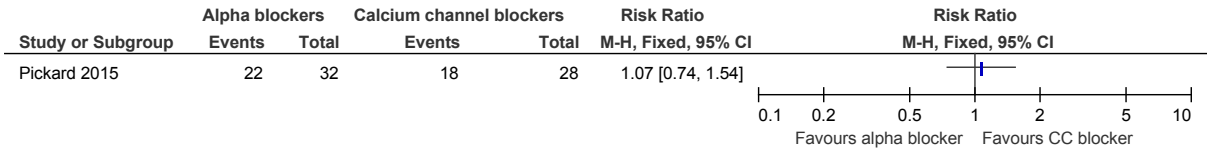
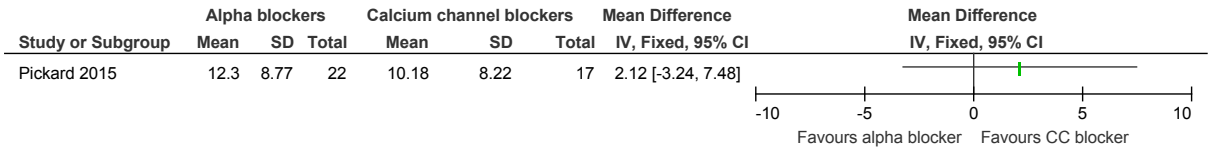


Figure 135: Analgesic use (number of days of pain medication use)



E.3 Proximal ureteric stones <10mm in adults

E.3.1 Alpha blockers versus placebo

Figure 136: Time to stone passage (days)

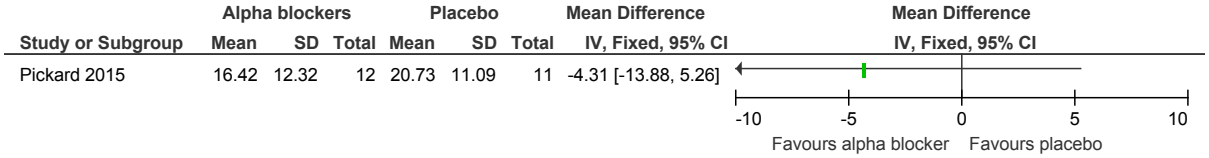


Figure 137: Stone passage

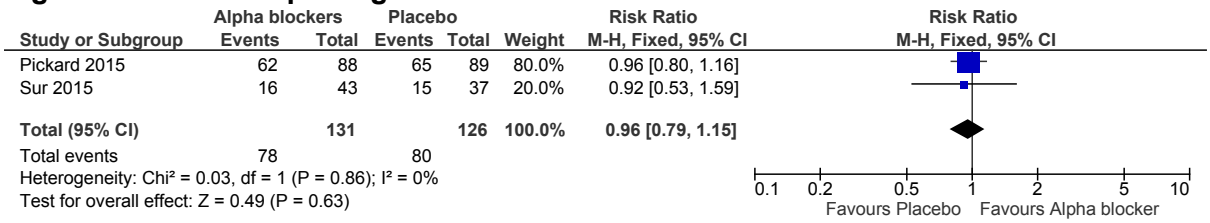


Figure 138: Hospitalisation (excess admission days)

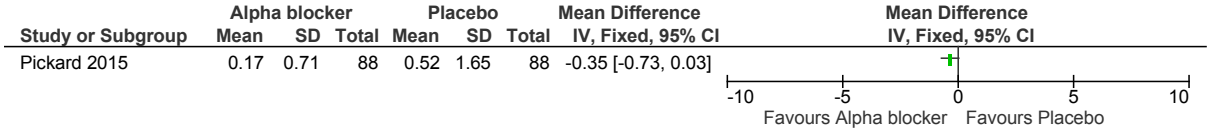


Figure 139: Use of healthcare services (visits)

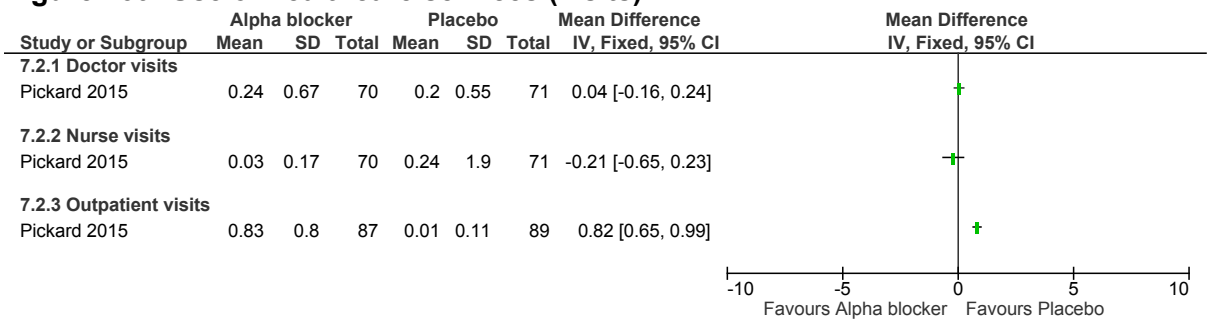


Figure 140: Quality of life (SF36)

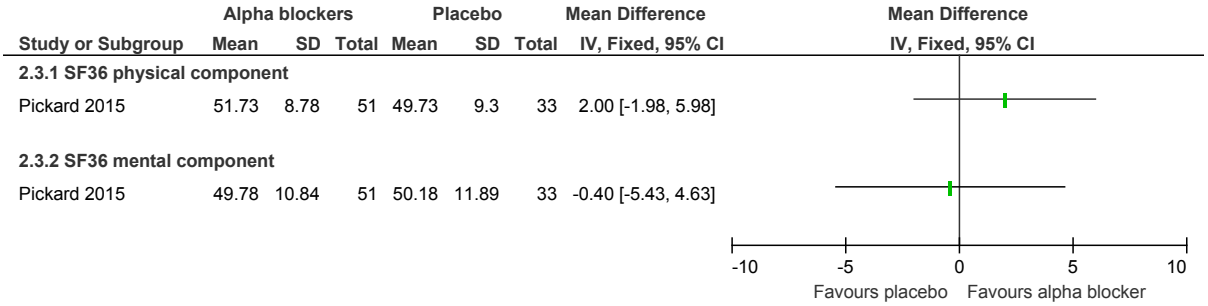


Figure 141: Quality of life (EQ5D)

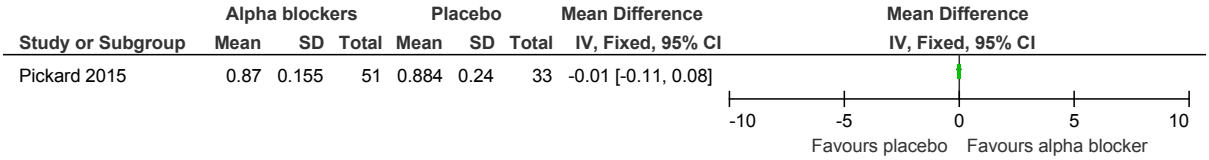


Figure 142: Adverse events (discontinuation due to adverse events)

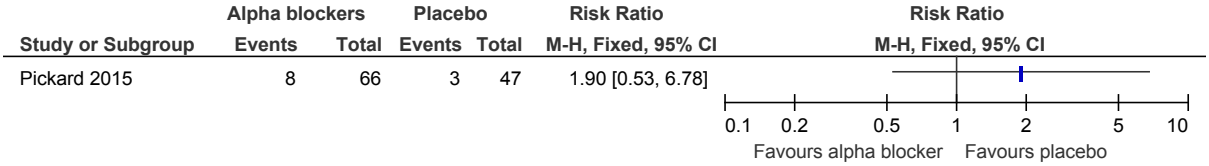


Figure 143: Pain intensity (VAS)

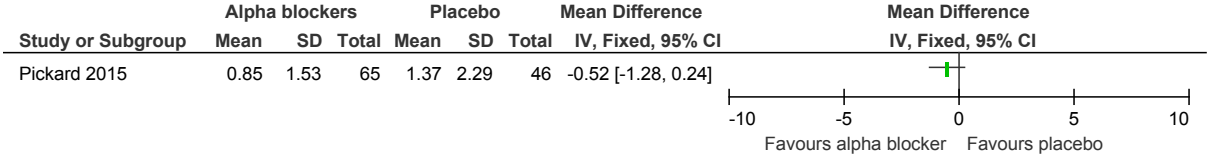


Figure 144: Pain intensity (EQD no pain/discomfort)

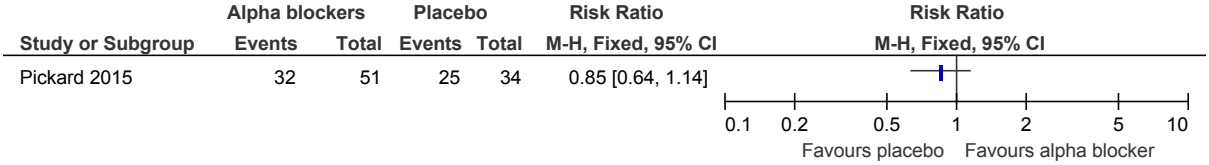


Figure 145: Pain intensity (EQD moderate pain/discomfort)

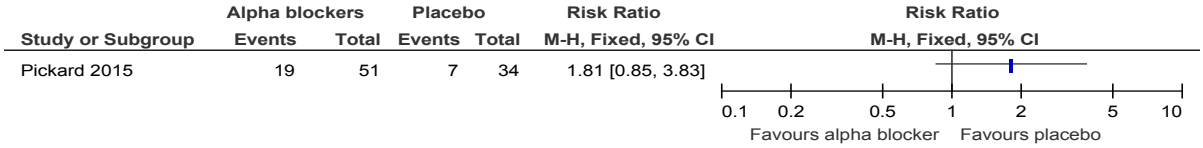


Figure 146: Pain intensity (EQD extreme pain/discomfort)

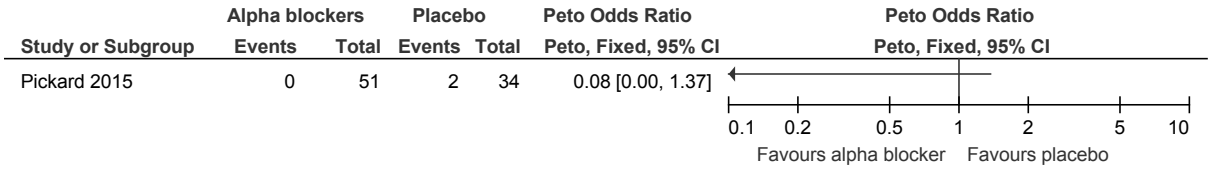


Figure 147: Analgesic use (pain medication use)

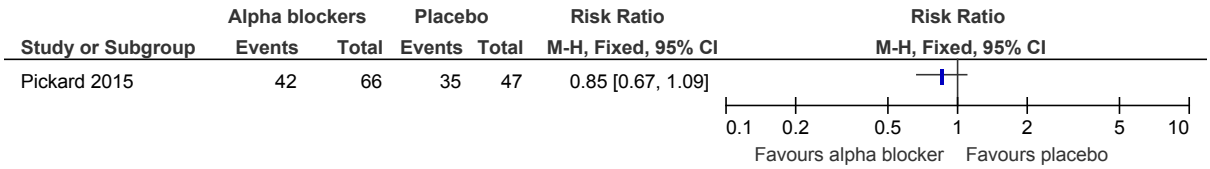
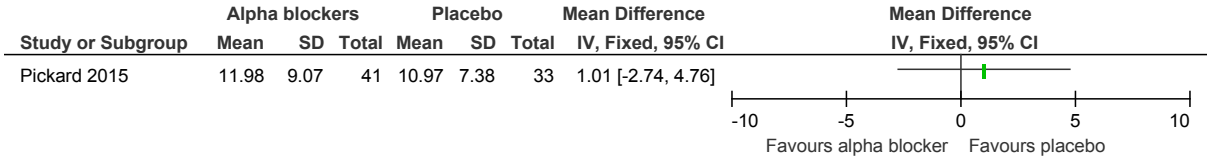


Figure 148: Analgesic use (number of days of pain medication use)



E.3.2 Alpha blockers versus no treatment (pain management only)

Figure 149: Time to stone passage (days)

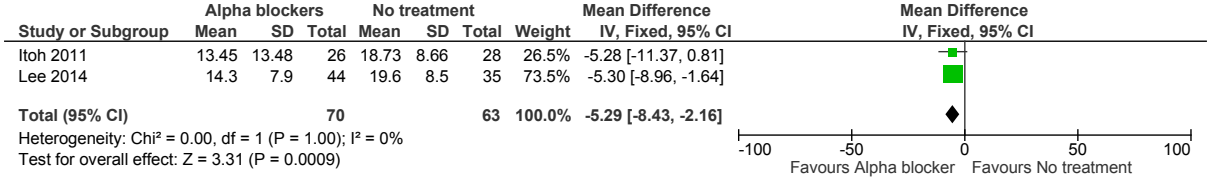


Figure 150: Stone passage

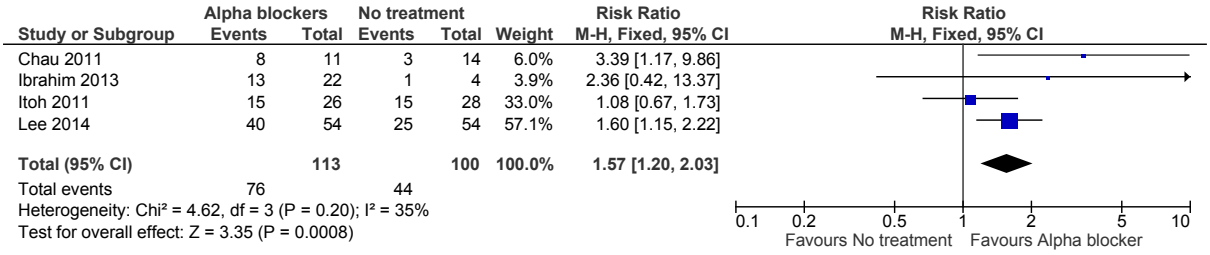


Figure 151: Quality of life (EuroQoL)

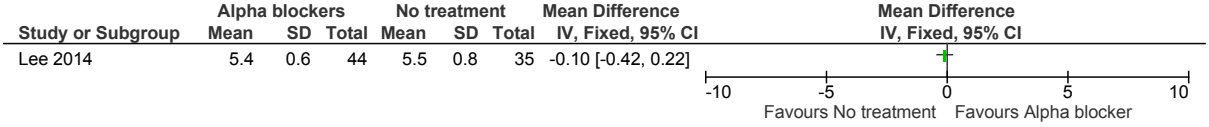
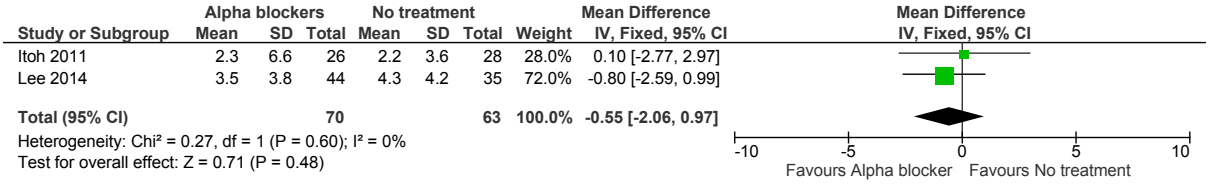


Figure 152: Analgesic use (number of times)



E.3.3 Calcium channel blockers versus placebo

Figure 153: Time to stone passage (days)

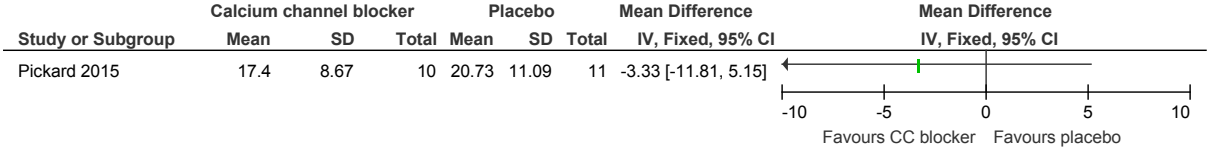


Figure 154: Stone passage

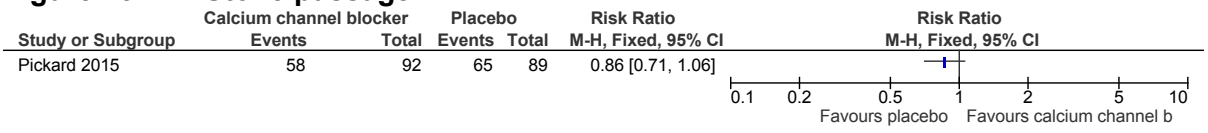


Figure 155: Hospitalisation (excess admission days)

Study or Subgroup	Calcium channel blocker Mean	SD	Total	Placebo Mean	SD	Total	Mean Difference IV, Fixed, 95% CI
Pickard 2015	0.44	1.56	91	0.52	1.65	88	-0.08 [-0.55, 0.39]

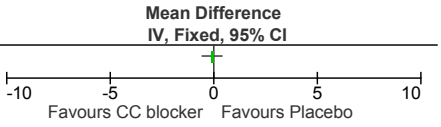


Figure 156: Use of healthcare services (visits)

Study or Subgroup	Calcium channel blocker Mean	SD	Total	Placebo Mean	SD	Total	Mean Difference IV, Fixed, 95% CI
8.2.1 Doctor visits							
Pickard 2015	0.19	0.61	67	0.2	0.55	71	-0.01 [-0.20, 0.18]
8.2.2 Nurse visits							
Pickard 2015	0.04	0.27	67	0.24	1.9	71	-0.20 [-0.65, 0.25]
8.2.3 Outpatient visits							
Pickard 2015	0.63	0.67	92	0.01	0.11	89	0.62 [0.48, 0.76]

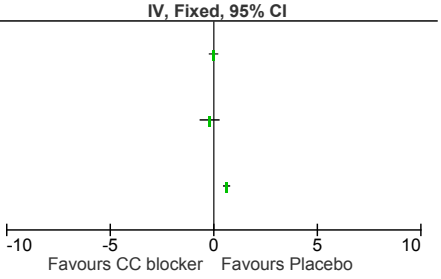


Figure 157: Quality of life (SF36)

Study or Subgroup	Calcium channel blocker Mean	SD	Total	Placebo Mean	SD	Total	Mean Difference IV, Fixed, 95% CI
4.3.1 SF36 physical component							
Pickard 2015	50.89	8.8	37	49.73	9.3	33	1.16 [-3.10, 5.42]
4.3.2 SF36 mental component							
Pickard 2015	49.25	9.93	37	50.18	11.89	33	-0.93 [-6.10, 4.24]

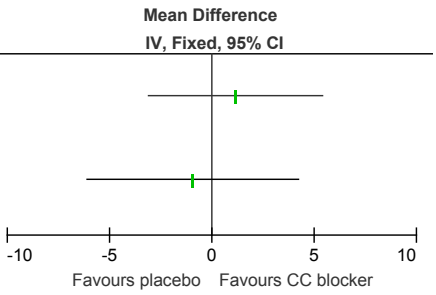


Figure 158: Quality of life (EQ5D)

Study or Subgroup	Calcium channel blocker Mean	SD	Total	Placebo Mean	SD	Total	Mean Difference IV, Fixed, 95% CI
Pickard 2015	0.894	0.183	40	0.884	0.24	33	0.01 [-0.09, 0.11]

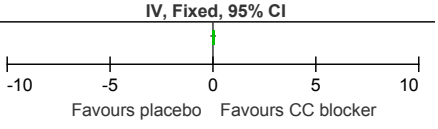


Figure 159: Adverse events (discontinuation due to adverse events)

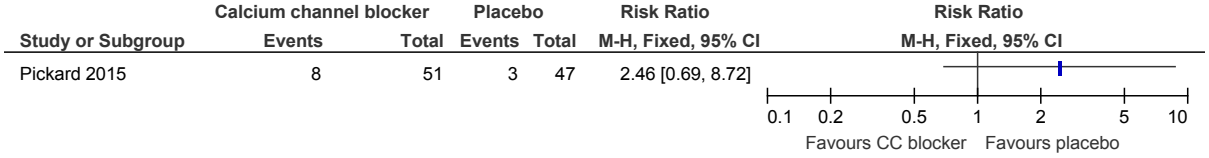


Figure 160: Pain intensity (VAS)

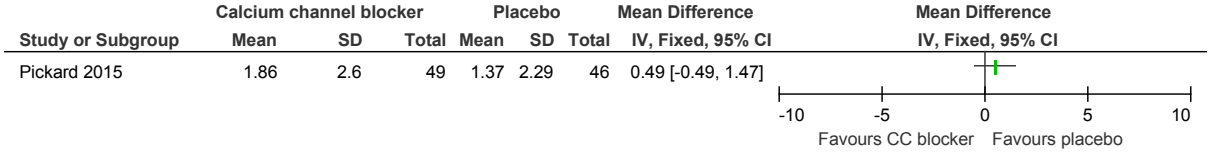


Figure 161: Pain intensity (EQ5D no pain/discomfort)

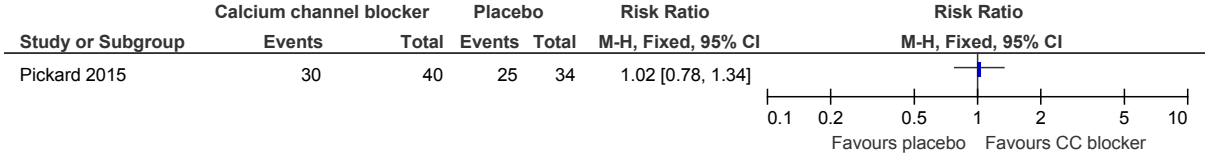


Figure 162: Pain intensity (EQ5D moderate pain/discomfort)

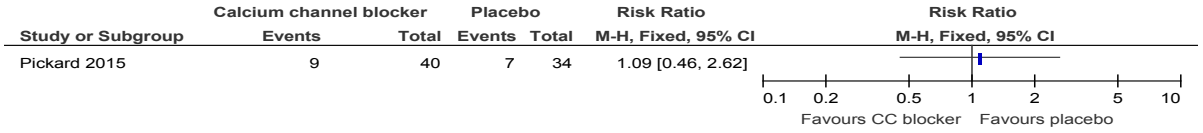


Figure 163: Pain intensity (EQ5D extreme pain/discomfort)

