Effect of alpha-adrenoceptor antagonists on sexual function. A systematic review and meta-analysis

Rawa Bapir [1, 13], Kamran Hassan Bhatti [2, 13], Ahmed Eliwa [3, 13], Herney Andrés García-Perdomo [4, 13], Nazim Gherabi [5, 13], Derek Hennessey [6, 13], Vittorio Magri [7, 13], Panagiotis Mourmouris [8, 13], Adama Ouattara [9, 13], Gianpaolo Perletti [10, 13], Joseph Philipraj [11, 13], Alberto Trinchieri [12, 13], Noor Buchholz [13]

[1] Smart Health Tower, Sulaymaniyah, Kurdistan region, Iraq;
[2] Urology Department, HMC, Hamad Medical Corporation, Qatar;
[3] Department of Urology, Zagazig University, Zagazig, Sharkia, Egypt;
[4] Universidad del Valle, Cali, Colombia;
[5] Faculty of Medicine Algiers 1, Algiers, Algeria;
[6] Department of Urology, Mercy University Hospital, Cork, Ireland;
[7] ASST Nord Milano, Milan, Italy;
[8] 2nd Department of Urology, National and Kapodistrian University of Athens, Sismanoglio Hospital, Athens, Greece;
[9] Division of Urology, Souro Sanou University Teaching Hospital, Bobo-Dioulasso, Burkina Faso;
[10] Department of Biotechnology and Life Sciences, Section of Medical and Surgical Sciences, University of Insubria, Varese, Italy;
[11] Department of Urology, Mahatma Gandhi Medical College and Research Institute, Sri Balaji Vidyapeeth, Puducherry, India;
[12] Urology School, University of Milan, Milan, Italy;
[13] U-merge Ltd. (Urology for emerging countries), London-Athens-Dubai *.

Authors 1-12 have equally contributed to the paper and share first authorship.
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ALPHA-BLOCKERS VS PLACEBO

PATIENTS WITH LUTS ASSOCIATED TO BPH (EFFECTS ON EJACULATION)

Chapple 2005	Men (> 45 years) with LUTS I-PSS > 13 suggestive of BPH maximum flow rate 4–12 ml/s	Tamsulosin OCAS 0.4 mg N=360 Tamsulosin MR 0.4 mg N=709 Tamsulosin OCAS 0.8 mg N=722 OCAS = oral controlled absorption system MR = modified release	Placebo N=356	12 wks	Retrograde Ejaculation Tamsulosin 6/360 10/709 18/722 Placebo 1/356	
Chapple 2011	Patients > 50 years IPSS > 13 Q_{max} 4-15	Silodosin 8 mg N = 381 Tamsulosin 0.4 mg N=384	Placebo N=190	12 weeks	Retrograde Ejaculation Silodosin 54/381 Tamsulosin 8/384 Placebo 2/190	

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No conflict of interest declared.

Homma 2010	Patients with BPH > 50 years IPSS 8, QoL 3, Q_{max} 15 mL/s, prostate volume 20 mL, postvoid residual urine volume of 100 mL	Silodosin (4 mg twice daily), N=175 Tamsulosin (0.2 mg once daily)	Placebo N=89	12 weeks	Ejaculation disorder silodosin 39/175 (22.3%) Tamsulosin 3/187 (1.6%) Placebo 0/89	
Kawabe 2006	Patients > 50 LUTS/BPH IPSS ≥ 8 QoL score ≥ 3 Q_{max}< 15	Silodosin: 4mg twice daily N=175 Tamsulosin: 0.2 mg daily N=192	Placebo: N=89	12 weeks	Abnormal ejaculation: Silodosin: 39/175 (22.3%) Tamsulosin 3/192(1.6%) Placebo 0/89	
Lepor 1998	Patients with BPH	Tamsulosin 0.4 mg/day N=254 0.8 mg/day N=248	placebo N=254		Abnormal ejaculation 15/254 (6%) 44/248 (18%) PBO 0/254	
Marks 2013	Patients > 50 years IPSS > 13 Q_{max} 4-15	Silodosin N=466	Placebo N=457	12 weeks	Retrograde Ejaculation Treated 131/466(28.1%) Placebo 4/457(0.9%)	
Mehik 2003	Patients with CP/CPPS	Alfuzosin 5 mg twice daily N=19 Standard therapy N=30	Placebo N=21	6 months	Decreased ejaculatory volume Alfuzosin 4/19	
Mohanty 2003	Patients 40–80 years with LUTS suggestive of BPH IPSS 10 or more flow rate between 5-13 mL/s voided volume ≥ 150 mL PSA < 4 ng/mL	Tamsulosin N=38	Placebo N=34	8 wks	Retrograde ejaculation 2/36 0/33	
Roehrborn 2011	Patients > 50 years IPSS > 13 Q_{max} 4-15	Silodosin N=466	Placebo N=457	12 weeks	Retrograde Ejaculation Silodosin 131/466 28.1% Placebo 4/457 0.9%	
Singh 2012	Men with symptomatic BPH	Tamsulosin 0.4 mg N=46	Placebo N=14	12 weeks	Ejaculation Disorder TAM 1 (2.1%) PBO 00	Decreased Libido TAM 00 PBO 00

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PATIENTS WITH URETERAL STONE (EFFECTS ON EJACULATION) (CONTROLLED WITH PLACEBO)

Al-Ansari 2010	Male patients with distal ureteral stones < 10 mm	Tamsulosin 0.4 mg N=32	Placebo N=35	4 wks	Retrograde Ejaculation 1/32 0/35	
Meltzer 2018	Male pts with Ureteral stones < 9 mm demonstrated CT (males subgroup)	Tamsulosin 0.4 mg N=154	Placebo N=135	28 days	Abnormal ejaculation Tamsulosin 28/154 (18.2%) PBO 10/135 (7.4%)	
Singh 2014	Male pts with double-J ureteral stent after PCNL or URS	Tamsulosin 0.4 mg N=14	Placebo N=20	4 wks	Retrograde Ejaculation Tamsulosin 2/14 PBO 0/20	
Sur 2015	Male pts with unilateral ureteral stone 4–10 mm	Silodosin 8 mg N=72	Placebo N=80	4 wks	Retrograde ejaculation SIL 11/72 PBO 1/80	
Ye 2018	Male with distal ureteral stones	Tamsulosin (0.4 mg) N=1086	Placebo N=1049	4 wks	Retrograde ejaculation TAM 67/1087 PBO 48/1049	

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PATIENTS WITH URETERAL STONE (EFFECTS ON EJACULATION) (CONTROLLED WITH STANDARD TREATMENT)

Cho 2013	Male patients after SWL for ureteral calculi 5 to 10 mm	Alfuzosin 10 mg + Loxoprofen N=29	Loxoprofen N=31	42 days	Ejaculatory disorders 0/29 0/31	
El Said 2015	Male with distal ureter stones ≤ 10 mm	Alfuzosin SR 5 mg BID (n=18)	Hydration + Diclofenac 75 mg on demand N=16	4 wks	Retrograde ejaculation 0/18 0/16	
Ferre 2009	Distal ureteral stones diagnosed by CT scan	Tamsulosin N=32	Ibuprofen and Oxycodone alone N=24	10 days	Retrograde ejaculation 0/32 0/24	
Itoh 2011	Male patients with ureteral stones	Silodosin 8 mg N=95	Hydratation 2 L N=92	8 weeks	Ejaculation disorder SIL 3/95 CON 0/92	
Moursy 2010	Management of steinstrasse (male pts)	Tamsulosin (0.4 mg) in addition to pain-relieving therapy N=28	Pain relieving therapy N=27	4 wks	Anejaculation Tamsulosin 6/28 0/27	
Naja 2008	Clearance of fragments after ESWL (male pts)	Tamsulosin 0.4 mg/d N=36	Not receiving Tamsulosin N=43	3 months	Retrograde ejaculation 1/36 0/43	
Resim 2005	Steinstrasse in the lower portion of the ureters (male pts)	Tamsulosin (0.4 mg daily) Hydration+ Tenoxicam 20 mg N=21	Hydration+ tenoxicam 20 mg N=22	6 wks	Abnormal Ejaculation 1/21 0/22	

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PATIENTS WITH LUTS ASSOCIATED TO BPH (EFFECTS ON EJACULATION AND ERECTION)

Chung 2018	Patients with LUTS associated with BPH	Tamsulosin 0.4 mg Tamsulosin 0.2 mg N=155 N=164	Placebo N=163	12 wks	Retrograde ejaculation 1/155 1/164 0/163 Ejaculation disorders 1/155 0/164 0/163	Erectile dysfunction 0/155 1/164 0/163
Höfner 1999	Patients with LUTS suggestive of BPO	Tamsulosin 0.4 mg once daily N=381	Placebo N=193	12 weeks	Abnormal ejaculation 17/381 (4.5%) 2/193 (1.0%) Decreased libido 3/381 (0.8%) 0/193 (0%)	Impotence 2/381 (0.8%) 3/193 (1.6%) The life-style questionnaire (3 questions sexual function) Baseline 3.35 2.28 Change at endpoint -0.31 +0.49
		Tamsulosin 0.4 mg once daily N=131	Alfuzosin 2.5 mg three times daily N=124		Abnormal ejaculation 1/131 (0.8%) 0/124 (0%) Decreased libido 0 (0%) 0 (0%)	Impotence 3/131 (2.3%) 1/124 (0.8%) Baseline 2.87 2.60 Change at endpoint -0.14 +0.15
Kirby 2003	Symptomatic treatment of BPH 50 to 80 years	Doxazosin 1-8 mg N=275 Finasteride (not included) doxazosin+ finasteride (not included)	Placebo N=269	52 wks	Abnormal ejaculation Doxazosin 1/275 (0.4%) PBO 4/269 (1.5%)	Impotence 16/275 (5.8) 9/269 (3.3) Libido decreased 10/275 (3.6) 5/269 (1.9)
Nordling 2005	Men aged ≥ 50 years with a clinical diagnosis of symptomatic BPH	Alfuzosin 10 mg N=154 Alfuzosin 15 mg N=159	Placebo N=154	12 wks	Ejaculation disorder 2/154 0/159 PBO 0/154	Impotence 2/154 2/159 0/154
		Tamsulosin 0.4 mg N=158			Tamsulosin 5/158	7/158
Roehrborn 2001	Patients > 50 years with LUTS/BPH IPSS ≥ 13 Q_{max} 5-12	Alfuzosin 10 mg N=176 Alfuzosin 15 mg N=177	Placebo N=175	3 months	Ejaculatory disorder ALF 1/176 ALF 1/177 PBO 0/175	Impotence ALF 5/176 (2.8) ALF 2/177 (1.1) PBO 2/175 (1.1)

Roehrborn 2006	Men at risk of having progression events from LUTS/BPH	Alfuzosin 10 mg once daily N=759	Placebo N=763	2 yrs	Ejaculation failure/retrograde ALF 3 (0.4) PBO 0	Erectile dysfunction ALF 15 (2.0) PBO 14 (1.8)
Rosen 2007	Patients > 50 years, LUTS/BPH IPSS > 13 Q_{max} 5-12	Alfuzosin 10 mg N=185	Placebo N=185	28 days	Ejaculatory disorders ALF 1/185 PBO 1/185	Erectile dysfunction 1/185 2/185 DAN-PSSsex ALF improved PBO decreased
Safarinejad 2006	Patients (21-40) years with painful ejaculation	Tamsulosin 0.4 mg N=59 50 patients completed the study	Placebo N=59 54 patients completed the study	6 weeks	Retrograde ejaculation Tamsulosin 2/50 Placebo 0/54	IIEF: Tamsulosin: Baseline 10 End 12 Placebo Baseline 11 End 10

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PATIENTS WITH LUTS ASSOCIATED TO BPH (EFFECTS ON ERECTION)

ERECTILE DYSFUNCTION						
Becker 1998	Patients with erectile dysfunction for < 3 years	Pral phentolamine 20, 40, 60 mg N=10 N=10 N=10	Placebo N=10	Time	Full erection 20 mg 3/10 40 mg 5/10 60 mg 4/10 Placebo 2/10	
Choppin 2001	24 men men with erectile dysfunction (mean age 44 year)	5 mg oral dose of Ro70-0004 a1A-adrenoceptor antagonist	Placebo or 50 mg Sildenafil (control)	4 dosing period at 7-day interval	Erection time Ro700004: 8.28minutes. Placebo: 9.69 minutes. Sildenafil: 22.64 minutes	
Resnick 2007	Patients aged > 50 years with symptomatic BPH	Alfuzosin N=185	Placebo N=185	28 days	Erectile dysfunction Alfuzosin 1/185 (0.5%) vs 2/185	
Shelbaia 2013	Patients LUTS and erectile dysfunction (ED)	Tamsulosin N=30	Placebo N=30	1 year	Erectile dysfunction < 17 0/30 vs 5/30	Total IIEF score Treated 22.2 ± 0.4 Placebo 20.0 ± 0.7 .047*
van Kerrebroeck 2000	LUTS suggestive of BPH	Alfuzosin 10 mg N=143 Alfuzosin 2.5 mg x 3 N=150	Placebo N=154	3 months	Impotence 0 (0%) 0 (0%) 1/154	Decreased libido 0 (0%) 1/150 1/154 Sexual dysfunction (total) 0 (0%) 1 (0.7%) 2 (1.3%) No ejaculation disorders

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COMPARISON BETWEEN ALPHA-BLOCKERS