Figure 164: Analgesic use (pain medication use)

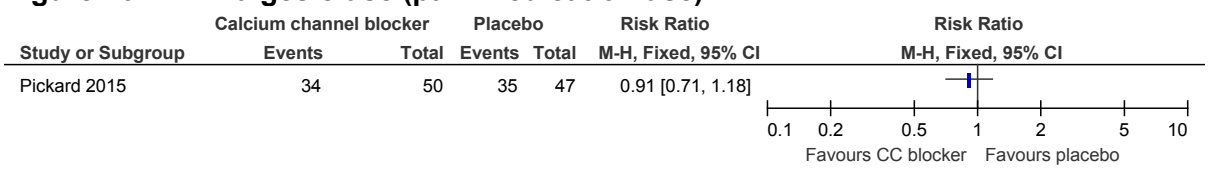
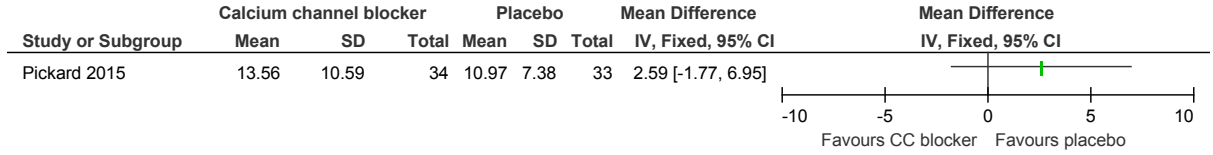


Figure 165: Analgesic use (number of days of pain medication use)



E.3.4 Alpha blockers versus Calcium channel blockers

Figure 166: Time to stone passage (days)

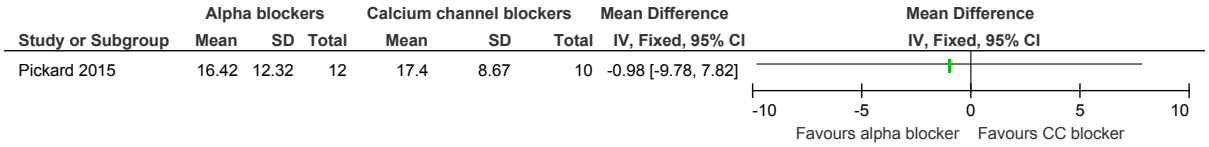


Figure 167: Stone passage

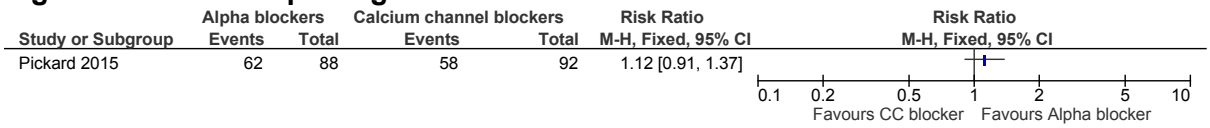


Figure 168: Hospitalisation (excess admission days)

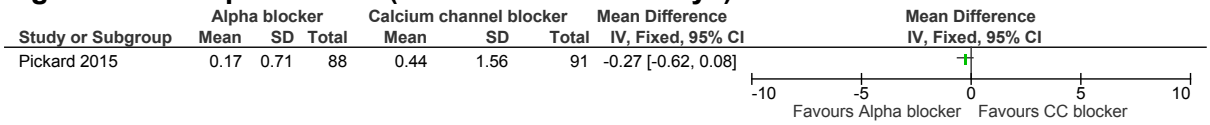


Figure 169: Use of healthcare services (visits)

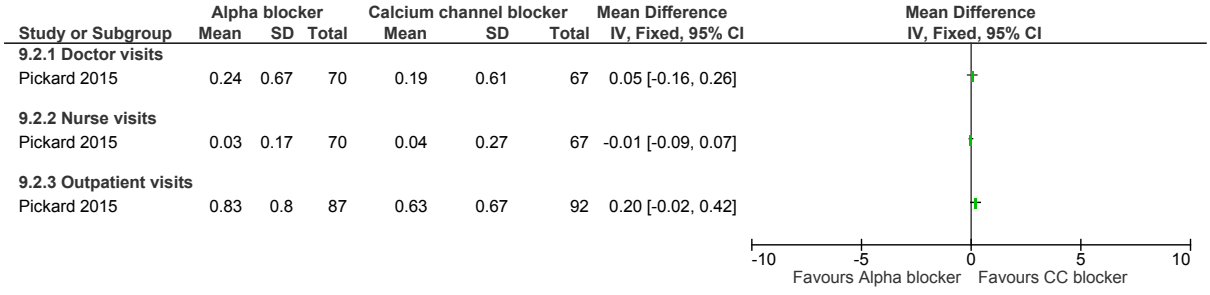


Figure 170: Quality of life (SF36)

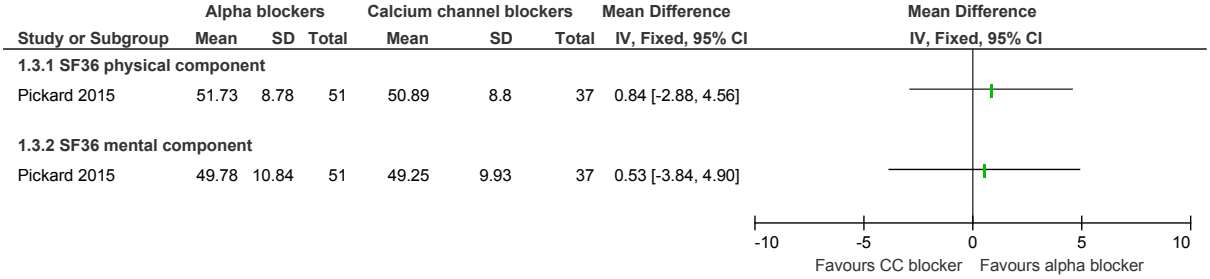


Figure 171: Quality of life (EQ5D)

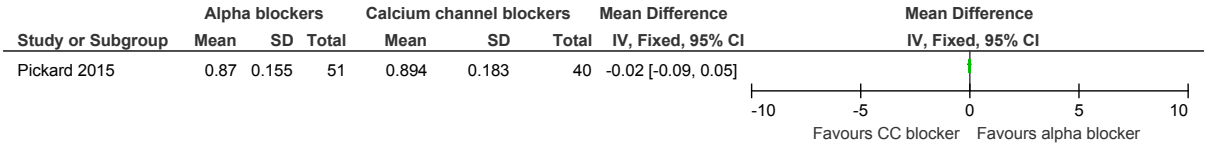


Figure 172: Adverse events (discontinuation due to adverse events)

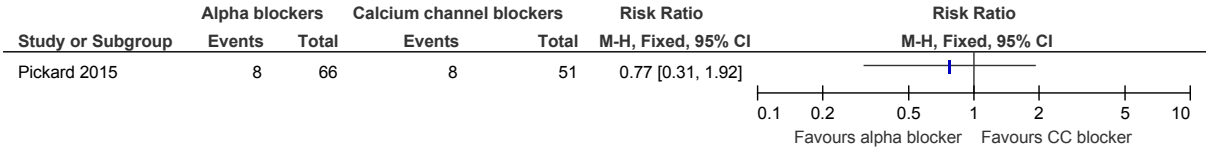


Figure 173: Pain intensity (VAS)

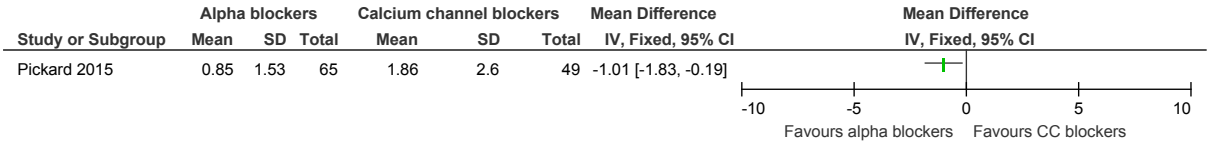


Figure 174: Pain intensity (EQ5D no pain/discomfort)

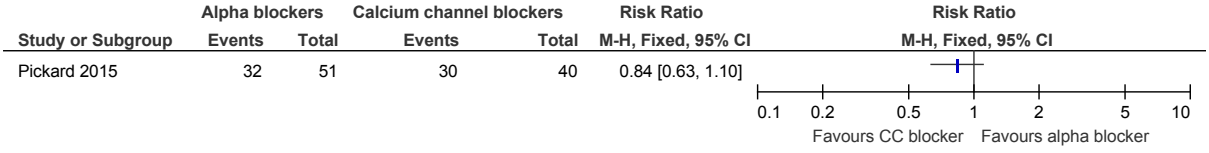


Figure 175: Pain intensity (EQ5D moderate pain/discomfort)

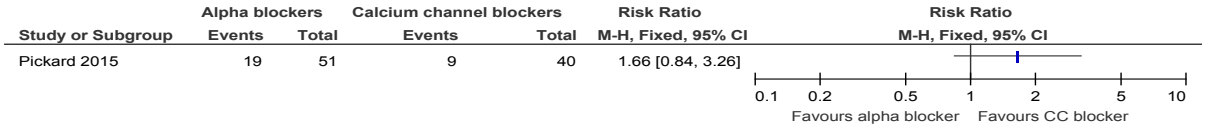


Figure 176: Pain intensity (EQ5D extreme pain/discomfort)

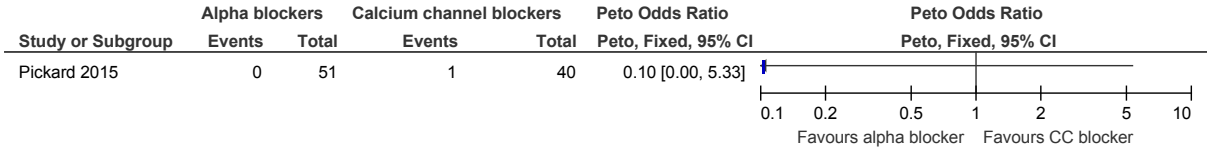


Figure 177: Analgesic use (pain medication use)

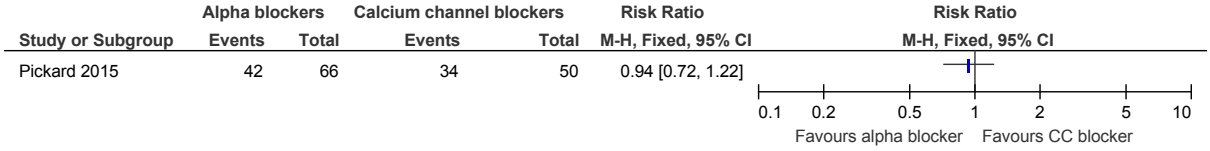
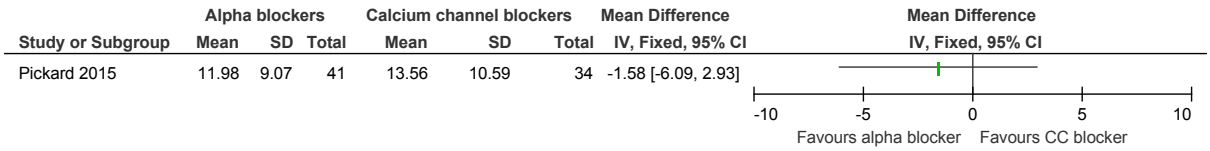


Figure 178: Analgesic use (number of days with pain medication use)



E.4 Distal ureteric stones <10mm in children

E.4.1 Alpha blockers versus placebo

Figure 179: Time to stone passage (days)

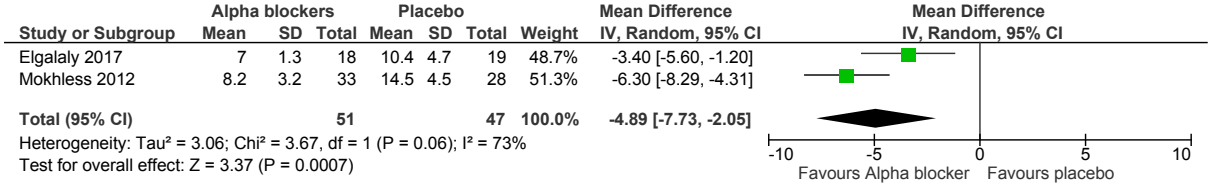


Figure 180: Stone passage (4 weeks)

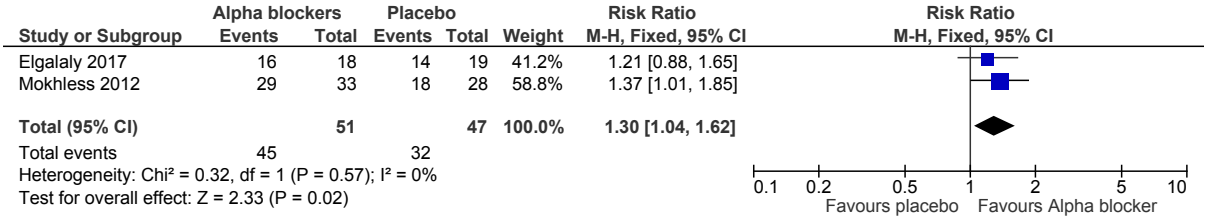


Figure 181: Adverse events (headaches/dizziness)

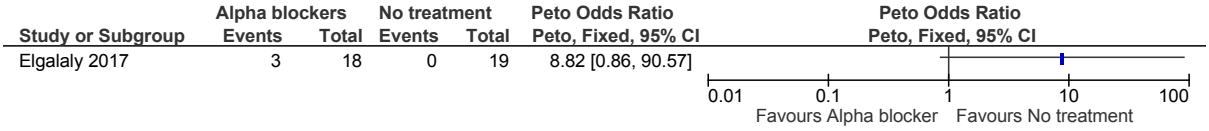


Figure 182: Adverse events (headache)

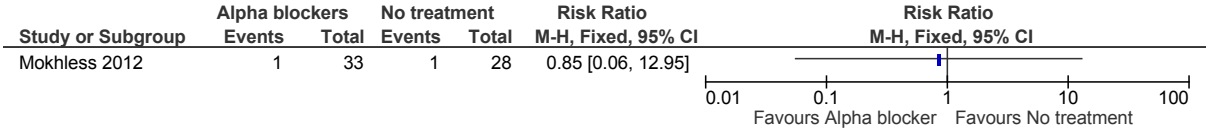


Figure 183: Adverse events (hypotension)

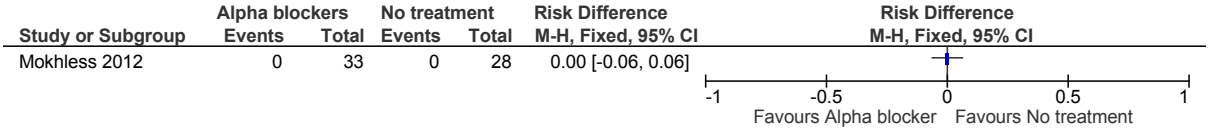
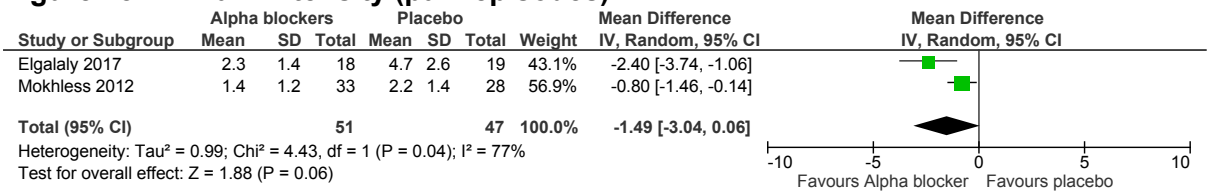


Figure 184: Pain intensity (pain episodes)



E.4.2 Alpha blockers versus no treatment (pain management only)

Figure 185: Time to stone passage (days)

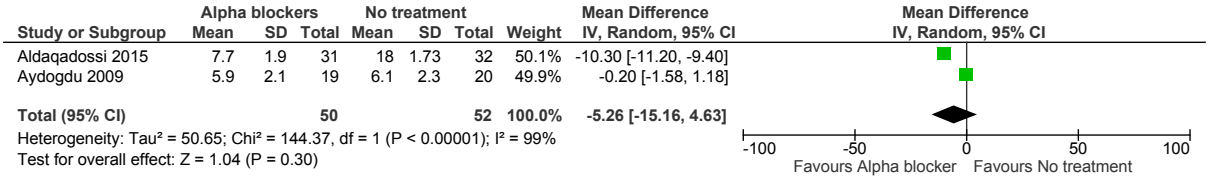


Figure 186: Stone passage

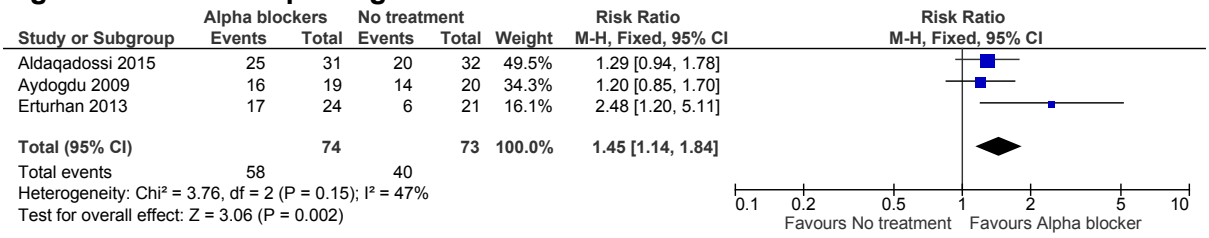


Figure 187: Adverse events (unspecified)

Figure 188: Pain intensity (daily pain episodes)

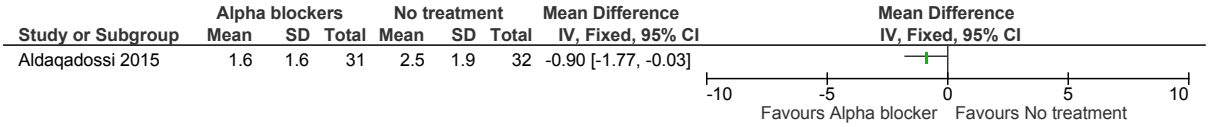
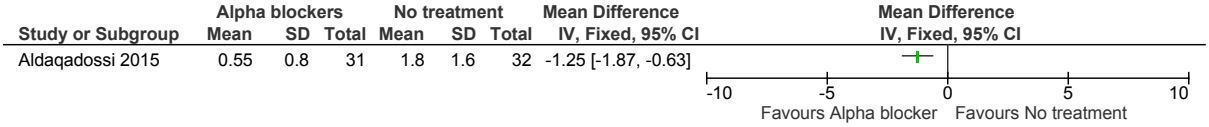


Figure 189: Analgesic use (ketorolac injections)



E.5 Adjunctive therapy: distal ureteric stones <10mm in adults

E.5.1 Alpha blockers as adjunctive therapy to shock wave lithotripsy versus shock wave lithotripsy only

Figure 190: Time to stone passage

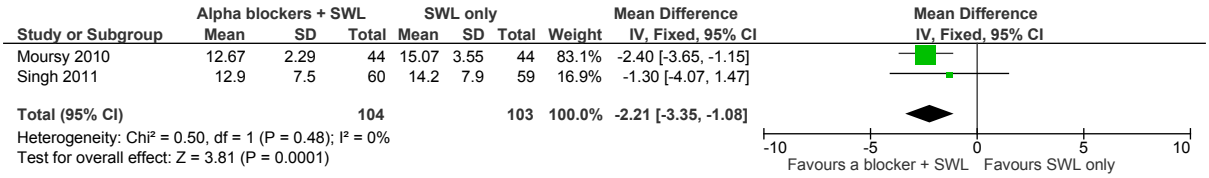


Figure 191: Stone passage

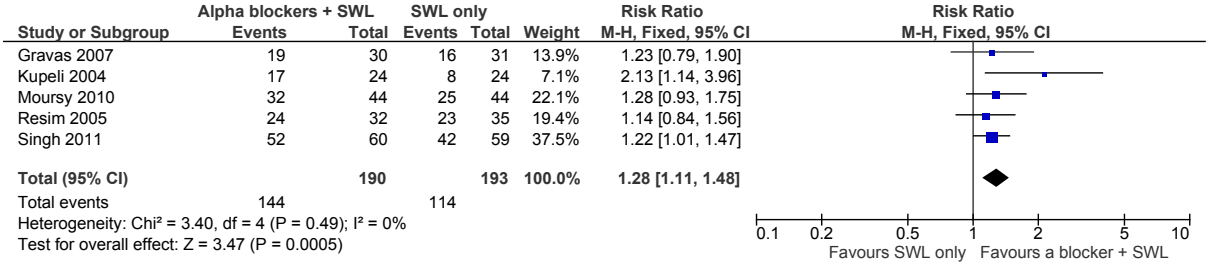


Figure 192: Hospitalisation

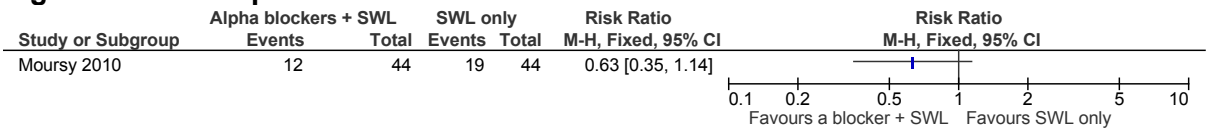


Figure 193: Adverse events (abnormal ejaculation)

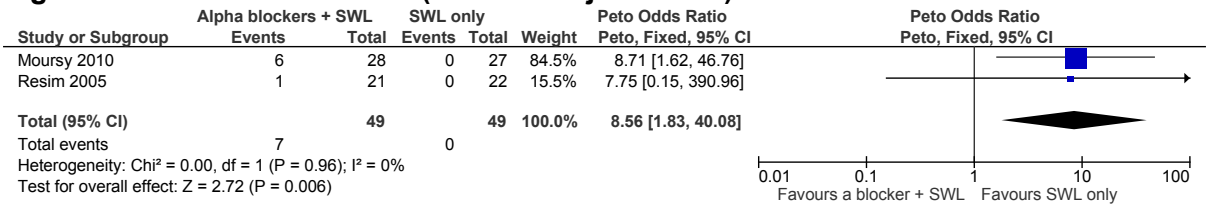


Figure 194: Adverse events (dizziness)

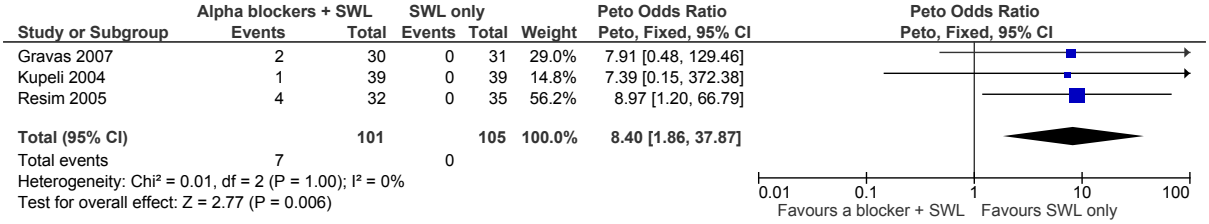


Figure 195: Adverse events (headache)

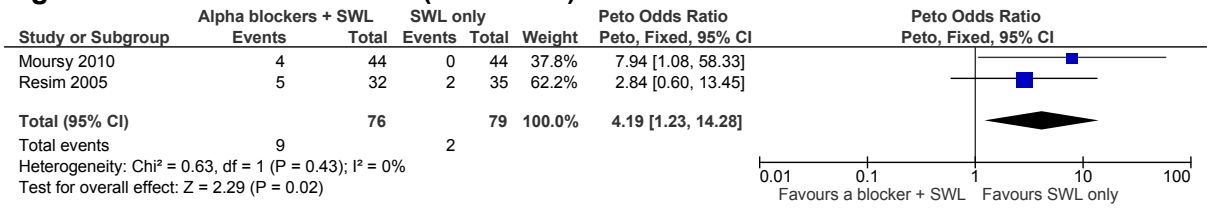


Figure 196: Adverse events (hypotension)

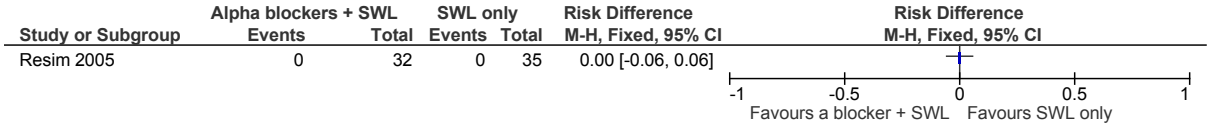


Figure 197: Analgesic use (number of analgesics)

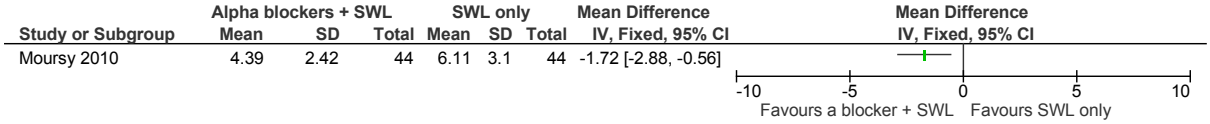
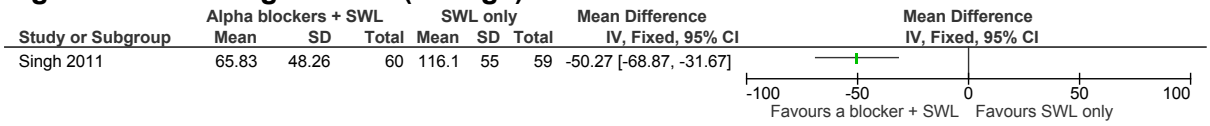


Figure 198: Analgesic use (dosage)



E.5.2 Alpha blockers as adjunctive therapy to ureteroscopy versus ureteroscopy only

Figure 199: Stone passage

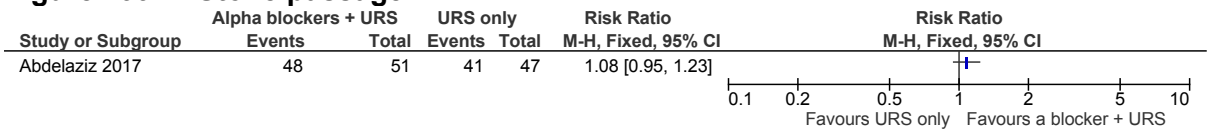
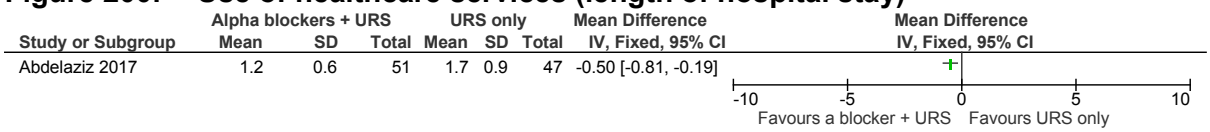


Figure 200: Use of healthcare services (length of hospital stay)



E.5.3 Alpha blockers as adjunctive therapy to ureteroscopy versus placebo and ureteroscopy

Figure 201: Stone passage

Study or Subgroup	Alpha blockers + URS Events	Total	Placebo + URS Events	Total	Risk Ratio M-H, Fixed, 95% CI
Ketabchi 2014	49	52	35	50	1.35 [1.11, 1.63]

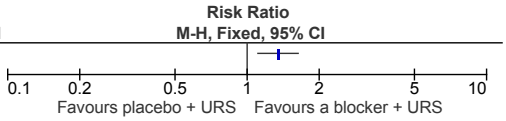


Figure 202: Pain intensity (colic episodes)

Study or Subgroup	Alpha blockers + URS Mean	SD	Total	Placebo + URS Mean	SD	Total	Mean Difference IV, Fixed, 95% CI
Ketabchi 2014	1	0.7	52	6	3.5	50	-5.00 [-5.99, -4.01]

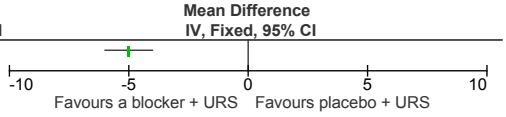
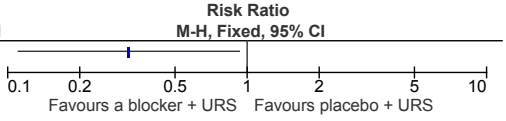


Figure 203: Analgesic use (number of people using analgesia)

Study or Subgroup	Alpha blockers + URS Events	Total	Placebo + URS Events	Total	Risk Ratio M-H, Fixed, 95% CI
Ketabchi 2014	4	52	12	50	0.32 [0.11, 0.93]



E.6 Adjunctive therapy: distal ureteric stones 10-20mm in adults

E.6.1 Alpha blockers as adjunctive therapy to shock wave lithotripsy versus shock wave lithotripsy only

Figure 204: Time to stone passage (days)

Study or Subgroup	Alpha blockers + SWL Mean	SD	Total	SWL only Mean	SD	Total	Mean Difference IV, Fixed, 95% CI
Basri 2013	9.86	6.94	14	12.42	9.38	24	-2.56 [-7.78, 2.66]

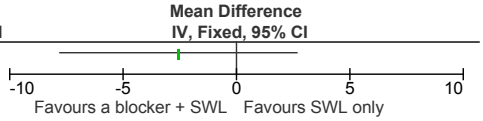
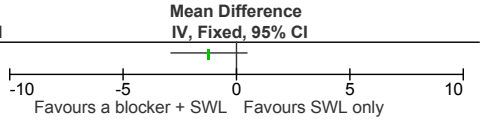


Figure 205: Pain intensity (VAS)

Study or Subgroup	Alpha blockers + SWL Mean	SD	Total	SWL only Mean	SD	Total	Mean Difference IV, Fixed, 95% CI
Basri 2013	2.79	2.42	14	4	2.71	24	-1.21 [-2.88, 0.46]



E.7 Adjunctive therapy: mid ureteric stones 10-20mm in adults

E.7.1 Alpha blockers as adjunctive therapy to shock wave lithotripsy versus shock wave lithotripsy only

Figure 206: Time to stone passage (days)

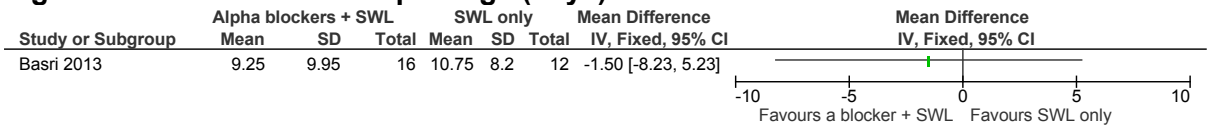
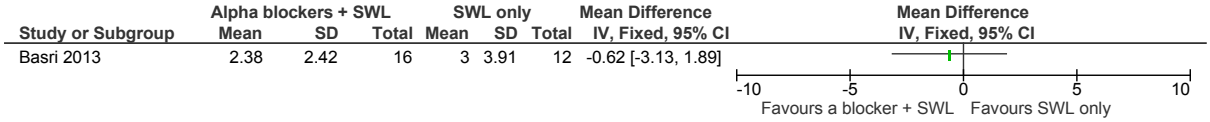


Figure 207: Pain intensity (VAS)



E.8 Adjunctive therapy: proximal ureteric stones <10mm in adults

E.8.1 Alpha blockers as adjunctive therapy to shock wave lithotripsy versus shock wave lithotripsy only

Figure 208: Time to stone passage (days)

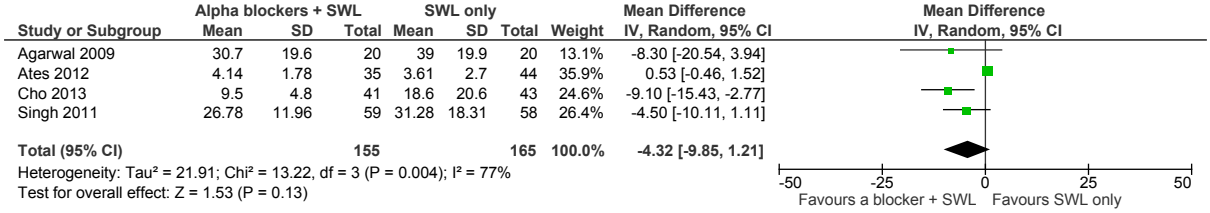


Figure 209: Stone passage

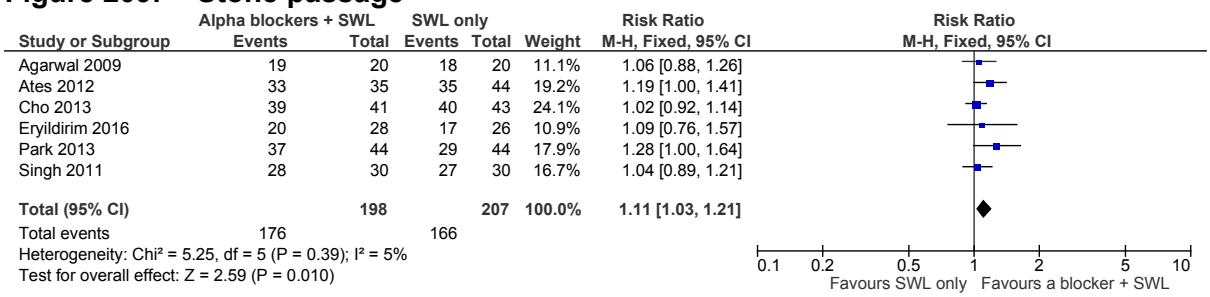


Figure 210: Hospitalisation

Study or Subgroup	Alpha blockers + SWL Mean	SD	Total	SWL only Mean	SD	Total	Mean Difference IV, Fixed, 95% CI
Ates 2012	0.51	0.7	35	0.52	0.62	44	-0.01 [-0.31, 0.29]

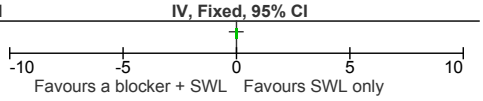


Figure 211: Use of healthcare services (ED visits)

Study or Subgroup	Alpha blockers + SWL Mean	SD	Total	SWL only Mean	SD	Total	Mean Difference IV, Fixed, 95% CI
Eryildirim 2016	0.82	0.9	28	1.42	1.07	26	-0.60 [-1.13, -0.07]

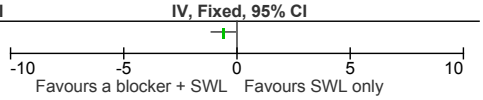


Figure 212: Quality of life (EQ5D)

Study or Subgroup	Alpha blockers + SWL Mean	SD	Total	SWL only Mean	SD	Total	Mean Difference IV, Fixed, 95% CI
Eryildirim 2016	0.82	0.11	28	0.78	0.09	26	0.04 [-0.01, 0.09]

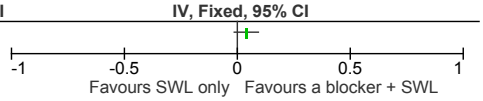


Figure 213: Quality of life (EQ5D VAS)

Study or Subgroup	Alpha blockers + SWL Mean	SD	Total	SWL only Mean	SD	Total	Mean Difference IV, Fixed, 95% CI
Eryildirim 2016	80.36	11.05	28	73.65	8.43	26	6.71 [1.49, 11.93]

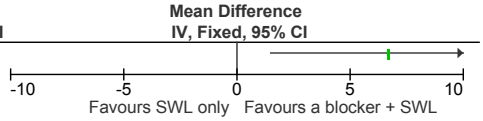


Figure 214: Adverse events (dizziness)

Study or Subgroup	Alpha blockers + SWL Events	Total	SWL only Events	Total	Weight	Peto Odds Ratio Peto, Fixed, 95% CI
Cho 2013	2	41	0	43	66.4%	7.95 [0.49, 129.44]
Park 2013	1	44	0	44	33.6%	7.39 [0.15, 372.38]
Total (95% CI)		**85**		**87**	**100.0%**	**7.76 [0.80, 75.32]**
Total events	3		0			

Heterogeneity: Chi² = 0.00, df = 1 (P = 0.98); I² = 0%
Test for overall effect: Z = 1.77 (P = 0.08)

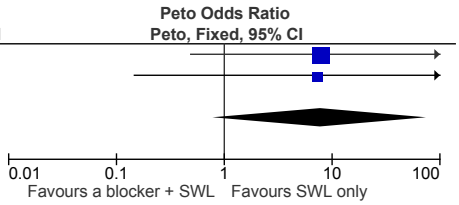


Figure 215: Adverse events (retrograde ejaculation)

Study or Subgroup	Alpha blockers + SWL Events	Total	SWL only Events	Total	Risk Difference M-H, Fixed, 95% CI
Cho 2013	0	41	0	43	0.00 [-0.05, 0.05]

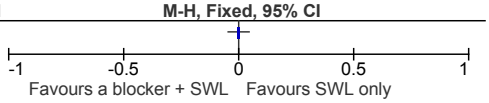


Figure 216: Pain intensity (VAS)

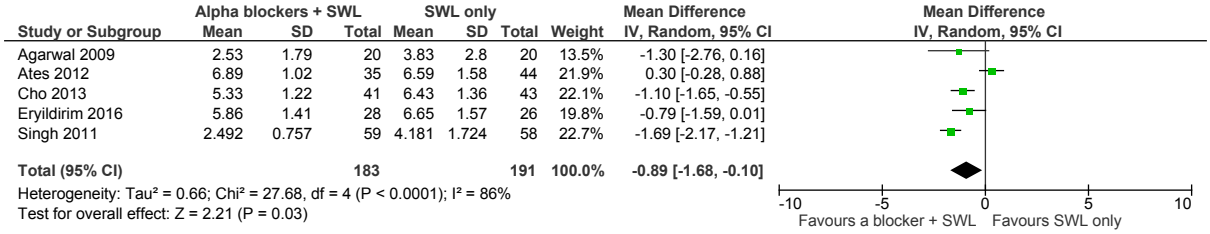


Figure 217: Pain intensity (colic episodes)

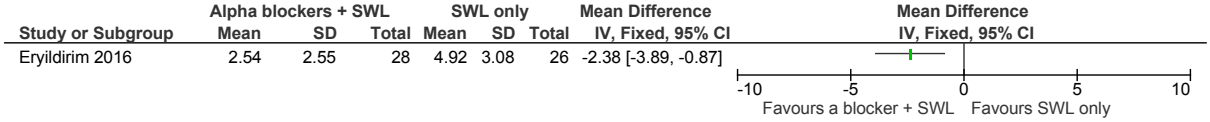


Figure 218: Analgesic use (dosage)

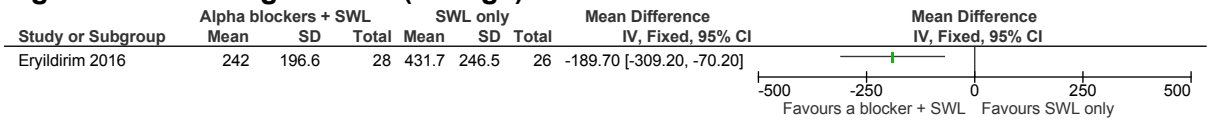
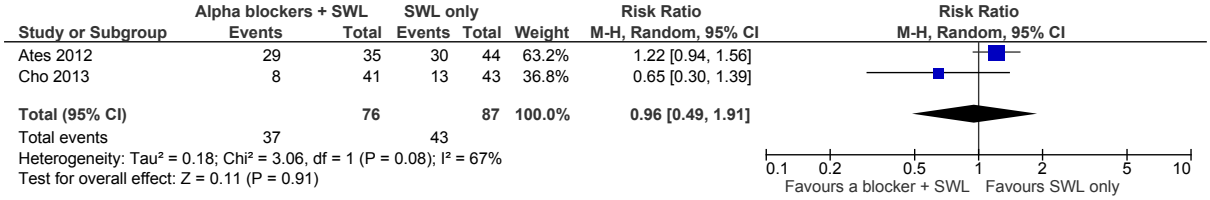


Figure 219: Analgesic use (number of people using analgesia)



E.8.2 Alpha blockers as adjunctive therapy to shock wave lithotripsy versus placebo and shock wave lithotripsy

Figure 220: Time to stone passage (days)

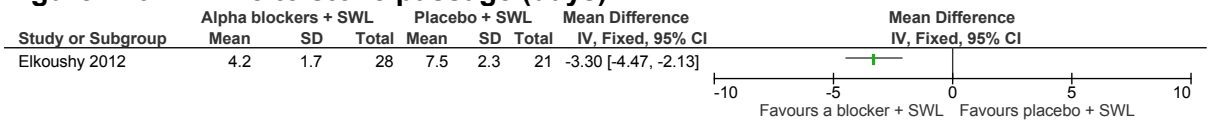
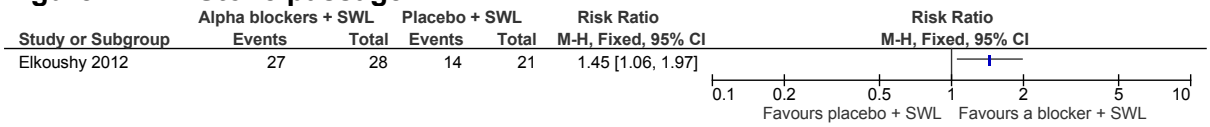


Figure 221: Stone passage



E.9 Adjunctive therapy: proximal ureteric stones 10-20mm in adults

E.9.1 Alpha blockers as adjunctive therapy to shock wave lithotripsy versus shock wave lithotripsy only

Figure 222: Time to stone passage (days)

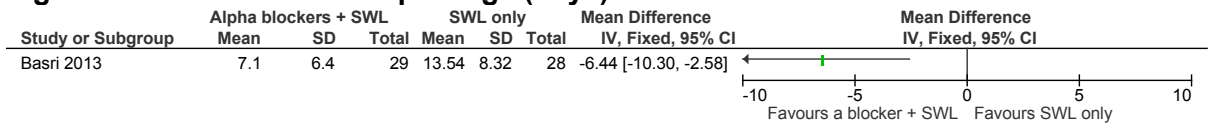


Figure 223: Stone passage

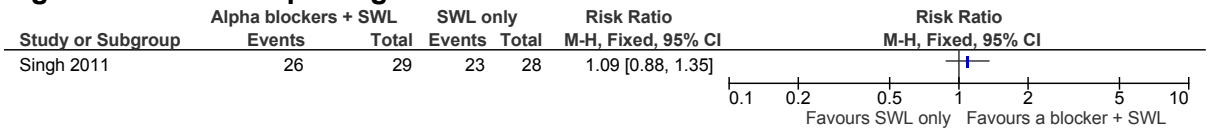
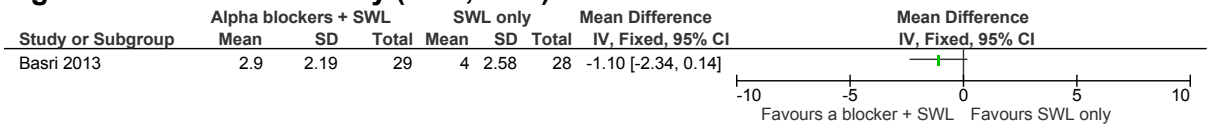


Figure 224: Pain intensity (VAS, 0-10)



E.9.2 Alpha blockers as adjunctive therapy to ureteroscopy versus ureteroscopy only

Figure 225: Time to stone passage (days)