Agrawal 2009	Male pts with stones < 1 cm size and located in the lower ureter	Tamsulosin 0.4/ mg N=26	Alfuzosin 10 mg N=28 Placebo N=24	4 wks	Retrograde ejaculation 3/26 0/28 0/24	
Agrawal 2009	Acute urinary Retention (AUR) due to BPH	Tamsulosin 0.4/mg N=34	Alfuzosin 10 mg N=34 Placebo N=34	3 months	Retrograde Ejaculation 4/34 0/34 0/34	
Ahmed 2010	Male pts with uncomplicated distal ureteral stones	Tamsulosin 0.4/ mg N=19	Alfuzosin 10 mg N=18 No alpha-blockers N=19	1 month	Retrograde ejaculation 2/19 0/18 0/19	
Dell'Atti 2015	Male pts with unilateral radiopaque, proximal ureteral stone	Tamsulosin 0.4/ mg N=39	Silodosin 8 mg N=44	3 wks	Retrograde ejaculation 4/39 10/44	
De Nunzio 2016	Male patients undergoing SWL	Tamsulosin 0.4/ mg N=11	Silodosin 8 mg N=12 Placebo N=9	3 wks	1/11 2/12 0/9	
Elgalaly 2016	Male pts with distal ureteric stones	Tamsulosin 0.4/ mg N=32	Silodosin 8 mg N=35	1 month	Abnormal ejaculation 3/32 9/35	
Georgescu 2015	Male pts with ureteral stones under 10 mm	Tamsulosin 0.4/ mg N=27	Silodosin 8 mg N=20 Placebo N=31	4 wks	Retrograde Ejaculation 3/27 5/31	
Gharib 2018	Male single unilateral stone 10 mm or less	Tamsulosin 0.4/ mg N=43	Silodosin 8 mg N=44	4 wks	5/41 10/43	
Gupta 2013	Male pts with unilateral, non-impacted, uncomplicated middle or lower ureteral stones < 1 cm	Tamsulosin 0.4/ mg N=20	Silodosin 8 mg N=18	4 wks	Retrograde ejaculation 0/20 2/18	
Hellstrom 2006	Healthy subjects N=48	Tamsulosin 0.8 mg	Alfuzosin 10 mg Placebo	5 days Cross-over	Anejaculation 17/48 0/48 0/48	
Ibrahim 2013	Male patients with ureteric stones of 6-10 mm	Tamsulosin 0.4 mg N=40	Alfuzosin 10 mg N=40 No alpha-blockers N=32	4 wks	3/32 2/34	
Karadağ 2011	Men with BPH with LUTS	Alfuzosin-Tamsulosin N=50	Tamsulosin-Alfuzosin N=50	8 wks + 8 wks	Tamsulosin 14/100 Alfuzosin 3/100	
Kirby 2003	Men aged 50-80 years with concomitant BPH and hypertension	Doxazosin-GITS 4-8 mg/d or Tamsulosin 0.4-0.8 mg/d	Tamsulosin or Doxazosin-GITS	8 wks + 8 wks	Retrograde ejaculation Doxazosin 0/48 Tamsulosin 2/50	
Kumar 2013	Distal ureteric stones of size 5 to 10 mm	Tamsulosin N=25	Naftopidil N=30 watchful waiting N=28	4 wks	Retrograde Ejaculation 1/25 1/30 0/28	

Manohar 2017	LUTS associated with BPH	Tamsulosin 0.4 mg N=89	Alfuzosin 10 mg N=87 Silodosin 8 mg N=93	12 wks	3/89 0/87 9/93	
Masumori 2009	LUTS/BPH who had IPSS > 8	Tamsulosin 0.2 mg/day N = 47	Naftopidil 50 mg/day N = 48	12 wks	Tamsulosin 8/47 Naftopidil 4/48	
Miyakita 2010	LUTS associated with BPH	Tamsulosin 0.2 mg N=97	Silodosin 4 mg N=97	4 wks + 4 wks crossover	Ejaculatory disorder 0/97 7/97	
Narayan 2005	Patients with signs and symptoms of BPH	Tamsulosin 0.4 mg/day N=1002	Terazosin 5 mg/day N=981	57 days	Anejaculation 21/1002 (2.1%) 0/981 Ejaculation disorder 37/1002 (3.7%) 3/981 (0.3%)	
Pande 2014	BPH patients, aged above 50 years	Tamsulosin 0.4 mg controlled release N=27	Silodosin 8 mg once daily N=26	12 wks	Retrograde Ejaculation 0/27 3/26	
Patil 2017	Acute urinary retention secondary to BPH	Tamsulosin 0.4 mg (80 patients) N=54	Silodosin 8 mg (80 patients) N=48	1 month after successful TWOC	Retrograde ejaculation 2/54 0/48	
Pompeo 2006	Patients with BPH	Tamsulosin 0.4 q.i.d. N=83	Doxazosin gastrointestinal therapeutic system (GITS) 4 mg q.i.d. N=82	12 wks	Abnormal ejaculation 4/83 2/82	
Samli 2004	Patients with lower urinary tract symptoms (LUTS)	Doxazosin N=25 once daily	Terazosin N=25 once daily	3 months		Erectile dysfunction 0/25 1/25
Shirakawa 2013	Patients presenting LUTS/BPH	Silodosin (4 mg twice daily) or N=59	Naftopidil (50 mg once daily) for 4 or 8 weeks N=57		Ejaculation disorders 1/59 0/57	
Takahashi 2011	Patients with (LUTS)/BPH who had IPSS of 8 or more	Silodosin 8 mg/day N=48	Naftopidil 75 mg/day N=41	12 wks	Self-assessed ejaculatory volume (Q1 score) Decreased in Silodosin ($p < 0.01$) No significant changes in naftopidil	IIEF-5 changes from baseline Silodosin more deteriorated than Naftopidil (NS)
Takeshita 2016	Japanese men with LUTS/BPH	S-T group Silodosin 4 m g daily + Tamsulosin 0.2 mg daily N=16	T-S group Tamsulosin 0.2 mg daily + Silodosin 4 mg daily N = 14	4+4 wks crossover	Abnormal ejaculation Tamsulosin 0/34 Silodosin 3/34	
Watanabe 2013	Japanese patients with LUTS associated with BPH	T–S group Tamsulosin 0.2 mg once daily + Silodosin 4 mg twice daily N=42	S–T group Silodosin 4 mg twice daily + Tamsulosin 0.2 mg once N=42	4 wks + 4wks	Ejaculation disorder Tamsulosin 1/91 Silodosin 11/88	Erectile dysfunction 0/91 1/88

Yamaguchi 2013	Patients with LUTS/BPH with IPSS > 8	Silodosin 8 mg/day N = 53 Sexually active N = 23	Naftopidil 75 mg/day N = 44 Sexually active N= 21	12 wks	Loss of ejaculation Silodosin 10/23 2/21 Changes from baseline of volume, time and orgasm deteriorated more in silodosin	Silodosin & Naftopidil significant decrease from IIEF-5 baseline Silodosin > 25% Naftopidil < 25%
Yokoyama 2011	LUTS patients aged 50–80 years with IPSS > 8	Silodosin 4 mg twice a day; N=41 Sexually active N=11	Tamsulosin 0.2 mg once a day N=39 N=12 Naftopidil at 50 mg once a day N=42 N=15	3 months	Reduced/absent ejaculation at 4 wks Silodosin 10/41 Tamsulosin 1/39 Naftopidil 1/42	IIEF-5 at 4 wks Tamsulosin 6.6+/-0.9 6.1+/-1.1 P=0.841 Naftopidil 7.0+/-1.0 7.4+/-1.1 P=0.010 Silodosin 6.2+/-0.8 5.4+/-0.7 P=0.111
Yokoyama 2012	Men > 50 years IPSS > 8	Tamsulosin 0.2 mg once daily followed by Silodosin 4 mg twice daily N=23	Silodosin followed by Tamsulosin N=23	3 months + 3 months	Ejaculatory dysfunction Tamsulosin 0/46 Silodosin 4/46	
Yu 2011	LUTS patients with BPH and IPSS > 13	Silodosin 4 mg twice daily N=105	Tamsulosin 0.2 mg once daily N=104	12 wks	Abnormal ejaculation Silodosin 10/105 Tamsulosin 1/104	
Zaytoun 2012	SWL for renal stones	Tamsulosin 0.4 mg once daily plus phloroglucinol N=50	Doxazosin 4 mg plus phloroglucinol N=50 phloroglucinol 240 mg daily N=50	12 wks	Ejaculatory disorders Tamsulosin 2/50 0/50 0/50	