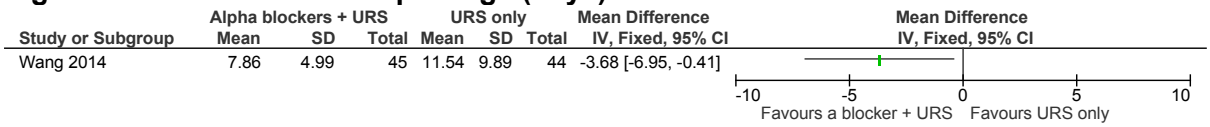


Figure 226: Stone passage

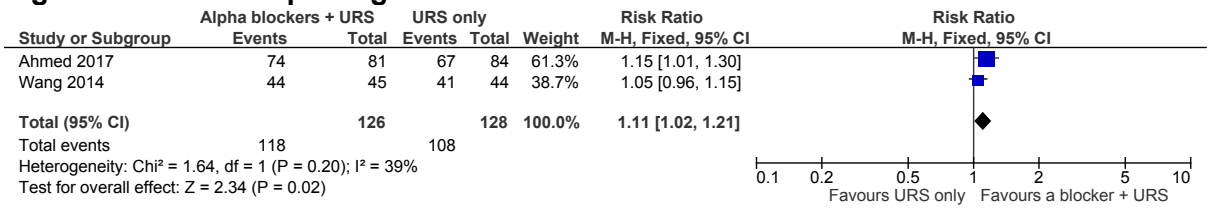


Figure 227: Use of healthcare services (Hospitalisation time)

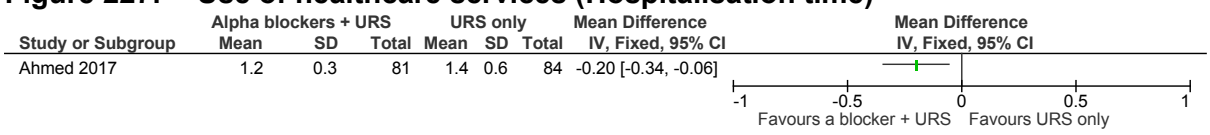


Figure 228: Hospitalisation (readmission)

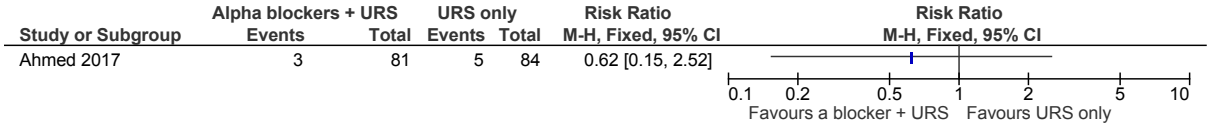


Figure 229: Adverse events (dizziness)

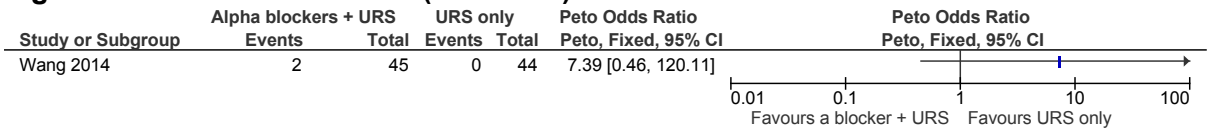
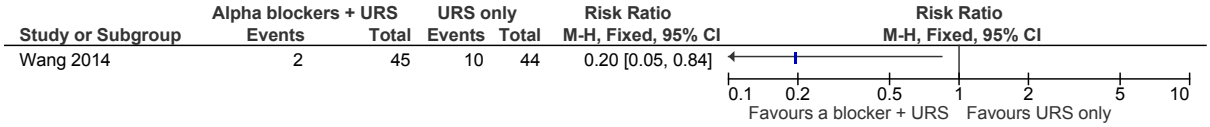


Figure 230: Pain intensity (colic episodes)



Appendix F: GRADE tables

Table 33: Clinical evidence profile: Alpha blockers versus placebo for distal ureteric stones <10mm in adults

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Alpha blockers	Placebo (<10mm)	Relative (95% CI)	Absolute		
Stone passage (follow-up 1-4 weeks; assessed with: number of people spontaneously passing stones during follow up)												
13	randomised trials	no serious risk of bias	serious[1]	no serious indirectness	serious[2]	none	2219/2614 (84.9%)	60.9%	RR 1.19 (1.09 to 1.29)	116 more per 1000 (from 55 more to 177 more)	⊕⊕OO LOW	CRITICAL
Time to stone passage (follow-up 2-4 weeks; measured with: mean number of days for spontaneous stone passage; Better indicated by lower values)												
6	randomised trials	very serious[3]	no serious inconsistency	no serious indirectness	serious[2]	none	1911	1877	-	MD 3.5 lower (2.66 to 3.93 lower)	⊕OOO VERY LOW	CRITICAL
Time to stone passage (follow-up 3 weeks; assessed with: mean number of hours for spontaneous stone passage)												
1	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	very serious[2]	none	-	0%	HR 0.99 (0.55 to 1.78)	-	⊕OOO VERY LOW	CRITICAL
Hospitalisation (follow-up 3-4 weeks; assessed with: number of people hospitalized during follow up)												
3	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[2]	none	26/292 (8.9%)	4.4%	RR 0.99 (0.59 to 1.64)	0 fewer per 1000 (from 18 fewer to 28 more)	⊕⊕OO LOW	CRITICAL

Hospitalisation (excess admission days) (follow-up 4 weeks; Better indicated by lower values)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	247	246	-	MD 0.03 lower (0.17 lower to 0.11 higher)	⊕⊕⊕⊕ HIGH	CRITICAL
Use of healthcare services (re-presentation to ED) (follow-up 4 weeks; assessed with: number of people who re-presented to ED during follow up)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[2]	none	31/198 (15.7%)	18%	RR 0.87 (0.56 to 1.36)	23 fewer per 1000 (from 79 fewer to 65 more)	⊕⊕OO LOW	CRITICAL
Use of healthcare services - Doctor visits (follow-up 4 weeks; Better indicated by lower values)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	224	215	-	MD 0.07 higher (0.04 lower to 0.18 higher)	⊕⊕⊕⊕ HIGH	CRITICAL
Use of healthcare services - Nurse visits (follow-up 4 weeks; Better indicated by lower values)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	224	215	-	MD 0.01 lower (0.04 lower to 0.02 higher)	⊕⊕⊕⊕ HIGH	CRITICAL
Use of healthcare services - Outpatient visits (follow-up 4 weeks; Better indicated by lower values)												
1	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	no serious imprecision	none	289	246	-	MD 0.01 lower (0.12 lower to 0.1 higher)	⊕⊕⊕O MODERATE	CRITICAL

Quality of life (SF36; 12 weeks) - SF36 physical component (follow-up 12 weeks; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	serious [3]	no serious inconsistency	no serious indirectness	serious[2]	none	100	110	-	MD 1.15 lower (3.75 lower to 1.45 higher)	⊕⊕OO LOW	CRITICAL
Quality of life (SF36; 12 weeks) - SF36 mental component (follow-up 12 weeks; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	serious [3]	no serious inconsistency	no serious indirectness	serious[2]	none	100	110	-	MD 1.79 lower (4.7 lower to 1.12 higher)	⊕⊕OO LOW	CRITICAL
Quality of life (EQ5D; 12 weeks) (follow-up 12 weeks; range of scores: 0-1; Better indicated by higher values)												
1	randomised trials	serious [3]	no serious inconsistency	no serious indirectness	no serious imprecision	none	103	114	-	MD 0.04 lower (0.1 lower to 0.02 higher)	⊕⊕⊕O MODERATE	CRITICAL
Adverse events (discontinuation due to AE)												
1	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	very serious[2]	none	15/149 (10.1%)	5.9%	RR 1.71 (0.77 to 3.79)	42 more per 1000 (from 14 fewer to 165 more)	⊕OOO VERY LOW	CRITICAL
Adverse events (unspecified) (follow-up 2-4 weeks; assessed with: number of people experiencing adverse events during follow up)												
3	randomised trials	very serious[3]	no serious inconsistency	serious[4]	no serious imprecision	none	17/205 (8.3%)	0%	RR 5.65 (1.5 to 21.29)	-	⊕OOO VERY LOW	CRITICAL
Adverse events (retrograde ejaculation) (follow-up 3-4 weeks; assessed with: number of people experiencing retrograde ejaculation during follow up)												

6	randomised trials	serious[3]	serious[1]	no serious indirectness	no serious imprecision	none	86/1868 (4.6%)	0%	Peto OR 1.78 (1.26 to 2.51)	20 more per 1000 (from 7 more to 32 more)[1]	⊕⊕OO LOW	CRITICAL
Adverse events (dizziness) (follow-up 1-4 weeks; assessed with: number of people experiencing dizziness during follow up)												
7	randomised trials	very serious[3]	no serious inconsistency	no serious indirectness	serious[2]	none	77/1990 (3.9%)	2.2%	RR 1.28 (0.92 to 1.79)	6 more per 1000 (from 2 fewer to 17 more)	⊕OOO VERY LOW	CRITICAL
Adverse events (headache) (follow-up 4 weeks; assessed with: number of people experiencing headache during follow up)												
4	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[2]	none	55/1879 (2.9%)	2.9%	RR 1.06 (0.72 to 1.56)	2 more per 1000 (from 8 fewer to 16 more)	⊕⊕OO LOW	CRITICAL
Adverse events (hypotension) (follow-up 4 weeks; assessed with: number of people experiencing hypotension during follow up)												
2	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	very serious[2]	none	1/118 (0.85%)	0%	Peto OR 6.82 (0.13 to 344.93)	9 more per 1000 (from 18 fewer to 35 more)[1]	⊕OOO VERY LOW	CRITICAL
Pain intensity (VAS score) (follow-up 4 weeks; range of scores: 0-10; Better indicated by lower values)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	137	142	-	MD 0.1 lower (0.49 lower to 0.29 higher)	⊕⊕⊕⊕ HIGH	IMPORTANT
Pain intensity (EQ5D No pain/discomfort) at 12 weeks												
1	randomised trials	serious [3]	no serious inconsistency	no serious indirectness	no serious imprecision	none	77/104 (74%)	77.4%	RR 0.96 (0.82 to 1.11)	31 fewer per 1000 (from 139 fewer to 85 more)	⊕⊕⊕O MODERATE	IMPORTANT

Pain intensity (EQ5D Moderate pain/discomfort) at 12 weeks												
1	randomised trials	serious [3]	no serious inconsistency	no serious indirectness	very serious[2]	none	22/104 (21.2%)	21.7%	RR 0.97 (0.59 to 1.62)	7 fewer per 1000 (from 89 fewer to 135 more)	⊕OOO VERY LOW	IMPORTANT
Pain intensity (EQ5D Extreme pain/discomfort) at 12 weeks												
1	randomised trials	serious [3]	no serious inconsistency	no serious indirectness	very serious[2]	none	5/104 (4.8%)	0.9%	RR 5.53 (0.66 to 46.55)	41 more per 1000 (from 3 fewer to 410 more)	⊕OOO VERY LOW	IMPORTANT
Pain intensity (pain episodes) (follow-up 4 weeks; assessed with: number of people experiencing episodes of renal colic)												
1	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	no serious imprecision	none	20/75 (26.7%)	77.3%	RR 0.34 (0.23 to 0.51)	510 fewer per 1000 (from 379 fewer to 595 fewer)	⊕⊕⊕O MODERATE	IMPORTANT
Pain intensity (pain episodes) (follow-up 2-4 weeks; measured with: mean number of pain episodes ; Better indicated by lower values)												
2	randomised trials	serious[3]	no serious inconsistency	no serious indirectness	serious[2]	none	112	107	-	MD 0.51 lower (0.86 to 0.15 lower)	⊕⊕OO LOW	IMPORTANT
Pain intensity (pain score >0) at 1 week (follow-up 1 weeks; assessed with: verbal numeric pain scale)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	142/185 (76.8%)	78.6%	RR 0.98 (0.88 to 1.09)	16 fewer per 1000 (from 94 fewer to 71 more)	⊕⊕⊕⊕ HIGH	IMPORTANT
Pain intensity (pain score >0) at 2 weeks (follow-up 2 weeks; assessed with: verbal numeric pain scale)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[2]	none	60/176 (34.1%)	32.8%	RR 1.04 (0.77 to 1.4)	13 more per 1000 (from 75	⊕⊕OO LOW	IMPORTANT

										fewer to 131 more)		
Pain intensity (pain score >0) at 3 weeks (follow-up 3 weeks; assessed with: verbal numeric pain scale)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[2]	none	34/170 (20%)	21.4%	RR 0.94 (0.62 to 1.42)	13 fewer per 1000 (from 81 fewer to 90 more)	⊕⊕OO LOW	IMPORTANT
Pain intensity (pain score >0) at 4 weeks (follow-up 4 weeks; assessed with: verbal numeric pain scale)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[2]	none	26/173 (15%)	16.1%	RR 0.93 (0.57 to 1.53)	11 fewer per 1000 (from 69 fewer to 85 more)	⊕⊕OO LOW	IMPORTANT
Analgesic use (follow-up 4 weeks; assessed with: number of people using analgesics during follow up period)												
3	randomised trials	serious[3]	very serious[1]	no serious indirectness	very serious[2]	none	115/1838 (6.3%)	39.6%	RR 0.45 (0.13 to 1.54)	218 fewer per 1000 (from 345 fewer to 214 more)	⊕OOO VERY LOW	IMPORTANT
Analgesic use (number of times) (follow-up 4-12 weeks; measured with: mean number of times analgesics were used during follow up; Better indicated by lower values)												
2	randomised trials	serious[3]	no serious inconsistency	serious[4]	no serious imprecision	none	84	81	-	MD 0.9 lower (1.35 to 0.45 lower)	⊕⊕⊕O MODERATE	IMPORTANT
Analgesic use (Buprenorphine dose) (measured with: mean dose of Buprenorphine used during follow up ; Better indicated by lower values)												
2	randomised trials	very serious[3]	no serious inconsistency	no serious indirectness	no serious imprecision	none	157	159	-	MD 0.07 lower (0.12 to 0.02 lower)	⊕⊕OO LOW	IMPORTANT
Analgesic use (Ketorolac dose) (follow-up 2 weeks; measured with: mean dose of Ketorolac used during follow up; Better indicated by lower values)												
2	randomised trials	very serious[3]	no serious inconsistency	no serious indirectness	no serious imprecision	none	156	159	-	MD 97.44 lower (124.25 to 70.62 lower)	⊕⊕OO LOW	IMPORTANT

Analgesic use (Diclofenac dose) (follow-up 4 weeks; measured with: mean dose of Diclofenac used during follow up; Better indicated by lower values)												
2	randomised trials	no serious risk of bias	very serious[1]	no serious indirectness	no serious imprecision	none	1692	1700	-	MD 149.03 lower (152.37 to 145.68 lower)	⊕⊕OO LOW	IMPORTANT
Analgesic use (days) (Better indicated by lower values)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	74	79	-	MD 0.41 higher (2.36 lower to 3.18 higher)	⊕⊕⊕⊕ HIGH	IMPORTANT

[1] Downgraded by 1 or 2 increments because the point estimate varies widely across studies, the confidence intervals across studies show minimal or no overlap, or heterogeneity, I2>50%, p<0.05, 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

[3] 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

[4] Downgraded by 1 or 2 increments because the majority of the evidence included an indirect population (downgrade by one increment) or a very indirect population (downgrade by two increments)

Table 34: Clinical evidence profile: Alpha blockers versus no treatment (pain management only) for distal ureteric stones <10mm in adults

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Alpha blockers**	**No treatment (pain management only) (<10mm)**	**Relative (95% CI)**	**Absolute**		
Stone passage (follow-up 10 days - 8 weeks ; assessed with: number of people spontaneously passing stones during follow up)												
32	randomised trials	very serious[1]	serious[1]	no serious indirectness	no serious imprecision	none	1144/1430 (80%)	50.6%	RR 1.64 (1.49 to 1.81)	324 more per 1000 (from 248 more to 410 more)	⊕OOO VERY LOW	CRITICAL
Time to stone passage (days) (follow-up 2-8 weeks; measured with: mean number of days for spontaneous stone passage ; Better indicated by lower values)												

18	randomised trials	very serious[1]	very serious[1]	no serious indirectness	no serious imprecision	none	967	675	-	MD 4.28 lower (5.36 to 3.2 lower)	⊕OOO VERY LOW	CRITICAL
Adverse events (unspecified) (follow-up 10 days - 4 weeks ; assessed with: number of people experiencing adverse events during follow up)												
9	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	10/407 (2.5%)	0%	Peto OR 5.89 (1.57 to 22.13)	-	⊕⊕OO LOW	CRITICAL
Adverse events (dizziness) (follow-up 2-6 weeks; assessed with: number of people experiencing dizziness during follow up)												
7	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[3]	none	23/277 (8.3%)	0%	RR 1.34 (0.74 to 2.4)	-	⊕OOO VERY LOW	CRITICAL
Adverse events (hypotension) (assessed with: number of people experiencing hypotension during follow up)												
8	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	11/366 (3%)	0%	Peto OR 5.72 (1.65 to 19.87)	-	⊕⊕OO LOW	CRITICAL
Adverse events (retrograde ejaculation) (follow-up 2-8 weeks; assessed with: number of people experiencing retrograde ejaculation during follow up)												
5	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[3]	none	4/223 (1.8%)	0.8%	Peto OR 2.05 (0.32 to 13.08)	8 more per 1000 (from 6 fewer to 89 more)	⊕OOO VERY LOW	CRITICAL
Adverse events (headache) (follow-up 2-6 weeks; assessed with: number of people experiencing headache during follow up)												
2	randomised trials	very serious[1]	no serious inconsistency	serious[2]	very serious[3]	none	8/100 (8%)	6.7%	RR 1.48 (0.47 to 4.69)	32 more per 1000 (from 36 fewer to 247 more)	⊕OOO VERY LOW	CRITICAL
Hospitalisation (follow-up 2-4 weeks; assessed with: number of people admitted to hospital during follow up)												

8	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	18/330 (5.5%)	10.2%	RR 0.3 (0.18 to 0.49)	71 fewer per 1000 (from 52 fewer to 84 fewer)	⊕⊕OO LOW	CRITICAL
Use of healthcare services (return to ED/primary care visit) (follow-up 2 weeks; assessed with: number of people returning to ED or having an unscheduled primary care visit)												
2	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[3]	none	6/104 (5.8%)	10.3%	RR 0.77 (0.29 to 2.01)	24 fewer per 1000 (from 73 fewer to 104 more)	⊕OOO VERY LOW	CRITICAL
Pain intensity (follow-up 10 days-4 weeks; assessed with: number of people experiencing pain during follow up)												
3	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[3]	none	56/121 (46.3%)	79.3%	RR 0.77 (0.64 to 0.94)	182 fewer per 1000 (from 48 fewer to 285 fewer)	⊕OOO VERY LOW	IMPORTANT
Pain intensity (colicky pain episodes) (follow-up 2 weeks; measured with: mean number of colicky pain episodes; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[3]	none	0	-	-	MD 0.05 lower (4.81 lower to 4.71 higher)	⊕OOO VERY LOW	IMPORTANT
Pain intensity (pain episodes) (follow-up 2-4 weeks; measured with: mean number of pain episodes during follow up; Better indicated by lower values)												
11	randomised trials	very serious[1]	very serious[1]	no serious indirectness	serious[1]	none	655	422	-	MD 0.68 lower (0.93 to 0.44 lower)	⊕OOO VERY LOW	IMPORTANT
Pain intensity (VAS score) at 3 days (follow-up 3 days; measured with: visual analogue scale; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	70	33	-	MD 1.37 higher (0.84 to 1.90 higher)	⊕⊕OO LOW	IMPORTANT
Pain intensity (VAS score) at 7 days (follow-up 7 days; measured with: visual analogue scale ; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	70	33	-	MD 1.63 higher (1.2 to 2.06 higher)	⊕⊕OO LOW	IMPORTANT

Analgesic use (follow-up 10 days-4 weeks; assessed with: number of people using analgesics)												
4	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	25/166 (15.1%)	48.5%	RR 0.42 (0.29 to 0.62)	281 fewer per 1000 (from 184 fewer to 344 fewer)	⊕⊕OO LOW	IMPORTANT
Analgesic use (number of times) (measured with: mean number of times analgesics were used during follow up ; Better indicated by lower values)												
4	randomised trials	very serious[1]	very serious[1]	no serious indirectness	serious[1]	none	210	211	-	MD 1.18 lower (2.49 lower to 0.13 higher)	⊕OOO VERY LOW	IMPORTANT
Analgesic use (Diclofenac dose) (follow-up 3-4 weeks; measured with: mean Diclofenac dose during follow up; Better indicated by lower values)												
3	randomised trials	very serious[1]	very serious[4]	no serious indirectness	no serious imprecision	none	146	144	-	MD 169.99 lower (314.6 to 25.37 lower)	⊕OOO VERY LOW	IMPORTANT
Analgesic use (days) (follow-up 2 weeks; measured with: mean number of days analgesics were used ; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[3]	none	0	-	-	MD 4.94 lower (12.04 lower to 2.16 higher)	⊕OOO VERY LOW	IMPORTANT
Analgesic use (Pethidine dose) (follow-up 4 weeks; measured with: mean dose of Pethidine used during follow up ; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	32	32	-	MD 27.7 lower (33.41 to 21.99 lower)	⊕⊕OO LOW	IMPORTANT
Analgesic use (Ketorolac dose) (follow-up 2 weeks; measured with: mean dose of Ketorolac used during follow up; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	64	62	-	MD 103.5 lower (141.57 to 65.43 lower)	⊕⊕OO LOW	IMPORTANT
Analgesic use (Buprenorphine dose) (follow-up 2 weeks; measured with: mean dose of Buprenorphine during follow up ; Better indicated by lower values)												

1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	64	62	-	MD 0.01 lower (0.12 lower to 0.09 higher)	⊕⊕OO LOW	IMPORTANT

[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 or 2 increments because the majority of the evidence included an indirect population or the majority of the evidence had indirect outcomes
[3] Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs
[4] Downgraded by 1 or 2 increments because the point estimate varies widely across studies, the confidence intervals across studies show minimal or no overlap or heterogeneity, I2>50%, p<0.04, unexplained by subgroup analysis

Table 35: Clinical evidence profile: Calcium channel blockers versus placebo for distal ureteric stones <10mm in adults

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Calcium channel blockers**	**placebo (<10mm)**	**Relative (95% CI)**	**Absolute**		
Stone passage rate												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	214/247 (86.6%)	82.1%	RR 1.06 (0.98 to 1.14)	49 more per 1000 (from 16 fewer to 115 more)	⊕⊕⊕⊕ HIGH	CRITICAL
Time to stone passage (Better indicated by lower values)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	53	60	-	MD 0 higher (5.28 lower to 5.28 higher)	⊕⊕⊕⊕ HIGH	CRITICAL
Adverse events (discontinuation due to AE)												