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COMPARISON BETWEEN ALPHA-BLOCKERS AT DIFFERENT DOSE AND TIMING OF ADMINISTRATION

Doxazosin					
Keten 2015	Patients with BPH related LUTS	4 mg Doxazosin XL N=108	8 mg Doxazosin XL N=54	1 month	Retrograde ejaculation 2/94 (2%) 1/44 (1.9%)
Kirby 2005	Men with BPH and aged 50–80 years 237 (35%) with ED at baseline	Doxazosin XL 4 or 8 mg once daily N=350 N=311 completed the study	or Doxazosin standard 1–8 mg once daily N=330 N=299 completed the study	13 weeks	Pts with ED IIEF improvement 13%-41% in the five domains No difference between groups
Silodosin					
Choo 2014	Korean patients with LUTS or BPH	Silodosin 8 mg (once/d) (breakfast) N=212	Silodosin 8 mg (4 mg bid) N=208	12 weeks	Retrograde ejaculation 32/212 vs 46/208
Seki 2015	Storage symptoms in patients with BPH	Silodosin 4 mg/day N=115	Silodosin 8 mg/day (4 mg bid) N=115	12 weeks	Ejaculation disorder 6/115 vs 10/115
Tamsulosin					
Kim 2014	Asian patients with LUTS secondary to BPH	Tamsulosin 0.2 mg N=91	Tamsulosin 0.4 mg N=95	12 weeks	Abnormal ejaculation 2/91 vs 2/95
Lojanapiwat 2008	Outpatients with distal ureteroliths in Thailand	Tamsulosin 0.2 mg/day N=25	Tamsulosin 0.4 mg/day N=25 Control N=25	28 days	Retrograde ejaculation 0/25 vs 0/25
Yanardag 2005	Patients with lower urinary tract symptoms	Tamsulosin 0.4 mg once daily N=31	Tamsulosin 0.4 mg once daily every other day N=43	24 weeks	Retrograde ejaculation 1/31 vs 0/43
Other					
Hareendran 2005	Men aged > 40 with LUTS resulting from BPH	New uro-selective alpha-blocker high, medium, and low dose N=125 N=129 N=127	Placebo N=65	12 weeks	Retrograde ejaculation 14.6% high 7.2% medium dose 0% placebo

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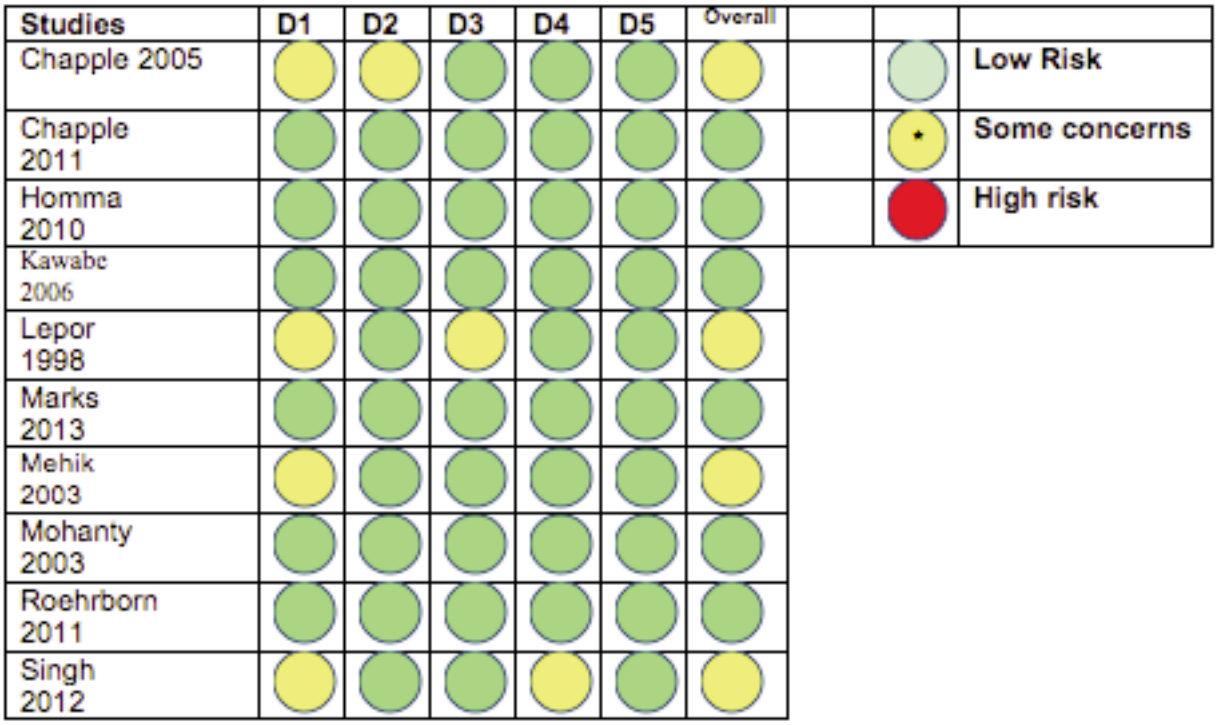
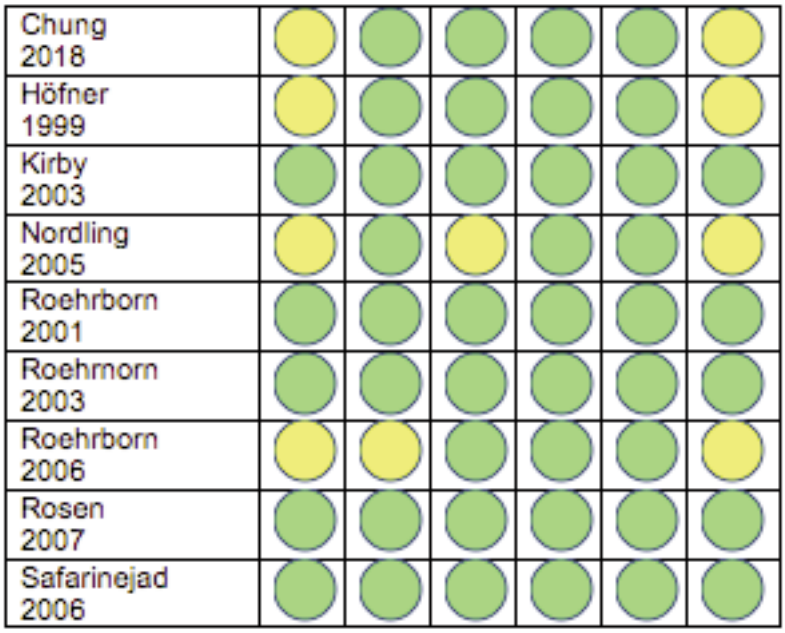
Risk of Bias