1	randomised trials	serious [1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	29/162 (17.9%)	5.9%	RR 3.04 (1.49 to 6.22)	120 more per 1000 (from 29 more to 308 more)	⊕⊕⊕O MODERATE	CRITICAL
Analgesic use												
1	randomised trials	serious [1]	no serious inconsistency	no serious indirectness	serious[2]	none	81/161 (50.3%)	53.6%	RR 0.94 (0.76 to 1.16)	32 fewer per 1000 (from 129 fewer to 86 more)	⊕⊕OO LOW	IMPORTANT
Analgesic use (days) (Better indicated by lower values)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	78	79	-	MD 1.22 lower (3.9 lower to 1.46 higher)	⊕⊕⊕⊕ HIGH	IMPORTANT
Quality of life (12 weeks) - SF36 physical component (follow-up 12 weeks; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	serious [1]	no serious inconsistency	no serious indirectness	very serious[2]	none	116	110	-	MD 0.11 lower (2.38 lower to 2.16 higher)	⊕OOO VERY LOW	CRITICAL
Quality of life (12 weeks) - SF36 mental component (follow-up 12 weeks; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	serious [1]	no serious inconsistency	no serious indirectness	serious[2]	none	116	110	-	MD 0.49 lower (3.09 lower to 2.11 higher)	⊕⊕OO LOW	CRITICAL
Quality of life (EQ5D) (follow-up 12 weeks; range of scores: 0-1; Better indicated by higher values)												
1	randomised trials	serious [1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	123	114	-	MD 0.02 lower (0.08 lower to 0.03 higher)	⊕⊕⊕O MODERATE	CRITICAL

Pain intensity (VAS scale) (follow-up 4 weeks; range of scores: 0-10; Better indicated by lower values)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	155	142	-	MD 0.05 lower (0.52 lower to 0.42 higher)	⊕⊕⊕⊕ HIGH	IMPORTANT
Pain intensity (EQ5D no pain/discomfort) (follow-up 12 weeks)												
1	randomised trials	serious [1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	92/123 (74.8%)	77.4%	RR 0.97 (0.84 to 1.11)	23 fewer per 1000 (from 124 fewer to 85 more)	⊕⊕⊕O MODERATE	IMPORTANT
Pain intensity (EQ5D moderate pain/discomfort) (follow-up 12 weeks)												
1	randomised trials	serious [1]	no serious inconsistency	no serious indirectness	very serious[2]	none	28/123 (22.8%)	21.7%	RR 1.05 (0.65 to 1.68)	11 more per 1000 (from 76 fewer to 148 more)	⊕OOO VERY LOW	IMPORTANT
Pain intensity (EQ5D extreme pain/discomfort) (follow-up 12 weeks)												
1	randomised trials	serious [1]	no serious inconsistency	no serious indirectness	very serious[2]	none	3/123 (2.4%)	0.9%	RR 2.8 (0.3 to 26.58)	16 more per 1000 (from 6 fewer to 230 more)	⊕OOO VERY LOW	IMPORTANT
Use of healthcare services - Doctor visits (follow-up 4 weeks; Better indicated by lower values)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	226	215	-	MD 0.08 higher (0.04 lower to 0.2 higher)	⊕⊕⊕⊕ HIGH	CRITICAL
Use of healthcare services - Nurse visits (follow-up 4 weeks; Better indicated by lower values)												

1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	226	215	-	MD 0.01 higher (0.04 lower to 0.02 higher)	⊕⊕⊕⊕ HIGH	CRITICAL
Use of healthcare services - Outpatient visits (follow-up 4 weeks; Better indicated by lower values)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	246	246	-	MD 0.05 lower (0.17 lower to 0.07 higher)	⊕⊕⊕⊕ HIGH	CRITICAL
Hospitalisation (excess admission days) (follow-up 4 weeks; Better indicated by lower values)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	247	246	-	MD 0.01 lower (0.17 lower to 0.15 higher)	⊕⊕⊕⊕ HIGH	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 36: Clinical evidence profile: Calcium channel blockers versus no treatment (pain management only) for distal ureteric stones <10mm in adults

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Calcium channel blockers**	**no treatment (pain management only) (<10mm)**	**Relative (95% CI)**	**Absolute**		
Stone passage (follow-up 4 weeks; assessed with: number of people spontaneously passing stones during follow up)												

3	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	59/91 (64.8%)	36%	RR 1.95 (1.4 to 2.71)	342 more per 1000 (from 144 more to 616 more)	⊕⊕⊕O MODERATE	CRITICAL
Time to stone passage (follow-up 4 weeks; measured with: mean number of days for spontaneous stone passage ; Better indicated by lower values)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	35	35	-	MD 0.29 lower (4.13 lower to 3.55 higher)	⊕⊕⊕O MODERATE	CRITICAL
Hospitalisation (follow-up 4 weeks; assessed with: number of people admitted to hospital during follow up)												
2	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	11/66 (16.7%)	38.6%	RR 0.41 (0.24 to 0.69)	228 fewer per 1000 (from 120 fewer to 293 fewer)	⊕⊕⊕O MODERATE	CRITICAL
Pain intensity (pain episodes) (follow-up 4 weeks; measured with: mean number of pain episodes during follow up; Better indicated by lower values)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	35	35	-	MD 0.09 higher (0.41 lower to 0.59 higher)	⊕⊕OO LOW	IMPORTANT
Adverse events (hypotension) (follow-up 4 weeks; assessed with: number of people experiencing hypotension during follow up)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	1/31 (3.2%)	0%	Peto OR 6.71 (0.13 to 339.76)	-	⊕OOO VERY LOW	CRITICAL
Adverse events (dizziness) (follow-up 4 weeks; assessed with: number of people experiencing dizziness during follow up)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	0/25 (0%)	0%	see comment	0 fewer per 1000 (7 fewer to 7 more)[3]	⊕⊕OO LOW	CRITICAL
Analgesic use (Diclofenac dose) (follow-up 4 weeks; measured with: mean Diclofenac dose during follow up ; Better indicated by lower values)												

1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	25	25	-	MD 806 lower (1103.31 to 508.69 lower)	⊕⊕OO LOW	IMPORTANT

[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
[3] Risk difference calculated in Review Manager

Table 37: Clinical evidence profile: Alpha blockers versus Calcium channel blockers for distal ureteric stones <10mm in adults

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Alpha blockers**	**Calcium channel blockers (<10mm)**	**Relative (95% CI)**	**Absolute**		
Stone passage (follow-up 4 weeks; assessed with: number of people spontaneously passing stones during follow up)												
7	randomised trials	serious[1]	serious[2]	no serious indirectness	serious[3]	none	1948/2103 (92.6%)	68%	RR 1.2 (1.05 to 1.39)	136 more per 1000 (from 34 more to 265 more)	⊕OOO VERY LOW	CRITICAL
Time to stone passage (follow-up 4 weeks; measured with: mean number of days for spontaneous stone passage ; Better indicated by lower values)												
2	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	94	88	-	MD 0.16 higher (2.53 lower to 2.85 higher)	⊕⊕⊕O MODERATE	CRITICAL
Hospitalisation (follow-up 4 weeks; assessed with: number of people requiring hospitalisation during follow up)												
2	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[3]	none	5/67 (7.5%)	15.7%	RR 0.45 (0.18 to 1.17)	86 fewer per 1000 (from 129 fewer to 27 more)	⊕⊕OO LOW	CRITICAL

Hospitalisation (excess admission days) (follow-up 4 weeks; Better indicated by lower values)											
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	247	247	-	MD 0.02 lower (0.15 lower to 0.11 higher)	⊕⊕⊕⊕ HIGH	CRITICAL
Use of healthcare services - Doctor visits (follow-up 4 weeks; Better indicated by lower values)											
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	224	226	-	MD 0.01 lower (0.13 lower to 0.11 higher)	⊕⊕⊕⊕ HIGH	CRITICAL
Use of healthcare services - Nurse visits (follow-up 4 weeks; Better indicated by lower values)											
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	224	226	-	MD 0 higher (0.02 lower to 0.02 higher)	⊕⊕⊕⊕ HIGH	CRITICAL
Use of healthcare services - Outpatient visits (follow-up 4 weeks; Better indicated by lower values)											
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	289	246	-	MD 0.04 higher (0.07 lower to 0.15 higher)	⊕⊕⊕O MODERATE	CRITICAL
Quality of life (12 weeks) - SF36 physical component (follow-up 12 weeks; range of scores: 0-100; Better indicated by higher values)											
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[3]	none	100	116	-	MD 0.15 lower (2.68 lower to 2.38 higher)	⊕OOO VERY LOW	CRITICAL

Quality of life (12 weeks) - SF36 mental component (follow-up 12 weeks; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	serious [1]	no serious inconsistency	no serious indirectness	serious[3]	none	100	116	-	MD 1.3 lower (4.26 lower to 1.66 higher)	⊕⊕OO LOW	CRITICAL
Quality of life (EQ5D) (follow-up 12 weeks; range of scores: 0-1; Better indicated by higher values)												
1	randomised trials	serious [1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	103	123	-	MD 0.01 lower (0.08 lower to 0.05 higher)	⊕⊕⊕O MODERATE	CRITICAL
Adverse events (headache) (follow-up 4 weeks; assessed with: number of people experiencing headache during follow up)												
1	randomised trials	serious [1]	no serious inconsistency	no serious indirectness	very serious[3]	none	32/64 (50%)	43.1%	RR 1.16 (0.79 to 1.7)	69 more per 1000 (from 91 fewer to 302 more)	⊕OOO VERY LOW	CRITICAL
Adverse events (discontinuation due to AE)												
1	randomised trials	serious [1]	no serious inconsistency	no serious indirectness	serious[3]	none	15/149 (10.1%)	17.9%	RR 0.56 (0.31 to 1.01)	79 fewer per 1000 (from 124 fewer to 2 more)	⊕⊕OO LOW	CRITICAL
Adverse events (dizziness) (follow-up 4 weeks; assessed with: number of people experiencing dizziness during follow up)												
2	randomised trials	very serious[1]	no serious inconsistency	serious[4]	no serious imprecision	none	18/89 (20.2%)	2.6%	RR 4.86 (1.62 to 14.56)	100 more per 1000 (from 16	⊕OOO VERY LOW	CRITICAL

										more to 353 more)		
Adverse events (hypotension) (follow-up 4 weeks; assessed with: number of people experiencing hypotension during follow up)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[3]	none	0/32 (0%)	3.2%	Peto OR 0.13 (0 to 6.61)	28 fewer per 1000 (from 32 fewer to 147 more)	⊕OOO VERY LOW	CRITICAL
Adverse events (not specified) (follow-up 4 weeks; assessed with: number of people experiencing adverse events during follow up)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[3]	none	90/1596 (5.6%)	6.2%	RR 0.92 (0.69 to 1.21)	5 fewer per 1000 (from 19 fewer to 13 more)	⊕OOO VERY LOW	CRITICAL
Adverse events (flushing) (follow-up 4 weeks; assessed with: number of people experiencing flushing during follow up)												
1	randomised trials	very serious[1]	no serious inconsistency	serious[4]	serious[3]	none	0/64 (0%)	5.2%	Peto OR 0.12 (0.01 to 1.16)	45 fewer per 1000 (from 51 fewer to 8 more)	⊕OOO VERY LOW	CRITICAL
Analgesic use (mg) (follow-up 4 weeks; measured with: mean Diclofenac mg used during follow up; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[3]	none	25	25	-	MD 58 lower (315.47 lower to 199.47 higher)	⊕OOO VERY LOW	IMPORTANT
Analgesic use (follow-up 4 weeks; assessed with: number of people using analgesics during follow up)												

2	randomised trials	serious[1]	very serious[2]	no serious indirectness	serious[3]	none	99/1743 (5.7%)	27.6%	RR 0.57 (0.16 to 2.01)	119 fewer per 1000 (from 232 fewer to 279 more)	⊕OOO VERY LOW	IMPORTANT
Analgesic use (follow-up 4-12 weeks; measured with: mean analgesic use ; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	64	58	-	MD 0.77 lower (0.93 to 0.61 lower)	⊕⊕OO LOW	IMPORTANT
Pain intensity (pain episodes) (follow-up 4 weeks; measured with: mean number of pain episodes; Better indicated by lower values)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	35	35	-	MD 1.11 lower (1.54 to 0.68 lower)	⊕⊕⊕O MODERATE	IMPORTANT
Pain intensity (EQ5D no pain/discomfort) (follow-up 12 weeks)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	77/104 (74%)	74.8%	RR 0.99 (0.85 to 1.15)	7 fewer per 1000 (from 112 fewer to 112 more)	⊕⊕⊕O MODERATE	IMPORTANT
Pain intensity (EQ5D moderate pain/discomfort) (follow-up 12 weeks)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[3]	none	22/104 (21.2%)	22.8%	RR 0.93 (0.57 to 1.52)	16 fewer per 1000 (from 98 fewer to 119 more)	⊕OOO VERY LOW	IMPORTANT
Pain intensity (EQ5D extreme pain/discomfort) (follow-up 12 weeks)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[3]	none	5/104 (4.8%)	2.4%	RR 1.97 (0.48 to 8.05)	23 more per 1000 (from 12 fewer to 169 more)	⊕OOO VERY LOW	IMPORTANT
Pain intensity (VAS score) (follow-up 4 weeks; range of scores: 0-10; Better indicated by lower values)												

1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	137	155	-	MD 0.05 lower (0.49 lower to 0.39 higher)	⊕⊕⊕⊕ HIGH	IMPORTANT
Analgesic use (days) (Better indicated by lower values)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[3]	none	74	78	-	MD 1.63 higher (1.03 lower to 4.29 higher)	⊕⊕⊕O MODERATE	IMPORTANT

[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 or 2 increments because the point estimate varies widely across studies, the confidence intervals across studies show minimal or no overlap, or heterogeneity, I2>75%, p<0.05, unexplained by subgroup analysis.
[3] Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs
[4] Downgraded by 1 or 2 increments because the majority of the evidence included an indirect population (downgrade by one increment) or a very indirect population (downgrade by two increments) or the majority of the evidence had indirect outcomes

Table 38: Clinical evidence profile: Alpha blockers versus placebo for mid ureteric stones <10mm in adults

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Alpha blockers**	**Placebo (<10mm)**	**Relative (95% CI)**	**Absolute**		
Stone passage rate												
2	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	37/61 (60.7%)	64.7%	RR 0.86 (0.67 to 1.09)	91 fewer per 1000 (from 214 fewer to 58 more)	⊕⊕⊕O MODERATE	CRITICAL
Time to stone passage (days) (Better indicated by lower values)												

1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[2]	none	8	13	-	MD 7.73 higher (5.09 lower to 20.55 higher)	⊕⊕OO LOW	CRITICAL
Quality of life (SF36; 12 weeks) - SF36 physical component (follow-up 12 weeks; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	serious [1]	no serious inconsistency	no serious indirectness	very serious[2]	none	26	24	-	MD 0.64 lower (5.9 lower to 4.62 higher)	⊕OOO VERY LOW	CRITICAL
Quality of life (SF36; 12 weeks) - SF36 mental component (follow-up 12 weeks; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	serious [1]	no serious inconsistency	no serious indirectness	serious[2]	none	26	24	-	MD 4.86 lower (11.01 lower to 1.29 higher)	⊕⊕OO LOW	CRITICAL
Quality of life (EQ5D; 12 weeks) (follow-up 12 weeks; range of scores: 0-1; Better indicated by higher values)												
1	randomised trials	serious [1]	no serious inconsistency	no serious indirectness	serious[2]	none	28	28	-	MD 0.09 lower (0.21 lower to 0.03 higher)	⊕⊕OO LOW	CRITICAL
Analgesic use (pain medication use)												
1	randomised trials	serious [1]	no serious inconsistency	no serious indirectness	very serious[2]	none	22/32 (68.8%)	61.3%	RR 1.12 (0.78 to 1.61)	74 more per 1000 (from 135 fewer to 374 more)	⊕OOO VERY LOW	IMPORTANT
Analgesic use (number of days of pain medication use) (Better indicated by lower values)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[2]	none	22	19	-	MD 3.98 higher (0.55 lower to 8.51 higher)	⊕⊕OO LOW	IMPORTANT

Pain intensity (EQ5D no pain/discomfort; 12 weeks) (follow-up 12 weeks)												
1	randomised trials	serious [1]	no serious inconsistency	no serious indirectness	very serious[2]	none	17/28 (60.7%)	67.9%	RR 0.89 (0.6 to 1.32)	75 fewer per 1000 (from 272 fewer to 217 more)	⊕OOO VERY LOW	IMPORTANT
Pain intensity (EQ5D moderate pain/discomfort; 12 weeks) (follow-up 12 weeks)												
1	randomised trials	serious [1]	no serious inconsistency	no serious indirectness	very serious[2]	none	9/28 (32.1%)	32.1%	RR 1 (0.47 to 2.14)	0 fewer per 1000 (from 170 fewer to 366 more)	⊕OOO VERY LOW	IMPORTANT
Pain intensity (EQ5D extreme pain/discomfort; 12 weeks) (follow-up 12 weeks)												
1	randomised trials	serious [1]	no serious inconsistency	no serious indirectness	very serious[2]	none	2/28 (7.1%)	0%	Peto OR 6.89 (0.42 to 113.67)	71 more per 1000 (from 44 fewer to 186 more)[3]	⊕OOO VERY LOW	IMPORTANT
Pain intensity (VAS) (follow-up 4 weeks; range of scores: 0-10; Better indicated by lower values)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	31	28	-	MD 0.44 higher (0.88 lower to 1.76 higher)	⊕⊕⊕O MODERATE	IMPORTANT
Adverse events (discontinuation due to AE)												

1	randomised trials	serious [1]	no serious inconsistency	no serious indirectness	very serious[2]	none	2/32 (6.3%)	9.7%	RR 0.65 (0.12 to 3.61)	34 fewer per 1000 (from 85 fewer to 253 more)	⊕OOO VERY LOW	CRITICAL
Use of healthcare services - Doctor visits (follow-up 4 weeks; Better indicated by lower values)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	35	39	-	MD 0.09 lower (0.26 lower to 0.44 higher)	⊕⊕⊕O MODERATE	CRITICAL
Use of healthcare services - Nurse visits (follow-up 4 weeks; Better indicated by lower values)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[2]	none	35	39	-	MD 0.17 lower (0.12 lower to 0.46 higher)	⊕⊕OO LOW	CRITICAL
Use of healthcare services - Outpatient visits (follow-up 4 weeks; Better indicated by lower values)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	41	44	-	MD 0.05 lower (0.27 lower to 0.37 higher)	⊕⊕⊕O MODERATE	CRITICAL
Hospitalisation (excess admissions days) (follow-up 4 weeks; Better indicated by lower values)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	40	41	-	MD 0.21 higher (0.03 lower to 0.45 higher)	⊕⊕⊕O MODERATE	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

[3] Risk difference calculated with Review Manager

Table 39: Clinical evidence profile: Alpha blockers versus no treatment (pain management only) for mid ureteric stones <10mm in adults

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Alpha blockers	No treatment (<10mm)	Relative (95% CI)	Absolute		
Stone passage (follow-up 8 weeks; assessed with: number of people spontaneously passing stones during follow up)												
2	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	9/14 (64.3%)	16.3%	RR 4.09 (1.09 to 15.33)	504 more per 1000 (from 15 more to 1000 more)	⊕OOO VERY LOW	CRITICAL
Time to stone passage (follow-up 8 weeks; measured with: mean number of days for spontaneous stone passage ; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	8	8	-	MD 12.33 lower (17.26 to 7.4 lower)	⊕⊕OO LOW	CRITICAL
Analgesic use (follow-up 8 weeks; measured with: mean number of times analgesics were used during follow up ; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	8	8	-	MD 1.2 lower (2.67 lower to 0.27 higher)	⊕OOO VERY LOW	IMPORTANT

[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 40: Clinical evidence profile: Calcium channel blockers versus placebo for mid ureteric stones <10mm in adults

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Calcium channel blockers versus placebo	Control	Relative (95% CI)	Absolute		

Stone passage												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	32/40 (80%)	81.8%	RR 0.98 (0.79 to 1.2)	16 fewer per 1000 (from 172 fewer to 164 more)	⊕⊕⊕O MODERATE	CRITICAL
Time to stone passage (days) (Better indicated by lower values)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	11	13	-	MD 4.03 higher (2.16 lower to 10.22 higher)	⊕⊕⊕O MODERATE	CRITICAL
Quality of life (SF36; 12 weeks) - SF36 physical component (follow-up 12 weeks; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	serious [1]	no serious inconsistency	no serious indirectness	very serious[2]	none	24	24	-	MD 2.74 lower (8.96 lower to 3.48 higher)	⊕OOO VERY LOW	CRITICAL
Quality of life (SF36; 12 weeks) - SF36 mental component (follow-up 12 weeks; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	serious [1]	no serious inconsistency	no serious indirectness	very serious[2]	none	24	24	-	MD 2.17 lower (7.57 lower to 3.23 higher)	⊕OOO VERY LOW	CRITICAL
Quality of life (EQ5D; 12 weeks) (range of scores: 0-1; Better indicated by higher values)												
1	randomised trials	serious [1]	no serious inconsistency	no serious indirectness	serious[2]	none	24	28	-	MD 0.12 lower (0.26 lower to 0.02 higher)	⊕⊕OO LOW	CRITICAL
Analgesia use (pain medication use)												