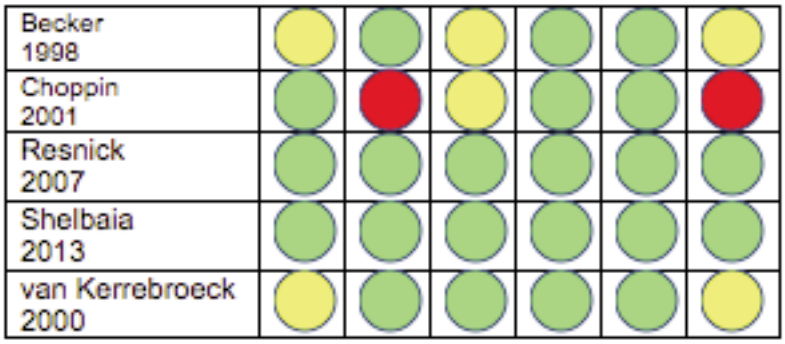
PATIENTS WITH LUTS ASSOCIATED TO BPH (EFFECTS ON EJACULATION)



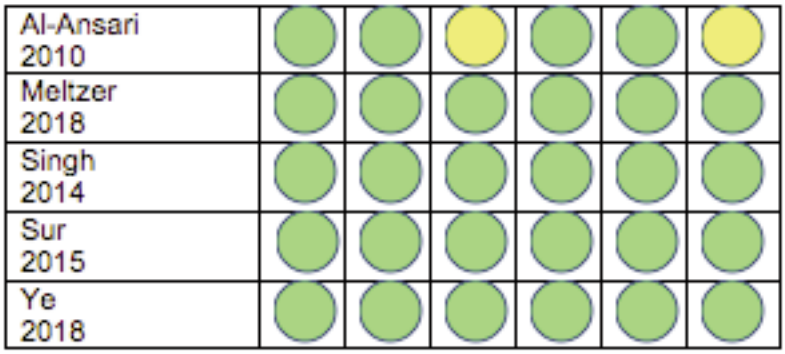
PATIENTS WITH LUTS ASSOCIATED TO BPH (EFFECTS ON EJACULATION AND ERECTION)

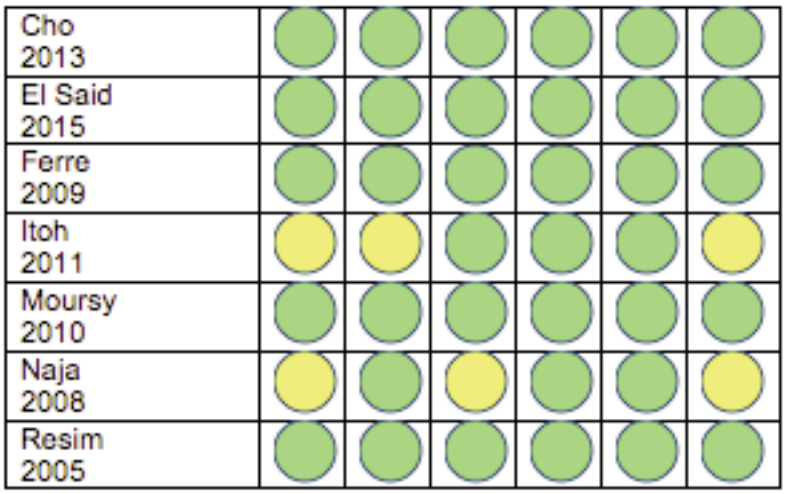


PATIENTS WITH LUTS ASSOCIATED TO BPH (EFFECTS ON ERECTION)

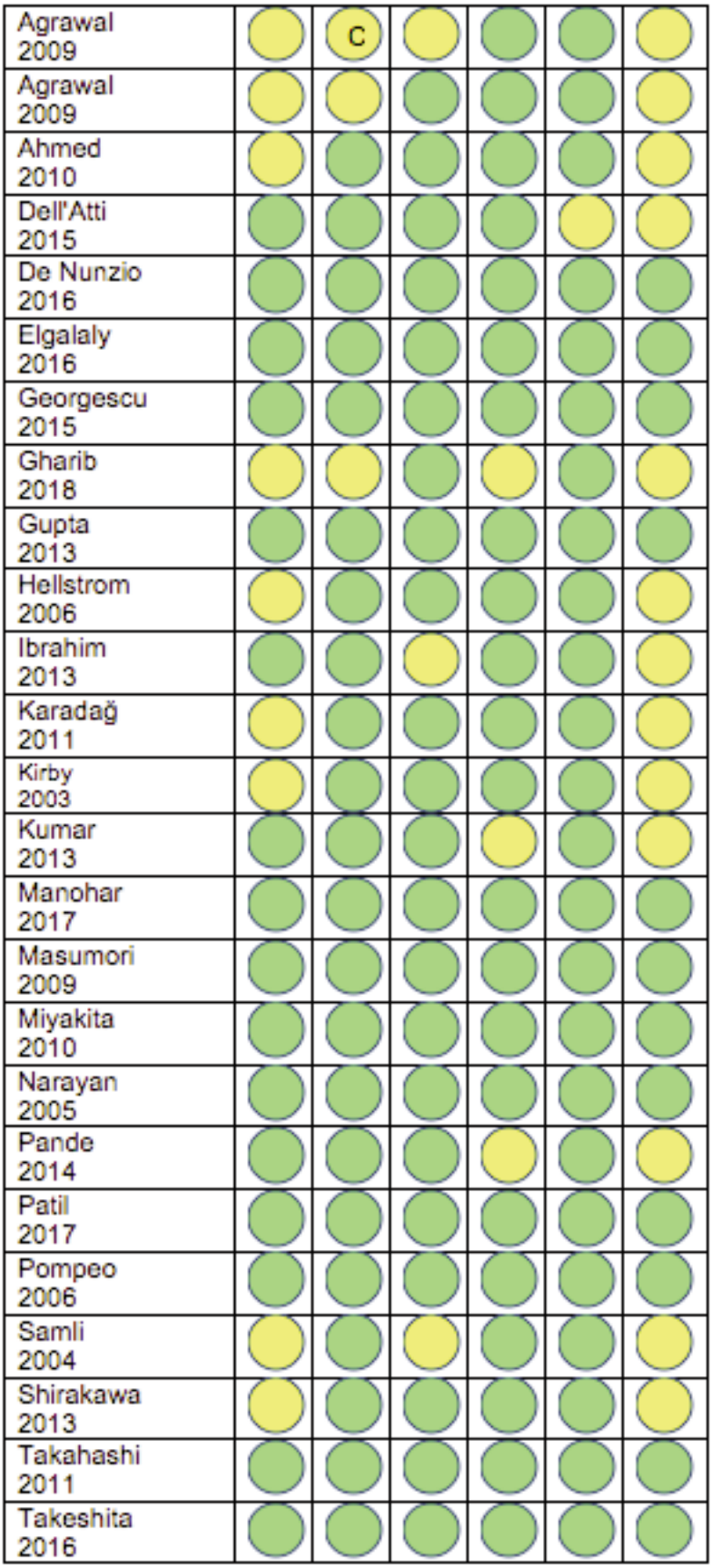


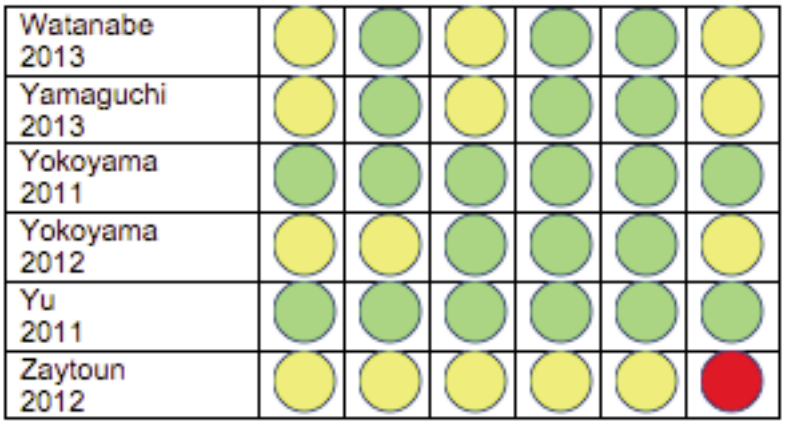
PATIENTS WITH URETERAL STONE (EFFECTS ON EJACULATION)



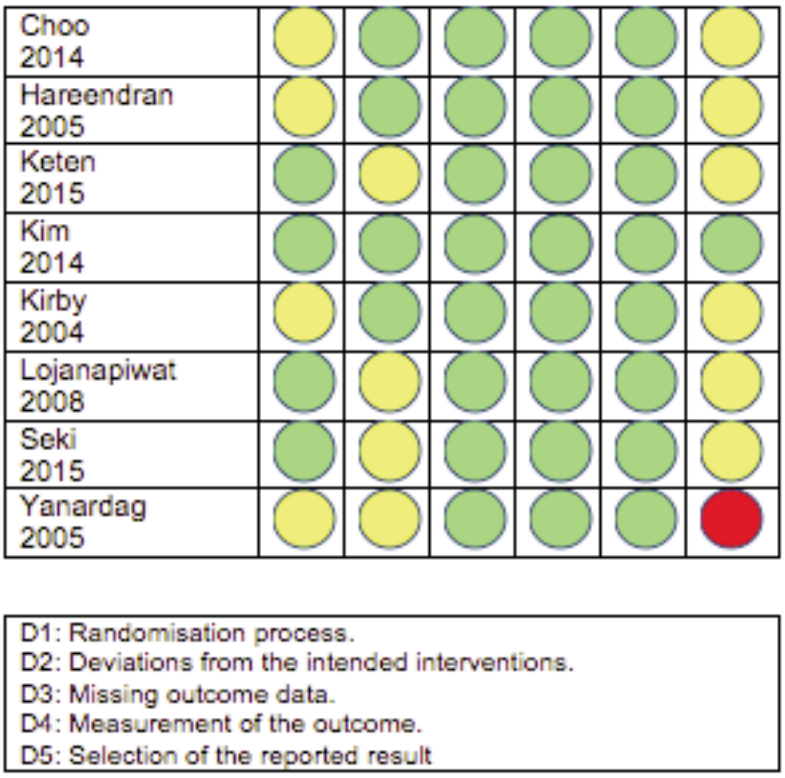


COMPARISON BETWEEN ALPHA-BLOCKERS (UROSELECTIVE VS NONSELECTIVE)



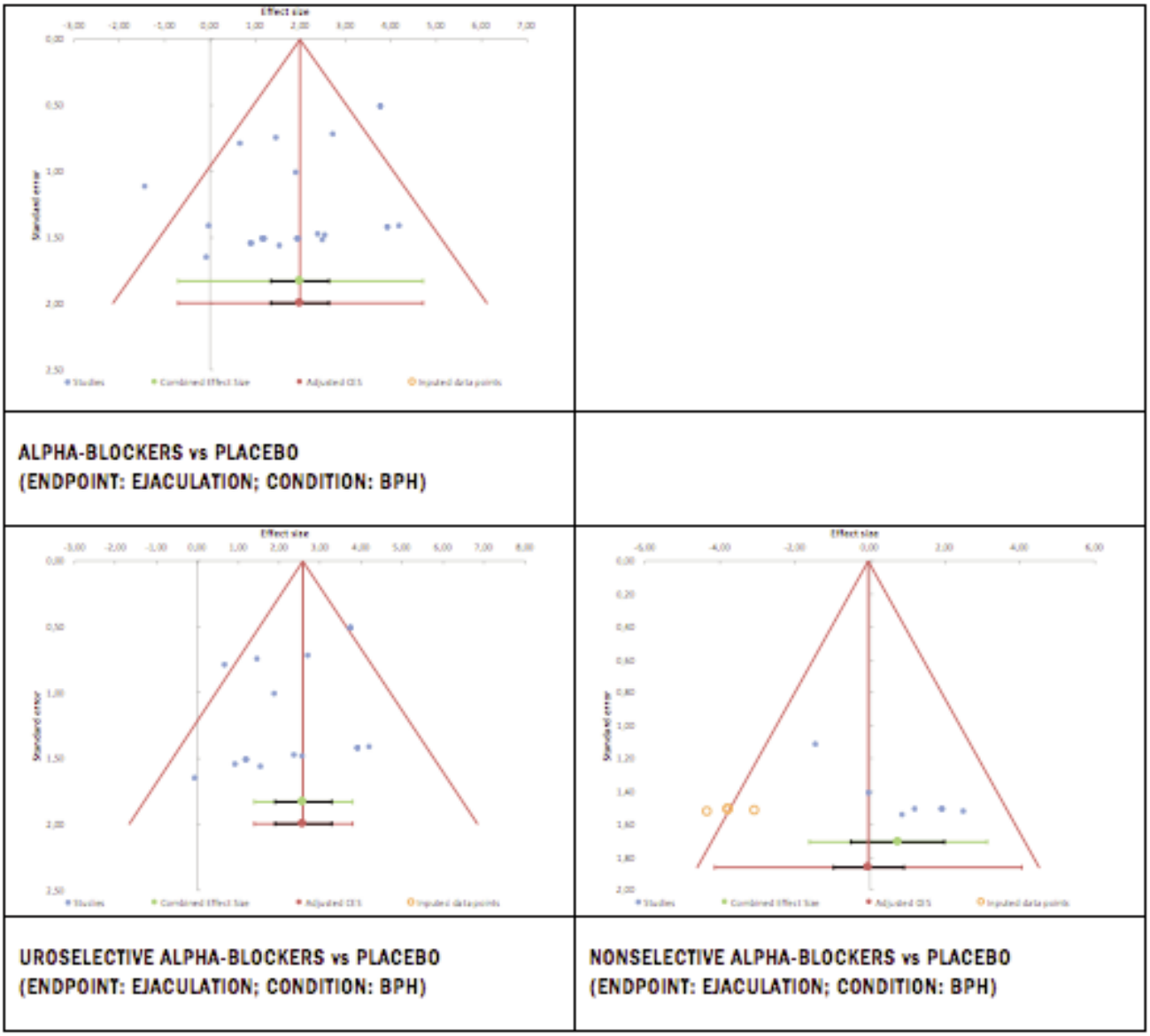


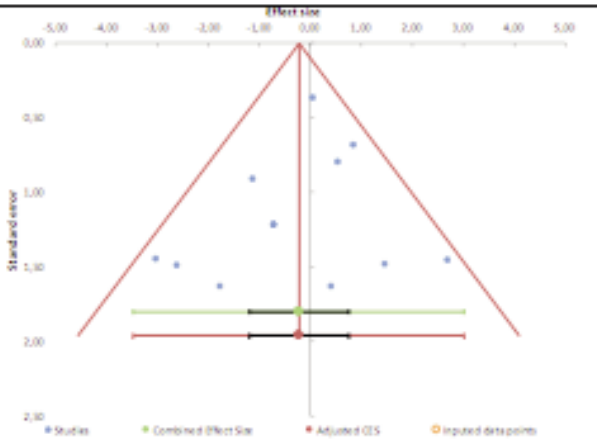
COMPARISON BETWEEN ALPHA-BLOCKERS (UROSELECTIVE VS NONSELECTIVE)