1	randomised trials	serious [1]	no serious inconsistency	no serious indirectness	very serious[2]	none	18/28 (64.3%)	61.3%	RR 1.05 (0.71 to 1.55)	31 more per 1000 (from 178 fewer to 337 more)	⊕OOO VERY LOW	IMPORTANT
Analgesia use (number of days of pain medication use) (follow-up 4 weeks; Better indicated by lower values)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	17	19	-	MD 1.86 higher (2.87 lower to 6.59 higher)	⊕⊕⊕O MODERATE	IMPORTANT
Pain intensity (EQ5D no pain/discomfort) (follow-up 12 weeks)												
1	randomised trials	serious [1]	no serious inconsistency	no serious indirectness	very serious[2]	none	14/25 (56%)	67.9%	RR 0.83 (0.54 to 1.27)	115 fewer per 1000 (from 312 fewer to 183 more)	⊕OOO VERY LOW	IMPORTANT
Pain intensity (EQ5D moderate pain/discomfort) (follow-up 12 weeks)												
1	randomised trials	serious [1]	no serious inconsistency	no serious indirectness	very serious[2]	none	9/25 (36%)	32.1%	RR 1.12 (0.53 to 2.37)	39 more per 1000 (from 151 fewer to 440 more)	⊕OOO VERY LOW	IMPORTANT
Pain intensity (EQ5D extreme pain/discomfort) (follow-up 12 weeks)												
1	randomised trials	serious [1]	no serious inconsistency	no serious indirectness	very serious[2]	none	2/25 (8%)	0%	Peto OR 8.68 (0.53 to 143.3)	80 more per 1000 (from 43 fewer to 203 more)3	⊕OOO VERY LOW	IMPORTANT
Pain intensity (VAS) (follow-up 4 weeks; range of scores: 0-10; Better indicated by lower values)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	27	28	-	MD 0.71 higher (0.75 lower to 2.17 higher)	⊕⊕⊕O MODERATE	IMPORTANT

Adverse events (discontinuation due to AE)												
1	randomised trials	serious [1]	no serious inconsistency	no serious indirectness	very serious[2]	none	3/28 (10.7%)	9.7%	RR 1.11 (0.24 to 5.04)	11 more per 1000 (from 74 fewer to 392 more)	⊕OOO VERY LOW	IMPORTANT
Use of healthcare services - Doctor visits (follow-up 4 weeks; Better indicated by lower values)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	38	39	-	MD 0.13 lower (0.41 lower to 0.15 higher)	⊕⊕⊕O MODERATE	CRITICAL
Use of healthcare services - Nurse visits (follow-up 4 weeks; Better indicated by lower values)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	38	39	-	MD 0.02 lower (0.11 lower to 0.07 higher)	⊕⊕⊕O MODERATE	CRITICAL
Use of healthcare services - Outpatient visits (follow-up 4 weeks; Better indicated by lower values)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	37	44	-	MD 0.74 lower (0.92 to 0.56 lower)	⊕⊕⊕⊕ HIGH	CRITICAL
Hospitalisation (excess admission days) (follow-up 4 weeks; Better indicated by lower values)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	40	41	-	MD 0.08 lower (0.09 lower to 0.25 higher)	⊕⊕⊕O MODERATE	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.
[3] Risk difference calculated with Review Manager

Table 41: Clinical evidence profile: Alpha blockers versus Calcium channel blockers for mid ureteric stones <10mm in adults

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Alpha blockers	Calcium channel blockers (<10mm)	Relative (95% CI)	Absolute		
Stone passage rate												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	29/41 (70.7%)	80%	RR 0.88 (0.69 to 1.14)	96 fewer per 1000 (from 248 fewer to 112 more)	⊕⊕⊕O MODERATE	CRITICAL
Time to stone passage (days) (Better indicated by lower values)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[2]	none	8	11	-	MD 3.7 higher (9.33 lower to 16.73 higher)	⊕⊕OO LOW	CRITICAL
Quality of life (SF36; 12 weeks) - SF36 physical component (follow-up 12 weeks; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	serious [1]	no serious inconsistency	no serious indirectness	very serious[2]	none	26	24	-	MD 2.1 higher (4.17 lower to 8.37 higher)	⊕OOO VERY LOW	CRITICAL
Quality of life (SF36; 12 weeks) - SF36 mental component (follow-up 12 weeks; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	serious [1]	no serious inconsistency	no serious indirectness	very serious[2]	none	26	24	-	MD 2.69 lower (9.47 lower to 4.09 higher)	⊕OOO VERY LOW	CRITICAL

Quality of life (EQ5D; 12 weeks) (follow-up 12 weeks; range of scores: 0-1; Better indicated by higher values)												
1	randomised trials	serious [1]	no serious inconsistency	no serious indirectness	serious[2]	none	28	24	-	MD 0.03 higher (0.14 lower to 0.2 higher)	⊕⊕OO LOW	CRITICAL
Analgesic use (pain medication use) (follow-up 4 weeks)												
1	randomised trials	serious [1]	no serious inconsistency	no serious indirectness	very serious[2]	none	22/32 (68.8%)	64.3%	RR 1.07 (0.74 to 1.54)	45 more per 1000 (from 167 fewer to 347 more)	⊕OOO VERY LOW	IMPORTANT
Analgesic use (number of days of pain medication use) (Better indicated by lower values)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	22	17	-	MD 2.12 higher (3.24 lower to 7.48 higher)	⊕⊕⊕O MODERATE	IMPORTANT
Pain intensity (EQ5D no pain/discomfort; 12 weeks) (follow-up 12 weeks)												
1	randomised trials	serious [1]	no serious inconsistency	no serious indirectness	very serious[2]	none	17/28 (60.7%)	56%	RR 1.08 (0.69 to 1.71)	45 more per 1000 (from 174 fewer to 398 more)	⊕OOO VERY LOW	IMPORTANT
Pain intensity (EQ5D moderate pain/discomfort; 12 weeks) (follow-up 12 weeks)												
1	randomised trials	serious [1]	no serious inconsistency	no serious indirectness	very serious[2]	none	9/28 (32.1%)	36%	RR 0.89 (0.42 to 1.89)	40 fewer per 1000 (from 209 fewer to 320 more)	⊕OOO VERY LOW	IMPORTANT
Pain intensity (EQ5D extreme pain/discomfort; 12 weeks)												

1	randomised trials	serious [1]	no serious inconsistency	no serious indirectness	very serious[2]	none	2/28 (7.1%)	8%	RR 0.89 (0.14 to 5.88)	9 fewer per 1000 (from 69 fewer to 390 more)	⊕OOO VERY LOW	IMPORTANT
Pain intensity (VAS) (follow-up 4 weeks; range of scores: 0-10; Better indicated by lower values)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	31	27	-	MD 0.27 lower (1.83 lower to 1.29 higher)	⊕⊕⊕O MODERATE	IMPORTANT
Adverse events (discontinuation due to AE)												
1	randomised trials	serious [1]	no serious inconsistency	no serious indirectness	very serious[2]	none	2/32 (6.3%)	10.7%	RR 0.58 (0.1 to 3.24)	45 fewer per 1000 (from 96 fewer to 240 more)	⊕OOO VERY LOW	IMPORTANT
Use of healthcare services - Doctor visits (Better indicated by lower values)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	35	38	-	MD 0.22 higher (0.15 lower to 0.59 higher)	⊕⊕OO LOW	CRITICAL
Use of healthcare services - Nurse visits (follow-up 4 weeks; Better indicated by lower values)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	None	35	38	-	MD 0.19 higher (0.09 lower to 0.47 higher)	⊕OOO VERY LOW	CRITICAL
Use of healthcare services - Outpatient visits (follow-up 4 weeks; Better indicated by lower values)												

1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision[2]	none	41	37	-	MD 0.79 higher (0.52 lower to 1.06 higher)	⊕⊕⊕⊕ HIGH	CRITICAL
Hospitalisation (excess admissions days) (follow-up 4 weeks; Better indicated by lower values)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	40	40	-	MD 0.13 higher (0.15 lower to0.41 higher)	⊕⊕⊕O MODERATE	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 42: Clinical evidence profile: Alpha blockers versus placebo for proximal ureteric stones <10mm in adults

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Alpha blockers**	**Placebo (<10mm)**	**Relative (95% CI)**	**Absolute**		
Stone passage rate												
2	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	78/131 (59.5%)	56.8%	RR 0.96 (0.79 to 1.15)	23 fewer per 1000 (from 119 fewer to 85 more)	⊕⊕⊕O MODERATE	CRITICAL
Time to stone passage (days) (Better indicated by lower values)												
1	randomised trials	serious [1]	no serious inconsistency	no serious indirectness	serious[2]	none	12	11	-	MD 4.31 lower (13.88 lower to 5.26 higher)	⊕⊕OO LOW	CRITICAL

Quality of life (SF36; 12 weeks) - SF36 physical component (follow-up 12 weeks; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	serious [1]	no serious inconsistency	no serious indirectness	serious[2]	none	51	33	-	MD 2 higher (1.98 lower to 5.98 higher)	⊕⊕OO LOW	CRITICAL
Quality of life (SF36; 12 weeks) - SF36 mental component (follow-up 12 weeks; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	serious [1]	no serious inconsistency	no serious indirectness	very serious[2]	none	51	33	-	MD 0.4 lower (5.43 lower to 4.63 higher)	⊕OOO VERY LOW	CRITICAL
Quality of life (EQ5D; 12 weeks) (follow-up 12 weeks; range of scores: 0-1; Better indicated by higher values)												
1	randomised trials	serious [1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	51	33	-	MD 0.01 lower (0.11 lower to 0.08 higher)	⊕⊕⊕O MODERATE	CRITICAL
Analgesic use (pain medication use)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	42/66 (63.6%)	74.5%	RR 0.85 (0.67 to 1.09)	112 fewer per 1000 (from 246 fewer to 67 more)	⊕⊕⊕O MODERATE	IMPORTANT
Analgesic use (number of days of pain medication use) (follow-up 4 weeks; Better indicated by lower values)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	41	33	-	MD 1.01 higher (2.74 lower to 4.76 higher)	⊕⊕⊕O MODERATE	IMPORTANT
Pain intensity (EQ5D no pain/discomfort) (follow-up 12 weeks)												

1	randomised trials	serious [1]	no serious inconsistency	no serious indirectness	serious[2]	none	32/51 (62.7%)	73.5%	RR 0.85 (0.64 to 1.14)	110 fewer per 1000 (from 265 fewer to 103 more)	⊕⊕OO LOW	IMPORTANT
Pain intensity (EQ5D moderate pain/discomfort) (follow-up 12 weeks)												
1	randomised trials	serious [1]	no serious inconsistency	no serious indirectness	serious[2]	none	19/51 (37.3%)	20.6%	RR 1.81 (0.85 to 3.83)	167 more per 1000 (from 31 fewer to 583 more)	⊕⊕OO LOW	IMPORTANT
Pain intensity (EQ5D extreme pain/discomfort) (follow-up 12 weeks)												
1	randomised trials	serious [1]	no serious inconsistency	no serious indirectness	very serious[2]	none	0/51 (0%)	5.9%	OR 0.08 (0 to 1.37)	54 fewer per 1000 (from 59 fewer to 20 more)	⊕OOO VERY LOW	IMPORTANT
Pain (VAS) (follow-up 4 weeks; range of scores: 0-10; Better indicated by lower values)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	65	46	-	MD 0.52 lower (1.28 lower to 0.24 higher)	⊕⊕⊕O MODERATE	IMPORTANT
Adverse events (discontinuation due to AE)												
1	randomised trials	serious [1]	no serious inconsistency	no serious indirectness	very serious[2]	none	8/66 (12.1%)	6.4%	RR 1.9 (0.53 to 6.78)	58 more per 1000 (from 30 fewer to 370 more)	⊕OOO VERY LOW	CRITICAL
Use of healthcare services - Doctor visits (follow-up 4 weeks; Better indicated by lower values)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	70	71	-	MD 0.04 higher (0.16 lower to 0.24 higher)		CRITICAL

											⊕⊕⊕O MODERATE	
Use of healthcare services - Nurse visits (follow-up 4 weeks; Better indicated by lower values)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	70	71	-	MD 0.21 lower (0.65 lower to 0.23 higher)	⊕⊕⊕O MODERATE	CRITICAL
Use of healthcare services - Outpatients visits (follow-up 4 weeks; Better indicated by lower values)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	87	89	-	MD 0.82 higher (0.65 lower to 0.99 higher)	⊕⊕⊕⊕ HIGH	CRITICAL
Hospitalisation (excess admission days) (follow-up 4 weeks; Better indicated by lower values)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	88	88	-	MD 0.35 higher (0.73 lower to 0.03 higher)	⊕⊕⊕⊕ HIGH	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 43: Clinical evidence profile: Alpha blockers versus no treatment (pain management only) for proximal ureteric stones <10mm in adults

Quality assessment	No of patients	Effect	Quality	Importance

No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Alpha blockers	No treatment (pain management only) (<10mm)	Relative (95% CI)	Absolute		
Stone passage (follow-up 4-8 weeks; assessed with: number of people spontaneously passing stones during follow up)												
4	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	76/113 (67.3%)	35.7%	RR 1.57 (1.2 to 2.03)	203 more per 1000 (from 71 more to 368 more)	⊕⊕OO LOW	CRITICAL
Time to stone passage (follow-up 4-8 weeks; measured with: mean number of days for spontaneous stone passage ; Better indicated by lower values)												
2	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	70	63	-	MD 5.29 lower (8.43 to 2.16 lower)	⊕OOO VERY LOW	CRITICAL
Analgesic use (follow-up 4-8 weeks; measured with: mean number of times analgesics were used ; Better indicated by lower values)												
2	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	70	63	-	MD 0.55 lower (2.06 lower to 0.97 higher)	⊕⊕OO LOW	IMPORTANT
Quality of life (EuroQoL) (follow-up 4 weeks; measured with: mean score on EuroQol ; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	44	35	-	MD 0.1 lower (0.42 lower to 0.22 higher)	⊕OOO VERY 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 44: Clinical evidence profile: Calcium channel blockers versus placebo for proximal ureteric stones <10mm in adults

Quality assessment	No of patients	Effect	Quality	Importance

No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Calcium channel blockers versus placebo	Control	Relative (95% CI)	Absolute		
Stone passage												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	58/92 (63%)	73%	RR 0.86 (0.71 to 1.06)	102 fewer per 1000 (from 212 fewer to 44 more)	⊕⊕⊕O MODERATE	CRITICAL
Time to stone passage (days) (Better indicated by lower values)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	10	11	-	MD 3.33 lower (11.81 lower to 5.15 higher)	⊕⊕⊕O MODERATE	CRITICAL
Quality of life (SF36; 12 weeks) - SF36 physical component (follow-up 12 weeks; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	serious [1]		no serious indirectness	very serious[2]	none	37	33	-	MD 1.16 higher (3.1 lower to 5.42 higher)	⊕⊕OO LOW	CRITICAL
Quality of life (SF36; 12 weeks) - SF36 mental component (follow-up 12 weeks; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	serious [1]	no serious inconsistency	no serious indirectness	very serious[2]	none	37	33	-	MD 0.93 lower (6.1 lower to 4.24 higher)	⊕OOO VERY LOW	CRITICAL
Quality of life (EQ5D; 12 weeks) (range of scores: 0-1; Better indicated by higher values)												

1	randomised trials	serious [1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	40	33	-	mean 0 higher (0.09 lower to 0.11 higher)	⊕⊕⊕O MODERATE	CRITICAL
Analgesic use (pain medication use)												
1	randomised trials	serious [1]	no serious inconsistency	no serious indirectness	serious[2]	none	34/50 (68%)	74.5%	RR 0.91 (0.71 to 1.18)	67 fewer per 1000 (from 216 fewer to 134 more)	⊕⊕OO LOW	IMPORTANT
Analgesic use (number of days of pain medication use) (follow-up 4 weeks; Better indicated by lower values)												
1	randomised trials	serious [1]	no serious inconsistency	no serious indirectness	serious[2]	none	34	33	-	MD 2.59 higher (1.77 lower to 6.95 higher)	⊕⊕OO LOW	IMPORTANT
Pain intensity (EQ5D no pain/discomfort) (follow-up 12 weeks)												
1	randomised trials	serious [1]	no serious inconsistency	no serious indirectness	very serious[2]	none	30/40 (75%)	73.5%	RR 1.02 (0.78 to 1.34)	15 more per 1000 (from 162 fewer to 250 more)	⊕OOO VERY LOW	IMPORTANT
Pain intensity (EQ5D moderate pain/discomfort)												
1	randomised trials	serious [1]	no serious inconsistency	no serious indirectness	very serious[2]	none	9/40 (22.5%)	20.6%	RR 1.09 (0.46 to 2.62)	19 more per 1000 (from 111 fewer to 334 more)	⊕OOO VERY LOW	IMPORTANT
Pain intensity (EQ5D extreme pain/discomfort) (follow-up 12 weeks)												
1	randomised trials	serious [1]	no serious inconsistency	no serious indirectness	very serious[2]	none	1/40 (2.5%)	5.9%	RR 0.43 (0.04 to 4.49)	34 fewer per 1000 (from 57 fewer to 206 more)	⊕OOO VERY LOW	IMPORTANT

Adverse events (discontinuation due to AE)												
1	randomised trials	serious [1]	no serious inconsistency	no serious indirectness	very serious[2]	none	8/51 (15.7%)	6.4%	RR 2.46 (0.69 to 8.72)	93 more per 1000 (from 20 fewer to 494 more)	⊕OOO VERY LOW	CRITICAL
Use of healthcare services - Doctor visits (follow-up 4 weeks; Better indicated by lower values)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	67	71	-	MD 0.01 higher (0.2 lower to 0.18 higher)	⊕⊕⊕O MODERATE	CRITICAL
Use of healthcare services - Nurse visits (follow-up 4 weeks; Better indicated by lower values)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision[2]	none	67	71	-	MD 0.2 lower (0.65 lower to 0.25 higher)	⊕⊕⊕O MODERATE	CRITICAL
Use of healthcare services - Outpatients visits (follow-up 4 weeks; Better indicated by lower values)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	92	89	-	MD 0.62 higher (0.48 to 0.76 higher)	⊕⊕⊕⊕ HIGH	CRITICAL
Pain intensity (VAS) (follow-up 4 weeks; range of scores: 0-10; Better indicated by lower values)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	49	46	-	MD 0.49 higher (0.49 lower to 1.47 higher)	⊕⊕⊕O MODERATE	IMPORTANT
Hospitalisation (excess admission days) (follow-up 4 weeks; Better indicated by lower values)												

1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision[2]	none	91	88	-	MD 0.08 lower (0.55 lower to 0.39 higher)	⊕⊕⊕⊕ HIGH	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 45: Clinical evidence profile: Alpha blockers versus Calcium channel blockers for proximal ureteric stones <10mm in adults

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Alpha blockers**	**Calcium channel blockers (<10mm)**	**Relative (95% CI)**	**Absolute**		
Stone passage rate												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	62/88 (70.5%)	63%	RR 1.12 (0.91 to 1.37)	76 more per 1000 (from 57 fewer to 233 more)	⊕⊕⊕O MODERATE	CRITICAL
Time to stone passage (days) (Better indicated by lower values)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[2]	none	12	10	-	MD 0.98 lower (9.78 lower to 7.82 higher)	⊕⊕OO LOW	CRITICAL
Quality of life (SF36; 12 weeks) - SF36 physical component (follow-up 12 weeks; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	serious [1]	no serious inconsistency	no serious indirectness	very serious[2]	none	51	37	-	MD 0.84 higher (2.88 lower to 4.56 higher)	⊕OOO VERY LOW	CRITICAL

Quality of life (SF36; 12 weeks) - SF36 mental component (follow-up 12 weeks; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	serious [1]	no serious inconsistency	no serious indirectness	very serious[2]	none	51	37	-	MD 0.53 higher (3.84 lower to 4.9 higher)	⊕OOO VERY LOW	CRITICAL
Quality of life (EQ5D; 12 weeks) (follow-up 12 weeks; range of scores: 0-1; Better indicated by higher values)												
1	randomised trials	serious [1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	51	40	-	MD 0.02 lower (0.09 lower to 0.05 higher)	⊕⊕⊕O MODERATE	CRITICAL
Analgesic use (pain medication use)												
1	randomised trials	serious [1]	no serious inconsistency	no serious indirectness	serious[2]	none	42/66 (63.6%)	68%	RR 0.94 (0.72 to 1.22)	41 fewer per 1000 (from 190 fewer to 150 more)	⊕⊕OO LOW	IMPORTANT
Analgesic use (number of days of pain medication use) (follow-up 4 weeks; Better indicated by lower values)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	41	34	-	MD 1.58 lower (6.09 lower to 2.93 higher)	⊕⊕⊕O MODERATE	IMPORTANT
Pain intensity (EQ5D no pain/discomfort) (follow-up 12 weeks)												
1	randomised trials	serious [1]	no serious inconsistency	no serious indirectness	serious[2]	none	32/51 (62.7%)	75%	RR 0.84 (0.63 to 1.1)	120 fewer per 1000 (from 278 fewer to 75 more)	⊕⊕OO LOW	IMPORTANT
Pain intensity (EQ5D moderate pain/discomfort) (follow-up 12 weeks)												

1	randomised trials	serious [1]	no serious inconsistency	no serious indirectness	serious[2]	none	19/51 (37.3%)	22.5%	RR 1.66 (0.84 to 3.26)	148 more per 1000 (from 36 fewer to 508 more)	⊕⊕OO LOW	IMPORTANT
Pain intensity (EQ5D extreme pain/discomfort)												
1	randomised trials	serious [1]	no serious inconsistency	no serious indirectness	very serious[2]	none	0/51 (0%)	2.5%	OR 0.1 (0 to 5.33)	22 fewer per 1000 (from 25 fewer to 95 more)	⊕OOO VERY LOW	IMPORTANT
Pain intensity (VAS) (follow-up 4 weeks; range of scores: 0-10; Better indicated by lower values)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	65	49	-	MD 1.01 lower (1.83 to 0.19 lower)	⊕⊕⊕O MODERATE	IMPORTANT
Adverse events (discontinuation due to AE)												
1	randomised trials	serious [1]	no serious inconsistency	no serious indirectness	very serious[2]	none	8/66 (12.1%)	15.7%	RR 0.77 (0.31 to 1.92)	36 fewer per 1000 (from 108 fewer to 144 more)	⊕OOO VERY LOW	CRITICAL
Use of healthcare services - Doctor visits (follow-up 4 weeks; Better indicated by lower values)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	70	67	-	MD 0.05 higher (0.16 lower to 0.26 higher)	⊕⊕⊕O MODERATE	CRITICAL
Use of healthcare services - Nurse visits (follow-up 4 weeks; Better indicated by lower values)												

1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	70	67	-	MD 0.01 lower (0.09 lower to 0.07 higher)	⊕⊕⊕O MODERATE	CRITICAL
Use of healthcare services - Outpatients visits (follow-up 4 weeks; Better indicated by lower values)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	87	92	-	MD 0.2 higher (0.02 lower to 0.42 higher)	⊕⊕⊕O MODERATE	CRITICAL
Hospitalisation (excess admission days) (follow-up 4 weeks; Better indicated by lower values)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	88	91	-	MD 0.27 lower (0.62 lower to 0.08 higher)	⊕⊕⊕⊕ HIGH	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 46: Clinical evidence profile: Alpha blockers versus placebo for distal ureteric stones <10mm in children

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Alpha blockers**	**Placebo**	**Relative (95% CI)**	**Absolute**		
Stone passage (follow-up 4 weeks)												
2	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	45/51 (88.2%)	69%	RR 1.3 (1.04 to 1.62)	207 more per 1000 (from 28 more to 428 more)	⊕⊕OO LOW	CRITICAL

Time to stone passage (days) (follow-up (4 weeks); Better indicated by lower values)												
2	randomised trials	serious[1]	serious[3]	no serious indirectness	serious[2]	none	51	47	-	MD 4.89 lower (7.73 to 2.05 lower)	⊕OOO VERY LOW	CRITICAL
Adverse events (headaches/dizziness) (follow-up 4 weeks)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	3/18 (16.7%)	0%	Peto OR 8.82 (0.86 to 90.57)	167 more per 1000 (from 21 fewer to 354 more)[4]	⊕⊕OO LOW	CRITICAL
Adverse events (headaches) (follow-up 4 weeks)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	1/33 (3%)	3.6%	RR 0.85 (0.06 to 12.95)	5 fewer per 1000 (from 34 fewer to 430 more)	⊕OOO VERY LOW	CRITICAL
Adverse events (hypotension)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious	none	0/33 (0%)	0%	See comment	0 fewer per 1000 (from 62 fewer to 62 more)[4]	⊕OOO VERY LOW	CRITICAL
Pain intensity (number of pain episodes) (follow-up 4 weeks; Better indicated by lower values)												
2	randomised trials	serious[1]	very serious[5]	no serious indirectness	serious[2]	none	51	47	-	MD 1.49 lower (3.04 lower to 0.06 higher)	⊕OOO VERY LOW	IMPORTANT

[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.
[3] Downgraded by 1 or 2 increments because heterogeneity, I2= 73%, p= > 0.1, unexplained by subgroup analysis
[4] Risk difference calculated in Review Manager
[5] Downgraded by 1 or 2 increments because heterogeneity, I2= 77%, p= > 0.1, unexplained by subgroup analysis

Table 47: Clinical evidence profile: Alpha blockers versus no treatment (pain management only) for distal ureteric stones <10mm in children

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Alpha blockers	No treatment (<10mm)	Relative (95% CI)	Absolute		
Stone passage (follow-up 3-4 weeks; assessed with: number of people spontaneously passing stones)												
3	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	58/74 (78.4%)	62.5%	RR 1.45 (1.14 to 1.84)	281 more per 1000 (from 87 more to 525 more)	⊕OOO VERY LOW	CRITICAL
Time to stone passage (follow-up 3-4 weeks; measured with: mean number of days for spontaneous stone passage ; Better indicated by lower values)												
2	randomised trials	very serious[1]	very serious[3]	no serious indirectness	very serious[2]	none	50	52	-	MD 5.26 lower (15.16 lower to 4.63 higher)	⊕OOO VERY LOW	CRITICAL
Pain intensity (daily pain episodes) (follow-up 4 weeks; measured with: mean number of daily pain episodes during follow up ; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	31	32	-	MD 0.9 lower (1.77 to 0.03 lower)	⊕OOO VERY LOW	IMPORTANT
Analgesic use (follow-up 4 weeks; measured with: mean number of times analgesics were used during follow up ; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	31	32	-	MD 1.25 lower (1.87 to 0.63 lower)	⊕OOO VERY LOW	IMPORTANT
Adverse events (follow-up 3-4 weeks; assessed with: number of people experiencing adverse events (unspecified))												
2	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	0	0%	see comment	MD 0 more per 1000 (50 fewer to 50 more)[4]	⊕⊕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
[3] Downgraded by 1 or 2 increments because the point estimate varies widely across studies, the confidence intervals across studies show minimal or no overlap, or heterogeneity, I2>50%, p<0.04, unexplained by subgroup analysis.
[4] Risk difference calculated in Review Manager

Table 48: Clinical evidence profile: Alpha blockers as adjunctive therapy to shock wave lithotripsy versus shock wave lithotripsy only for distal ureteric stones <10mm in adults

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Alpha blockers + SWL	SWL (<10mm)	Relative (95% CI)	Absolute		
Stone passage (follow-up 15 days - 6 weeks; assessed with: number of people stone free at the end of follow up)												
5	randomised trials	serious[1]	no serious inconsistency	serious[2]	serious[3]	none	144/190 (75.8%)	56.8%	RR 1.28 (1.11 to 1.48)	159 more per 1000 (from 62 more to 273 more)	⊕OOO VERY LOW	CRITICAL
Time to stone passage (follow-up 4-6 weeks; measured with: number of days for stone passage ; Better indicated by lower values)												
2	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[3]	none	104	103	-	MD 2.21 lower (3.35 to 1.08 lower)	⊕OOO VERY LOW	CRITICAL
Adverse events (dizziness) (follow-up 15 days - 6 weeks; assessed with: number of people experiencing dizziness during follow up)												
3	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	7/101 (6.9%)	0%	Peto OR 8.4 (1.86 to 37.87)	69 more per 1000 (from 17 more to 122 more)[4]	⊕⊕OO LOW	CRITICAL
Analgesic use (follow-up 4 weeks; measured with: mean number of times analgesics were used during follow up ; Better indicated by lower values)												

1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[3]	none	44	44	-	MD 1.72 lower (2.88 to 0.56 lower)	⊕OOO VERY LOW	IMPORTANT
Hospitalisation (follow-up 4 weeks; assessed with: number of people hospitalized during follow up)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[3]	none	12/44 (27.3%)	43.2%	RR 0.63 (0.35 to 1.14)	160 fewer per 1000 (from 281 fewer to 60 more)	⊕⊕OO LOW	CRITICAL
Adverse events (abnormal ejaculation) (follow-up 4-6 weeks; assessed with: number of people experiencing abnormal ejaculation during follow up)												
2	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	7/49 (14.3%)	0%	Peto OR 8.56 (1.83 to 40.08)	142 more per 1000 (from 40 more to 246 more)[4]	⊕⊕OO LOW	CRITICAL
Adverse events (headache) (follow-up 4-6 weeks; assessed with: number of people experiencing headache during follow up)												
2	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[3]	none	9/76 (11.8%)	2.9%	Peto OR 4.19 (1.23 to 14.28)	88 more per 1000 (from 1 more to 427 more)	⊕OOO VERY LOW	CRITICAL
Adverse events (hypotension) (follow-up 6 weeks; assessed with: number of people experiencing hypotension during follow up)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	0/32 (0%)	0%	See comment	0 more per 1000 (from 60 fewer to 60 more)[4]	⊕⊕OO LOW	CRITICAL
Analgesic use (dosage) (follow-up 4 weeks; measured with: mean dosage (mg) of Diclofenac during follow up; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	serious[2]	no serious imprecision	none	60	59	-	MD 50.27 lower (68.87 to 31.67 lower)	⊕OOO VERY LOW	IMPORTANT

[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 or 2 increments because the majority of the evidence included an indirect population (downgrade by one increment) or a very indirect population (downgrade by two increments)

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

[4] Risk difference calculated in Review Manager

Table 49: Clinical evidence profile: Alpha blockers as adjunctive therapy to ureteroscopy versus ureteroscopy only for distal ureteric stones <10mm in adults

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Alpha blockers + URS	URS (<10mm)	Relative (95% CI)	Absolute		
Stone passage (follow-up 2 weeks; assessed with: number of people stone-free at the end of follow up)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	48/51 (94.1%)	87.2%	RR 1.08 (0.95 to 1.23)	70 more per 1000 (from 44 fewer to 201 more)	⊕⊕⊕O MODERATE	CRITICAL
Use of healthcare services (measured with: length of hospital stay; Better indicated by lower values)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	51	47	-	MD 0.5 lower (0.81 to 0.19 lower)	⊕⊕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 50: Clinical evidence profile: Alpha blockers as adjunctive therapy to ureteroscopy versus placebo and ureteroscopy for distal ureteric stones <10mm in adults

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Alpha blockers + URS	placebo + URS (<10mm)	Relative (95% CI)	Absolute		
Stone passage (follow-up 2 weeks; assessed with: number of people stone free at the end of follow up)												

1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	49/52 (94.2%)	70%	RR 1.35 (1.11 to 1.63)	245 more per 1000 (from 77 more to 441 more)	⊕OOO VERY LOW	CRITICAL
Analgesic use (follow-up 2 weeks; assessed with: number of people using analgesia during follow up)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	4/52 (7.7%)	24%	RR 0.32 (0.11 to 0.93)	163 fewer per 1000 (from 17 fewer to 214 fewer)	⊕OOO VERY LOW	IMPORTANT
Pain intensity (colic episodes) (follow-up 2 weeks; measured with: mean number of colic episodes during follow up ; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	52	50	-	MD 5 lower (5.99 to 4.01 lower)	⊕⊕OO LOW	IMPORTANT

[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 51: Clinical evidence profile: Alpha blockers as adjunctive therapy to shock wave lithotripsy versus shock wave lithotripsy only for distal ureteric stones 10-20mm in adults

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Alpha blockers + SWL**	**SWL (10-20mm)**	**Relative (95% CI)**	**Absolute**		
Time to stone passage (follow-up unclear; measured with: number of days for stone passage; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	serious[2]	serious[3]	none	14	24	-	MD 2.56 lower (7.78 lower to 2.66 higher)	⊕OOO VERY LOW	CRITICAL
Pain intensity (VAS) (follow-up unclear; measured with: visual analogue scale; range of scores: 0-10; Better indicated by lower values)												

1	randomised trials	serious[1]	no serious inconsistency	serious[2]	serious[3]	none	14	24	-	MD 1.21 lower (2.88 lower to 0.46 higher)	⊕OOO VERY LOW	IMPORTANT

[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 or 2 increments because the majority of the evidence included an indirect population (downgrade by one increment) or a very indirect population (downgrade by two increments)
[3] Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

Table 52: Clinical evidence profile: Alpha blockers as adjunctive therapy to shock wave lithotripsy versus shock wave lithotripsy only for mid ureteric stones 10-20mm in adults

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Alpha blockers + SWL**	**SWL (10-20mm)**	**Relative (95% CI)**	**Absolute**		
Time to stone passage (follow-up unclear; measured with: number of days for stone passage; Better indicated by lower values)												
1	randomised trials	serious[1]	no serious inconsistency	serious[2]	very serious[3]	none	16	12	-	MD 1.5 lower (8.23 lower to 5.23 higher)	⊕OOO VERY LOW	CRITICAL
Pain intensity (VAS) (follow-up unclear; measured with: visual analogue scale; range of scores: 0-10; Better indicated by lower values)												
1	randomised trials	serious[1]	no serious inconsistency	serious[2]	serious[3]	none	16	12	-	MD 0.62 lower (3.13 lower to 1.89 higher)	⊕OOO VERY LOW	IMPORTANT

[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 or 2 increments because the majority of the evidence included an indirect population (downgrade by one increment) or a very indirect population (downgrade by two increments)
[3] Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

Table 53: Clinical evidence profile: Alpha blockers as adjunctive therapy to shock wave lithotripsy versus shock wave lithotripsy only for proximal ureteric stones <10mm in adults

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Alpha blockers + SWL	SWL (<10mm)	Relative (95% CI)	Absolute		
Stone passage (follow-up 2-12 weeks; assessed with: number of people stone free at the end of follow up)												
6	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	176/198 (88.9%)	84.8%	RR 1.11 (1.03 to 1.21)	93 more per 1000 (from 25 more to 178 more)	⊕⊕⊕O MODERATE	CRITICAL
Time to stone passage (follow-up 2-12 weeks; measured with: number of days for stone passage ; Better indicated by lower values)												
4	randomised trials	very serious[1]	serious[2]	no serious indirectness	no serious imprecision	none	155	165	-	MD 4.32 lower (9.85 lower to 1.21 higher)	⊕OOO VERY LOW	CRITICAL
Pain intensity (VAS) (follow-up 2-12 weeks; measured with: visual analogue scale ; range of scores: 0-10; Better indicated by lower values)												
5	randomised trials	very serious[1]	serious[2]	no serious indirectness	serious[3]	none	183	191	-	MD 0.89 lower (1.68 to 0.1 lower)	⊕OOO VERY LOW	IMPORTANT
Hospitalisation (follow-up 2 weeks; measured with: mean number of Hospitalisations; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	serious[4]	no serious imprecision	none	35	44	-	MD 0.01 lower (0.31 lower to 0.29 higher)	⊕OOO VERY LOW	CRITICAL
Analgesic use (follow-up 2-6 weeks; assessed with: number of people using analgesia during follow up)												
2	randomised trials	very serious[1]	serious[2]	serious[4]	very serious[3]	none	37/76 (48.7%)	49.2%	RR 0.96 (0.49 to 1.91)	20 fewer per 1000 (from 251 fewer to 448 more)	⊕OOO VERY LOW	IMPORTANT
Adverse events (dizziness) (follow-up 3-6 weeks; assessed with: number of people experiencing dizziness during follow up)												

2	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[3]	none	3/85 (3.5%)	0%	Peto OR 7.76 (0.8 to 75.32)	35 more per 1000 (from 9 fewer to 80 more)[5]	⊕OOO VERY LOW	CRITICAL
Adverse events (retrograde ejaculation) (follow-up 6 weeks; assessed with: number of people experiencing retrograde ejaculation during follow up)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	0/41 (0%)	0%	See comment	0 more per 1000 (from 45 fewer to 45 more)[5]	⊕⊕OO LOW	CRITICAL
Analgesic use (dosage) (follow-up 4 weeks; measured with: mean dosage (mg) of Diclofenac used during follow up; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[3]	none	28	26	-	MD 189.7 lower (309.2 to 70.2 lower)	⊕OOO VERY LOW	IMPORTANT
Use of healthcare services (ED visits) (follow-up 4 weeks; measured with: mean number of ED visits during follow up ; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[3]	none	28	26	-	MD 0.6 lower (1.13 to 0.07 lower)	⊕OOO VERY LOW	CRITICAL
Pain intensity (renal colic episodes) (follow-up 4 weeks; measured with: mean number of renal colic episodes during follow up ; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[3]	none	28	26	-	MD 2.38 lower (3.89 to 0.87 lower)	⊕OOO VERY LOW	IMPORTANT
Quality of life (EQ5D) (follow-up 4 weeks; measured with: mean score on EQ5D; range of scores: 0-1; Better indicated by higher values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[3]	none	28	26	-	MD 0.04 higher (0.01 lower to 0.09 higher)	⊕OOO VERY LOW	CRITICAL
Quality of life (EQ5D VAS) (follow-up 4 weeks; measured with: mean score on EQ5D visual analogue scale ; range of scores: 0-100; Better indicated by higher values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[3]	none	28	26	-	MD 6.71 higher (1.49 to 11.93 higher)	⊕OOO VERY 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 or 2 increments because the point estimate varies widely across studies, the confidence intervals across studies show minimal or no overlap or heterogeneity, I2=50%, p=0.04,
[3] Risk difference calculated in Review Manager

Table 54: Clinical evidence profile: Alpha blockers as adjunctive therapy to shock wave lithotripsy versus placebo and shock wave lithotripsy for proximal ureteric stones <10mm in adults

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Alpha blockers + SWL	Placebo + SWL (<10mm)	Relative (95% CI)	Absolute		
Stone passage (follow-up 3 months; assessed with: number of people stone free at the end of follow up)												
1	randomised trials	no serious risk of bias	no serious inconsistency	serious[1]	serious[2]	none	27/28 (96.4%)	66.7%	RR 1.45 (1.06 to 1.97)	300 more per 1000 (from 40 more to 647 more)	⊕⊕OO LOW	CRITICAL
Time to stone passage (follow-up 3 months; measured with: number of days for stone passage ; Better indicated by lower values)												
1	randomised trials	serious[3]	no serious inconsistency	serious[1]	no serious imprecision	none	28	21	-	MD 3.3 lower (4.47 to 2.13 lower)	⊕⊕OO LOW	CRITICAL

[1] Downgraded by 1 or 2 increments because the majority of the evidence included an indirect population (downgrade by one increment) or a very indirect population (downgrade by two increments)
[2] Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs
[3] 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

Table 55: Clinical evidence profile: Alpha blockers as adjunctive therapy to shock wave lithotripsy versus shock wave lithotripsy only for proximal ureteric stones 10-20mm in adults

Quality assessment	No of patients	Effect	Quality	Importance

No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Alpha blockers + SWL	SWL (10-20mm)	Relative (95% CI)	Absolute		
Time to stone passage (follow-up unclear; measured with: number of days to stone passage ; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	serious[2]	serious[3]	none	29	28	-	MD 6.44 lower (10.3 to 2.58 lower)	⊕OOO VERY LOW	CRITICAL
Pain intensity (VAS) (follow-up unclear; measured with: visual analogue scale; range of scores: 0-10; Better indicated by lower values)												
1	randomised trials	serious[1]	no serious inconsistency	serious[2]	serious[3]	none	29	28	-	MD 1.1 lower (2.34 lower to 0.14 higher)	⊕OOO VERY LOW	IMPORTANT
Stone passage (follow-up 3 months; assessed with: number of people stone free at the end of follow up)												
1	randomised trials	very serious[1]	no serious inconsistency	serious[2]	serious[3]	none	26/29 (89.7%)	82.1%	RR 1.09 (0.88 to 1.35)	74 more per 1000 (from 99 fewer to 287 more)	⊕OOO VERY 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 or 2 increments because the majority of the evidence included an indirect population (downgrade by one increment) or a very indirect population (downgrade by two increments)

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

Table 56: Clinical evidence profile: Alpha blockers as adjunctive therapy to ureteroscopy versus ureteroscopy only for proximal ureteric stones 10-20mm in adults

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Alpha blockers + URS	URS (10-20mm)	Relative (95% CI)	Absolute		
Stone passage (follow-up 4-6 weeks; assessed with: number of people stone free at the end of follow up)												

2	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	118/126 (93.7%)	86.5%	RR 1.11 (1.02 to 1.21)	95 more per 1000 (from 17 more to 182 more)	⊕⊕⊕O MODERATE	CRITICAL
Use of healthcare services (Hospitalisation time) (follow-up admission; measured with: length of hospital stay for procedure; Better indicated by lower values)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	81	84	-	MD 0.2 lower (0.34 to 0.06 lower)	⊕⊕OO LOW	CRITICAL
Hospitalisation (readmission) (follow-up 8 weeks; assessed with: number of people readmitted to hospital during follow up)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	3/81 (3.7%)	6%	RR 0.62 (0.15 to 2.52)	23 fewer per 1000 (from 51 fewer to 91 more)	⊕OOO VERY LOW	CRITICAL
Time to stone passage (follow-up 6 weeks; measured with: number of days for stone passage; Better indicated by lower values)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	45	44	-	MD 3.68 lower (6.95 to 0.41 lower)	⊕OOO VERY LOW	CRITICAL
Pain intensity (ureteral colic rate) (follow-up 6 weeks; assessed with: number of people experiencing ureteral colic during follow up)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	2/45 (4.4%)	22.7%	RR 0.2 (0.05 to 0.84)	182 fewer per 1000 (from 36 fewer to 216 fewer)	⊕OOO VERY LOW	IMPORTANT
Adverse events (dizziness) (follow-up 6 weeks; assessed with: number of people experiencing dizziness during follow up)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	2/45 (4.4%)	0%	Peto OR 7.39 (0.46 to 120.11)	44 more per 1000 (from 28 fewer to 117 more)[3]	⊕OOO VERY LOW	CRITICAL

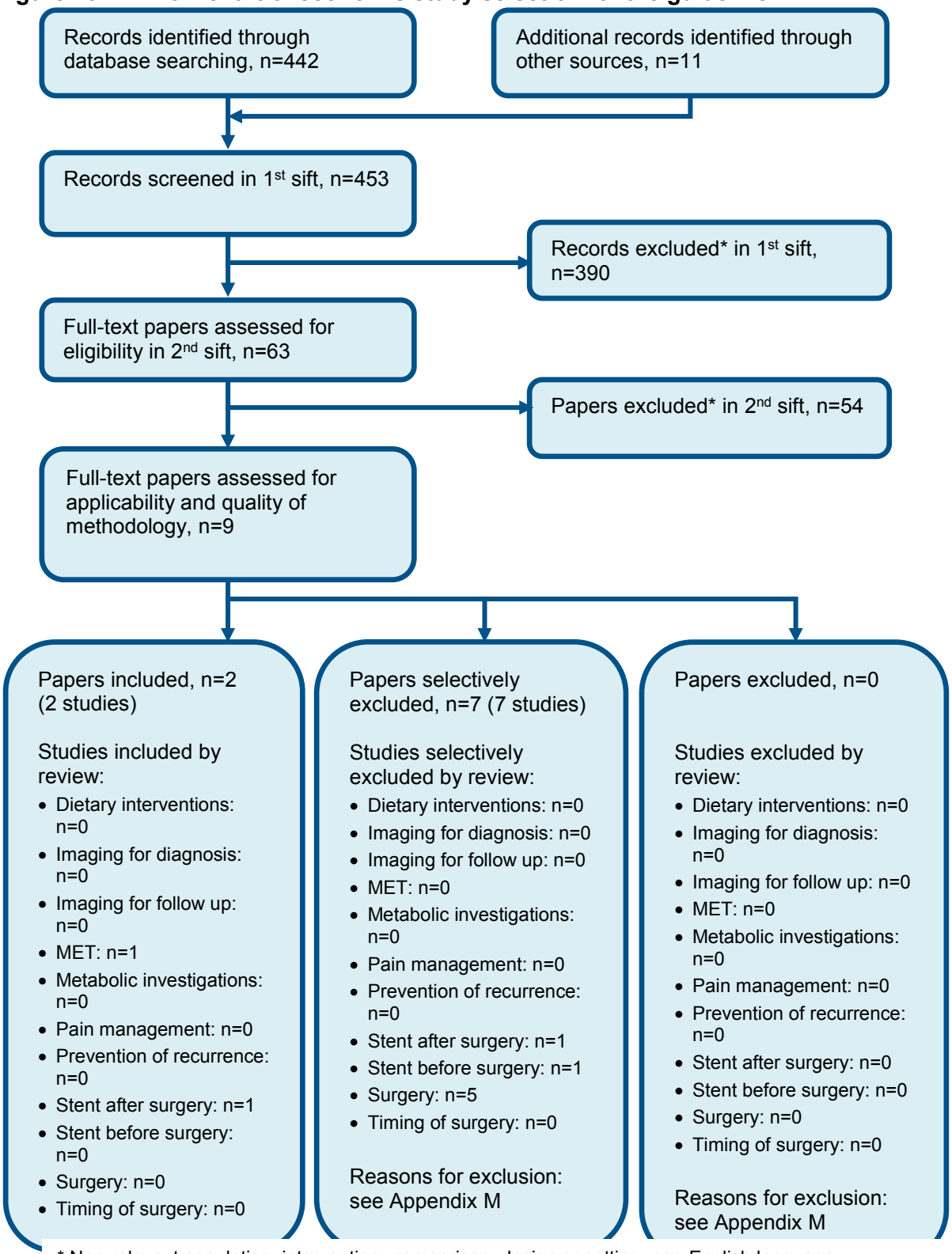
[1] Downgraded by 1 increment if the majority of the evidence was at high risk of bias, and downgraded by 2 increments if the majority of the evidence was at very high risk of bias