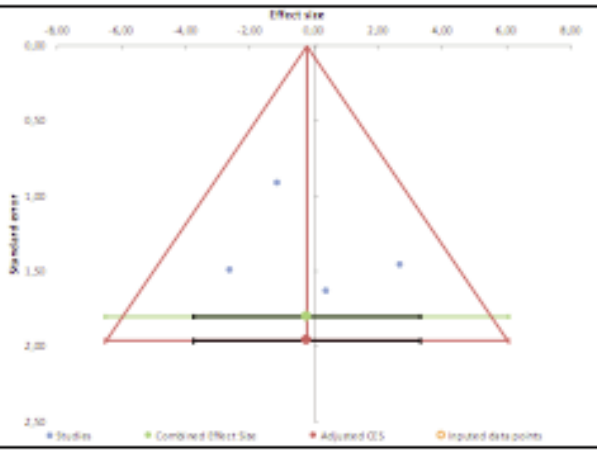
PUBLICATION BIAS

Funnel plots for publication bias analysis.
The combined effect size of each meta-analysis is presented as the natural logarithm of the odds ratio (green dots). Missing studies (orange circles) imputed by the trim-and-fill procedure were merged with included studies (blue dots) to calculate adjusted combined effect sizes (red dots).





ALPHA-BLOCKERS vs PLACEBO
(ENDPOINT: ERECTION; CONDITION: BPH)



UROSELECTIVE ALPHA-BLOCKERS vs PLACEBO
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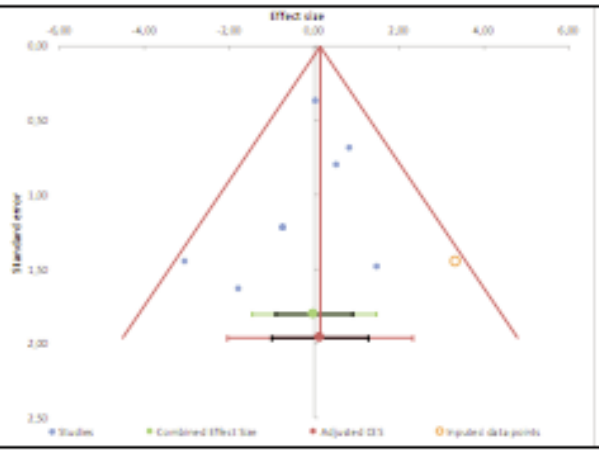

NONSELECTIVE ALPHA-BLOCKERS vs PLACEBO
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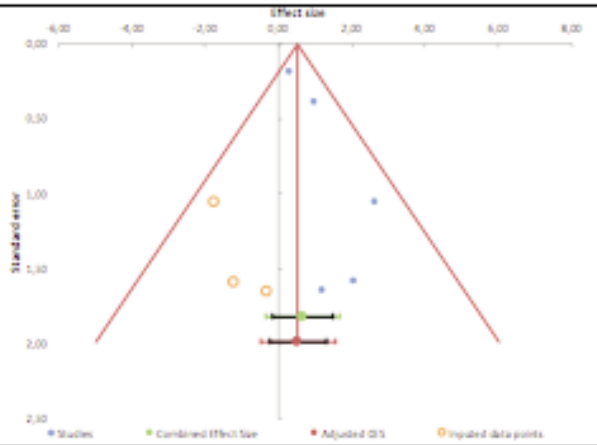
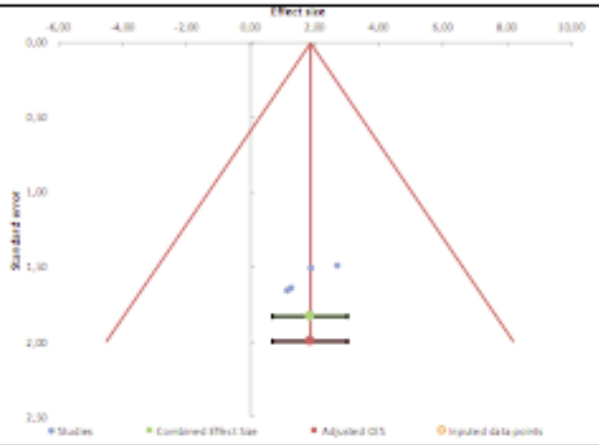
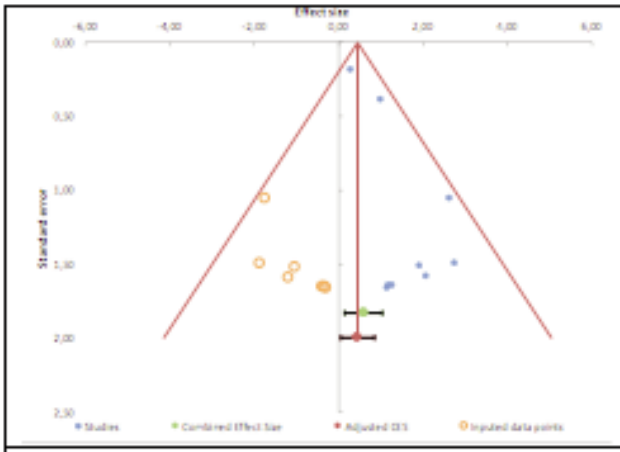


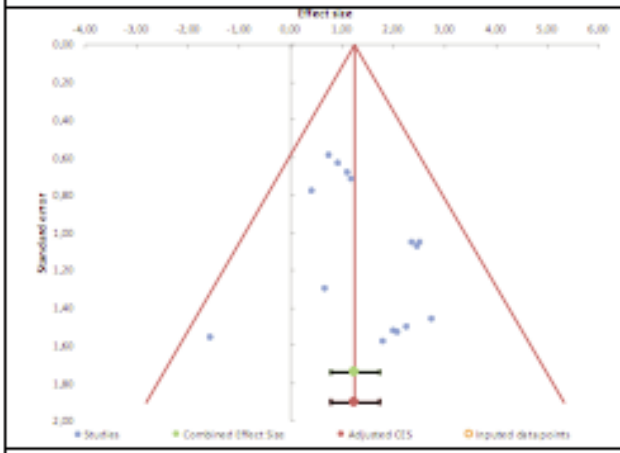
ALPHA-BLOCKERS VS PLACEBO
(ENDPOINT: EJACULATION; CONDITION: STONES)