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

[3] Risk difference calculated in Review Manager

Appendix G: Health economic evidence selection

Figure 231: 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

[Please note, only cite studies using the Main Endnote library for the guideline. This can be found at N:\NCGC Guidelines\[guideline]\5-Development\Searches\[Guideline] main database. **Under no circumstances should you cite from the search results library.**]

Study	Pickard 2015[153]			
Study details	**Population & interventions**	**Costs**	**Health outcomes**	**Cost effectiveness**
Economic analysis: CUA (health outcome: QALYs) **Study design:** CUA (health outcome: QALYs) **Approach to analysis:** This within trial analysis comparing the cost effectiveness of MET (nifedipine or tamsulosin) vs placebo and MET drugs to each other (tamsulosin vs nifedipine). The data were taken from 24 UK hospitals from 1167 participants and data on resource use and quality of life data was collected in all patients at baseline, 4 and 12 weeks after	**Population:** Patients presented as an emergency with a diagnosis of ureteric colic at UK NHS hospitals and diagnosed with a symptomatic ureteric stone of ≤ 10 mm in maximum dimension **Patient characteristics:** N: unclear as only complete data was used for the economic analysis Mean age: 43.1 (tamsulosin group), 42.3 (nifedipine group), 42.8 (placebo) Male [(a)]:82.2% (tamsulosin group), 82.8% (nifedipine group), 77.9% (placebo) **Intervention 1:** Placebo	**Total costs (mean per patient):** Intervention 1: NR Intervention 2: NR Intervention 3: NR Intervention 4: NR Incremental (2−1): -£42 Incremental (4-3):-£87 **Currency & cost year:** 2012-13 British Pounds **Cost components incorporated:** Drugs costs (interventions, analgesics, antibiotics), Resource use costs (GP appointment, outpatient appointment and admissions), diagnostic tests costs, unit costs of further active intervention like stents use or cost of	**QALYs (mean per patient):** Intervention 1: 0.20 Intervention 2: 0.19 Intervention 3: 0.20 Intervention 4: 0.19 Incremental (2−1): -0.001 (adjusted) Incremental (4-3): -0.002 (adjusted)	**ICER (Intervention 2 versus Intervention 1):** Intervention 2 is less expensive and less effective than intervention 1, so the ICER of 1 versus 2 is presented for ease of interpretation; Placebo vs MET = £42,000 [(c)] Probability Intervention 2 cost effective (£20K/30K threshold):56%/51% **ICER (Intervention 3 versus Intervention 4):** Intervention 4 is less expensive and less effective than intervention 3, so the ICER of 3 versus 4 is presented for ease of interpretation; Nifedipine vs Tamsulosin = £43,500 Probability intervention 4 cost effective(£20K/30K threshold):61%/55% **Analysis of uncertainty:** Non-parametric bootstrapping was used to generate 1000 estimates of mean costs and QALYs for each treatment

randomisation. Mean costs and QALYs over the 12 week period were used to derive ICERs. **Perspective:** UK NHS **Time horizon/Follow-up**: the period of the clinical study (12 weeks) **Treatment effect duration:**4 weeks **Discounting:** N/A	**Intervention 2:** Medical Expulsive Therapy consisted of Nifedipine, 30mg-MR capsules, or Tamsulosin hydrochloride 0.4 mg, for a maximum of 28 days **Intervention 3**: Nifedipine (MR capsules), 30mg-once daily**,** for a maximum of 28 days **Intervention 4:** Tamsulosin hydrochloride (MR capsules) 0.4 mg once daily, for a maximum of 28 days [(b)]	lithotripsy, participants costs (self-purchased health care such as prescription costs, over the counter medications, visits to non NHS health care providers)		group. Various one way sensitivity analyses were undertaken; *Using SF-6D instead of EQ-5D* [(d)] There was uncertainty around the QALY estimates derived using the EQ-5D that its sensitivity to capture the loss in QoL particularly in reference to acute pain was questioned. Therefore SF-36 responses were mapped onto the SF-6D measure. - MET versus placebo: MET was again less expensive and less effective, and so comparing placebo to MET gave an ICER of £12,333 (placebo cost effective). - Tamsulosin versus nifedipine:, Tamsulosin was again less expensive and less effective, and so comparing nifedipine to tamsulosin gave an ICER of £23,000 (nifedipine borderline cost effective). *Multiple imputation for EQ-5D – replacing all missing EQ-5D data with highest EQ-5D score* - MET versus placebo: MET again less expensive and less effective, so comparing placebo to MET gave an ICER of £6,000 (placebo cost effective). Incremental cost only £6 so explains low ICER but incremental QALY still 0.001. - Tamsulosin versus nifedipine: Tamsulosin is more expensive and more effective (both only slightly), giving an ICER of £24,677. So tamsulosin is above the cost effectiveness threshold slightly.
Data sources				

Health outcomes: Results of the large RCT informing resource use for the cost effectiveness analysis. Questionnaires were designed to obtain information on stone passage or further intervention, pain, HRQoL and resource use, including NHS and personal costs. Participants were asked to complete trial questionnaires at baseline, 4 weeks post randomisation and 12 weeks post randomisation. The baseline questionnaire was completed in hospital before randomisation **Quality-of-life weights:** Health-related quality-of-life measures were collected at baseline, 4 weeks and 12 weeks by participant completion of the EQ-5D and the SF-36 questionnaires. Responses from the SF-36 questionnaire were also used as the basis of QALYs as a sensitivity analysis to validate the EQ-5D scores. They were mapped onto the existing Short Form questionnare-6 Dimensions (SF-6D) measure using a standard algorithm to allow utility values to be estimated for each time point. These utility scores were transformed to QALYs using the methods described above to provide an alternative measure of QALYs for each participant **Cost sources:** Unit costs (drug costs) were obtained from published sources such as the British National Formulary (BNF) and NHS reference costs (cost of diagnostic tests, outpatient costs for urology department for a consultant outpatient appointment, cost of interventions like lithotripsies, stents insertion and removal, cost of admission with no intervention, cost of any extra admission days using the long stay excess days tariff) Cost of a GP appointment were obtained from the Personal Social Services Research Unit costs of primary services. The unit cost data source year was 2012–13 and the currency was British pounds.

Comments

Source of funding: National Institute for Health Research **Limitations:** A cost utility analysis that is a within trial analysis based on a UK RCT, using an NHS perspective and the EQ-5D that reports changes in quality of life and costs coming from the use of MET (tamsulosin and nifedipine) and placebo. Study Included some participants costs that are not NHS costs related, and these were reported as part of NHS costs that they account for significant % of total costs of intervention; so it is difficult to separate participants' costs from the NHS costs in order to determine whether their magnitude is significant compared to the total costs of interventions. The categories where the patient reported outcomes fall include costs that are of similar amount in both interventions (MET, placebo), so unlikely changing the cost effectiveness results. Study used a time horizon of 12 weeks and not longer. That was justified by the authors as there weren't many people who still needed interventions at the end of the trial. However there were no extrapolation and therefore assumptions made about what this treatment would be which could impact incremental costs and effects because different numbers of people are stone free in each arm, and that is a potentially serious limitation detracting from overall study quality **Other:**

Overall applicability: Directly applicable **Overall quality:** Potentially serious limitations

Abbreviations: CUA: cost–utility analysis; da: deterministic analysis; EQ-5D: Euroqol 5 dimensions (scale: 0.0 [death] to 1.0 [full health], negative values mean worse than death); ICER: incremental cost-effectiveness ratio; MET: medical expulsive therapy; NR: not reported; pa: probabilistic analysis; SF-36: Short Form (36) Health Survey (scale: 0.0 (maximum disability to 100 no disability)QALYs: quality-adjusted life years WTP: Willingness to pay

(a) Study reported % female participants for each intervention group and % male participants was worked out using the data from female

(b) Interventions administered for up to 4 weeks until the stone passage

(c) Note that the ICER reported in the table for MET vs placebo is reported as £4,355. Taking the incremental cost and dividing by the incremental QALY (-42/-0.001) is £42,000 which is much larger than the ICER reported. Therefore there must be a reporting error. Additionally this is reported as cost saving per QALY lost for MET versus placebo because MET is an intervention appearing in the bottom left quadrant of the cost effectiveness plane. However for ease of interpretation in cases like this the intervention should be switched around i.e. to compare placebo versus MET so that the less effective intervention is used as the comparator and so the ICER can be interpreted as it normally would (if less than £20,000 then intervention is cost effective versus the comparison).

(d) At the different sensitivity analysis scenario where the uncertainty around the QALY estimates derived using EQ-5D is further investigated, costs also changed not just QALYs because they are using a different subset of people from the base case, because these are people who responded to the SF-36. Same applies to the multiple imputation analysis as well.

Appendix I: Excluded studies

I.1 Excluded clinical studies

Table 57: Studies excluded from the clinical review

Study	Exclusion reason
Abdelaziz 2017[2]	Inappropriate comparison
Afridi 2017[4]	Stone location not reported
Ahmed 2016[10]	Not review population
Ahmed 2014 [12]	Incorrect comparison
Ahmed Pechuho 2012[11]	Not available
Ahn 1997[13]	Article not in English
Amer 2017[19]	Systematic review is not relevant to review question or unclear PICO
Amer 2017[18]	Systematic review is not relevant to review question or unclear PICO
Aydin 2017[23]	Unclear stone size and location
Ayubov 2007[25]	abstract
Bahn Zobbe 1986[26]	Incorrect interventions
Bai 2017[27]	Inappropriate comparison
Beach 2006[32]	Systematic review is not relevant to review question or unclear PICO
Berger 2015[33]	Mixed stone location
Bhagat 2007[34]	Not review population
Borghi 1994[35]	Mixed stone location
Campschroer 2014[37]	Systematic review is not relevant to review question or unclear PICO
Campschroer 2018[36]	Systematic review is not relevant to review question or unclear PICO
Cao 2014[38]	Systematic review is not relevant to review question or unclear PICO
Caravati 1989[39]	Crossover study
Cervenakov 2002[40]	Inappropriate comparison
Cha 2012[41]	Inappropriate comparison
Cho 2017[44]	Mixed stone location
Clayman 2002[45]	editorial comment
Cooper 2000[46]	Inappropriate comparison
Daga 2016[47]	Inappropriate comparison
De Nunzio 2016[48]	Not review population
Dellabella 2003[51]	Inappropriate comparison
Dellabella 2005[52]	Inappropriate comparison
Dell'atti 2015[50]	Inappropriate comparison
Dellis 2017[53]	Stone location not reported
Ding 2016[54]	Systematic review is not relevant to review question or unclear PICO
Doluoglu 2015[55]	Inappropriate comparison

Study	Exclusion reason
Elgalaly 2016[59]	Inappropriate comparison
El-Gamal 2012[56]	Inappropriate comparison
Erkan 2011[61]	abstract
Eryildirim 2015[64]	Incorrect study design
Falahatkar 2011[66]	Not review population
Fan 2013[67]	Systematic review is not relevant to review question or unclear PICO
Georgescu 2015[71]	Mixed stone location
Georgiev 2011[72]	Incorrect study design
Glina 2015[73]	Systematic review is not relevant to review question or unclear PICO
Gottlieb 2017[74]	review of Pikard 2015
Goyal 2018[75]	Incorrect interventions
Gravina 2005[77]	Not review population
Griwan 2010[78]	Inappropriate comparison
Gupta 2008[80]	Comment
Gupta 2013[81]	Inappropriate comparison
Gupta 2014[79]	Review protocol
Gurbuz 2011[82]	Inappropriate comparison
Hamidi Madani 2011[83]	Incorrect interventions
Han 2006[84]	Article not in English
Han 2006[85]	Not in English
Hollingsworth 2016[87]	Systematic review is not relevant to review question or unclear PICO
Hong 2008[88]	Not in English
Huang 2016[89]	Systematic review is not relevant to review question or unclear PICO
Hussein 2010[90]	Not review population
Hwang 2012[91]	Incorrect study design
Itoh 2013[94]	Appears to be a sub-analysis of Itoh 2011
Janane 2014[96]	Not review population
Jayant 2014 [97]	Incorrect comparison
John 2010[98]	Not review population
Kang 2009 [101]	Not in English
Kaneko 2010[100]	Mixed stone location
Kc 2016 [102]	Incorrect comparison
Kim 2007[104]	Not in English
Kim 2008[105]	Article not in English
Kiraç 2013[106]	Inappropriate comparison
Kobayashi 2008[107]	Mixed stone location
Kohjimoto 2015[108]	Inappropriate comparison
Koski 2018[109]	Systematic review: references checked
Kroczak 2017[110]	Literature review
Kumar 2013[113]	Inappropriate comparison
Kumar 2014 [112]	Incorrect comparison
Kumar 2015[111]	Inappropriate comparison

Study	Exclusion reason
Lee 2012[115]	Systematic review is not relevant to review question or unclear PICO
Li 1995[117]	Not review population
Li 2015[119]	Systematic review is not relevant to review question or unclear PICO
Li 2017[118]	Systematic review is not relevant to review question or unclear PICO
Liatsikos 2007[120]	Incorrect study design
Liu 2012[123]	Systematic review is not relevant to review question or unclear PICO
Liu 2015[121]	Systematic review is not relevant to review question or unclear PICO
Liu 2017[124]	Systematic review is not relevant to review question or unclear PICO
Liu 2018[122]	Incorrect interventions
Losek 2008[126]	Systematic review is not relevant to review question or unclear PICO
Lu 2012[128]	Systematic review is not relevant to review question or unclear PICO
Lu 2012[127]	Inappropriate comparison
Lv 2013 [129]	Incorrect comparison
Malo 2014[131]	Systematic review is not relevant to review question or unclear PICO
McClinton 2014[132]	Study protocol
Micali 2006[135]	Not review population
Micali 2007[134]	Incorrect study design
Meltzer 2017[146]	Trial registry reference
Meltzer 2018[133]	No useable data available on request
Mohamed 2013[136]	Inappropriate comparison
Montiel-Jarquín Á 2017 [139]	Not in English
Mukhtarov 2007[142]	abstract
Naja 2008[144]	Not review population
Ohgaki 2010[148]	Inappropriate comparison
Ozsoy 2016[149]	Inappropriate comparison
Parsons 2007[151]	Systematic review is not relevant to review question or unclear PICO
Picozzi 2011[155]	Systematic review is not relevant to review question or unclear PICO
Pirzada 2011[156]	Not review population
Porpiglia 2000[157]	Inappropriate comparison
Porpiglia 2002[158]	Inappropriate comparison
Porpiglia 2004[160]	Inappropriate comparison
Porpiglia 2006[161]	Incorrect study design
Porpiglia 2009[159]	second line therapy
Portis 2018[162]	Incorrect study design
Puvvada 2016 [163]	Incorrect comparison
Qadri 2014[164]	Not review population
Rahman 2017[166]	Inappropriate comparison

Study	Exclusion reason
Raison 2017[167]	Systematic review is not relevant to review question or unclear PICO
Ramesh 2015[168]	Incorrect study design
Reddy 2016[169]	Incorrect study design
Romics 2011[172]	Incorrect interventions
Saita 2004[173]	Incorrect study design
Sarica 2006[175]	Not review population
Schuler 2009[177]	Systematic review is not relevant to review question or unclear PICO
Seitz 2009[178]	Systematic review is not relevant to review question or unclear PICO
Seungok 2009[180]	Abstract
Shaaban 2008[181]	Abstract
Shabana 2016[182]	Inappropriate comparison
Shahat 2016[183]	Not review population
Shokeir 2016 [184]	Incorrect comparison
Singh 2007[185]	Systematic review is not relevant to review question or unclear PICO
Skolarikos 2015[189]	Systematic review is not relevant to review question or unclear PICO
Skolarikos 2017[188]	Systematic review: references checked
Skrekas 2003[190]	abstract
Sridharan 2017[191]	Systematic review: references checked
Sridharan 2018[192]	Not available
Strohmaier 1994[193]	Not review population
Sumer 2012[195]	Not guideline condition. Not review population
Tasian 2014[198]	Incorrect study design
Tian 2017[200]	Systematic review is not relevant to review question or unclear PICO
Tsuzaka 2011 [201]	Incorrect comparison
Tuerxun 2017[202]	Incorrect study design
Velazquez 2015[203]	Systematic review is not relevant to review question or unclear PICO
Vicentini 2011[204]	Not review population
Vincendeau 2010[205]	Inappropriate comparison
Wang 2008[211]	Article not in English
Wang 2009[207]	Incorrect study design
Wang 2010[209]	Inappropriate comparison
Wang 2016[210]	Systematic review is not relevant to review question or unclear PICO
Wang 2017[212]	Systematic review is not relevant to review question or unclear PICO
Yang 2016[214]	Systematic review is not relevant to review question or unclear PICO
Yencilek 2010[217]	Inappropriate comparison
Zaytoun 2012[220]	Not review population
Zehri 2010[221]	Incorrect study design

Study	Exclusion reason
Zheng 2010[223]	Systematic review is not relevant to review question or unclear PICO
Zhu 2010[225]	Systematic review is not relevant to review question or unclear PICO

I.2 Excluded health economic studies

None

Appendix J: Research recommendations

J.1 Alpha blockers and ureteroscopy

Research Question: What is the clinical and cost effectiveness of tamsulosin as an adjunct to ureteroscopy?

Why this is important:

Kidney and ureteric stones affect about 15% of the male population and 5% of the female population at some point in their lives. The incidence of kidney stones has been increasing because of their link to poor diet, obesity and diabetes. Kidney and ureteric stones can cause severe pain and morbidity. Ureteroscopy is a commonly used method of treating stones in the kidney or ureter, whereby a narrow telescope is advanced up the ureter and laser energy is applied to the stone through a small fibre. Fragments may be left to wash out or removed with a basket.

The ureteric is intrinsically narrow but its wall contains muscle which is known to relax when the patient is given a medication called tamsulosin, which is in common use for prostatic problems. Tamsulosin has been shown to improve the spontaneous passage rate of small ureteric stones and also fragment-clearance following shockwave lithotripsy and NICE guidelines have recommended alpha blockers such as tamsulosin are considered for such purposes.

The success of ureteroscopic stone clearance can be inhibited by the ureter being excessively tight. This might prevent the insertion of the ureteroscope into the ureter (failed access) or reduce the effectiveness of laser fragmentation or the spontaneous clearance of fragments. Ureteric stents are often used as a post-treatment safety measure if the ureter is felt to be tight or swollen up during a procedure. Ureteric stents are known to cause significant irritation symptoms due to mechanical rubbing in the urinary tract. There is also some evidence that these symptoms might be reduced by tamsulosin. Nevertheless, the studies that these finding are based on are small and the evidence quality is low so tamsulosin is not in widespread routine use for these purposes. A definitive RCT is required to determine if such a recommendation would be appropriate.

PICO question	**Population:** Adults with ureteric or renal stones up to 20mm in size undergoing ureteroscopic treatment and no stent **Intervention(s):** Tamsulosin 400mcg od for 1 week prior to ureteroscopy and for 4 weeks after **Comparison:** Double-blind placebo controlled **Outcomes:** Primary outcome: Stone free rate as assessed by CT KUB at 4 weeks Secondary outcomes: failed access rate, operation time, stenting rate, needs for repeat ureteroscopy or adjunctive procedures, hospitalisation/ED attendance?, pain scores, quality of life (EQ-5D- 3L), stent symptoms, side effects, failed insertion of access sheath, cost per QALY.
Importance to patients or the population	Kidney stones are extremely common and cause significant morbidity. Ureteroscopy is a commonly used and effective method of treating kidney stones. The success of stone clearance can be inhibited by the tightness of the ureter. Simple measures to relax the ureter peri-operatively might improve the success of the procedure, reduce the need for secondary procedures and improve the procedure related morbidity and quality of life.

Relevance to NICE guidance	The NICE guidelines panel felt that the current evidence was of too low quality to make a current recommendation on the use of tamsulosin for this purpose.
Relevance to the NHS	Tamsulosin is inexpensive and widely used by urologists. Ureteroscopic stone treatments are very common and improvements in its success rate will reduce the need for expensive secondary procedures and may reduce the cost of treatment related morbidity
National priorities	There is a strong link between diabetes, obesity and kidney stones and limiting the impact of these conditions is one of the top research priorities of the NHS. It is also a priority to test interventions and maximize effectiveness and cost-effectiveness.
Current evidence base	The current evidence is restricted to one or two studies with small numbers of participants for most outcome measures.
Equality	The recommendation is unlikely to impact on equality issues.
Study design	Double-blind placebo controlled RCT with health economic analysis
Feasibility	The trial is feasible and should be straightforward to carry out. There are a large number of such patients and a UK kidney stone trial network has already been established. The SUSPEND and TISU trials demonstrate this.
Other comments	The length of pre-treatment tamsulosin might be reviewed.
Importance	• Medium: the research is relevant to the recommendations in the guideline, but the research recommendations are not key to future updates.