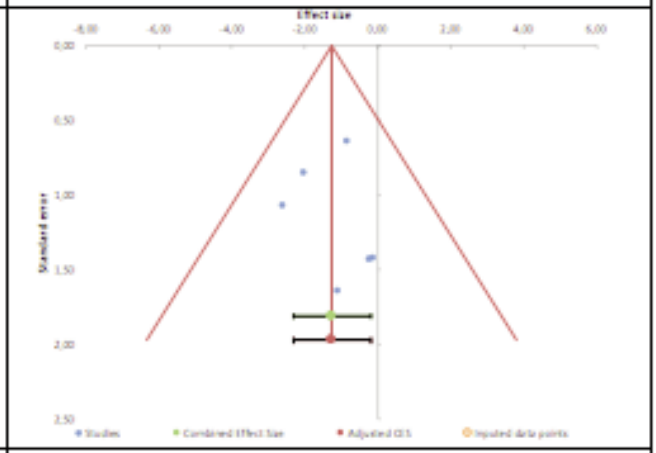
ALPHA-BLOCKERS VS STANDARD CARE
(ENDPOINT: EJACULATION; CONDITION: STONES)



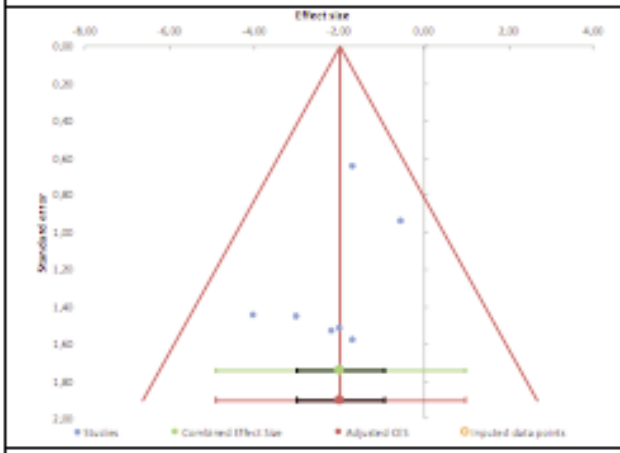
ALPHA-BLOCKERS VS PLACEBO OR STANDARD CARE
(ENDPOINT: EJACULATION; CONDITION: STONES)



SILODOSIN VS TAMSULOSIN
(ENDPOINT: EJACULATION; CONDITION: BPH OR STONES)



NAFTOPIDIL VS UROSELECTIVE ALPHA-BLOCKER
(ENDPOINT: EJACULATION; CONDITION: BPH OR STONES)



ALFUZOSIN VS UROSELECTIVE ALPHA-BLOCKER
(ENDPOINT: EJACULATION; CONDITION: BPH OR STONES)

SYMMETRY TESTS

Results of Funnel Plot Symmetry tests. Missing studies imputed to asymmetric plots and the adjusted odds ratio according to the Trim-and-fill method are presented.

Comparison	Imputed data points, "Trim and Fill"	Adjusted Odds Ratio (95% CI), "Trim and Fill"	Egger's test, significance (*)	Begg's test, significance (*)
Alpha-blockers vs. Placebo; Condition: BPH; Endpoint: Ejaculation	None	Same as non-adjusted	p = 0.001 (*)	p = 0.102
Uroselective Alpha-blockers vs. Placebo; Condition: BPH; Endpoint: Ejaculation	None	Same as non-adjusted	p = 0.142	p = 0.024 (*)
Non-uroselective alpha-blockers vs. Placebo; Condition: BPH; Endpoint: Ejaculation	4	0.97 (0.37 to 2.48)	p = 0.005 (*)	p = 0.176
Alpha-blockers vs. Placebo; Condition: BPH; Endpoint: Erection	None	Same as non-adjusted	p = 0.493	p = 0.064
Uroselective alpha-blockers vs. Placebo; Condition: BPH; Endpoint: Erection	None	Same as non-adjusted	p = 0.720	p = 0.999
Non-uroselective alpha-blockers vs. Placebo; Condition: BPH; Endpoint: Erection	1	1.16 (0.36 to 3.66)	p = 0.229	p = 0.174
Alpha-blockers vs. Placebo; Condition: Stones; Endpoint: Ejaculation	3	1.69 (0.78 to 3.70) (a)	p = 0.104	p = 0.999
Alpha-blockers vs. Standard care; Condition: Stones; Endpoint: Ejaculation	None	Same as non-adjusted	p = 0.071	p = 0.042 (*)
Alpha-blockers vs. Placebo or Standard care; Condition: Stones; Endpoint: Ejaculation	7	1.58 (1.05 to 2.36)	p = 0.007 (*)	p = 0.144
Silodosin vs. Tamsulosin; Endpoint: Ejaculation	None	Same as non-adjusted	p = 0.158	p = 0.729
Naftopidil vs. Uroselective alpha-blocker; Condition: BPH; Endpoint: Ejaculation	None	Same as non-adjusted	p = 0.800	p = 0.573
Alfuzosin vs. Uroselective alpha-blocker; Condition: BPH; Endpoint: Ejaculation	None	Same as non-adjusted	p = 0.228	p = 0.881

(a) After imputation of 3 missing studies, the adjusted odds ratio lost statistical significance (non-adjusted OR, 2.60; 95% CI, 1.20 to 5.65).

FOREST PLOTS NOT SHOWN IN THE TEXT

Figure 1.
Odds of ejaculatory disorders in patients with ureteral stones. Data to the right of the vertical no-effect axis indicate higher odds for ejaculatory disorders in patients treated with alpha adrenoceptor blockers compared to placebo.

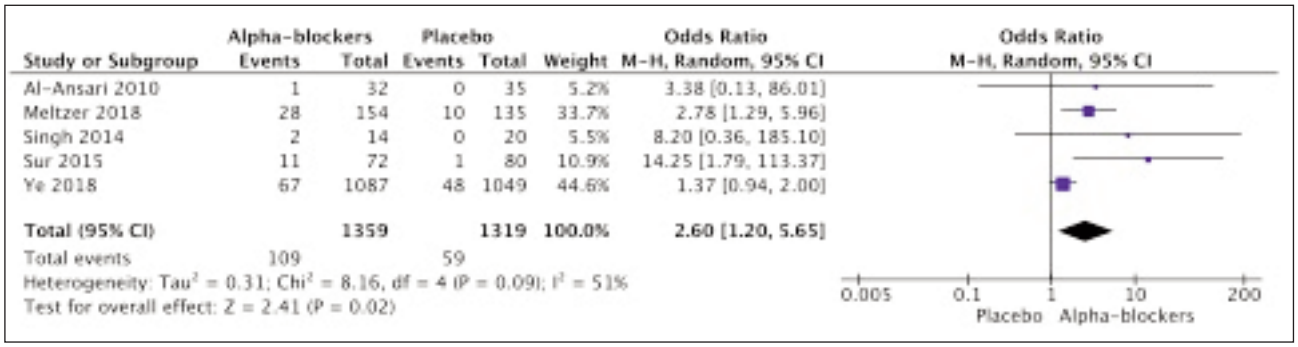


Figure 2.
Odds of ejaculatory disorders in patients with ureteral stones. Data to the right of the vertical no-effect axis indicate higher odds for ejaculatory disorders in patients treated with alpha adrenoceptor blockers compared to standard treatment.

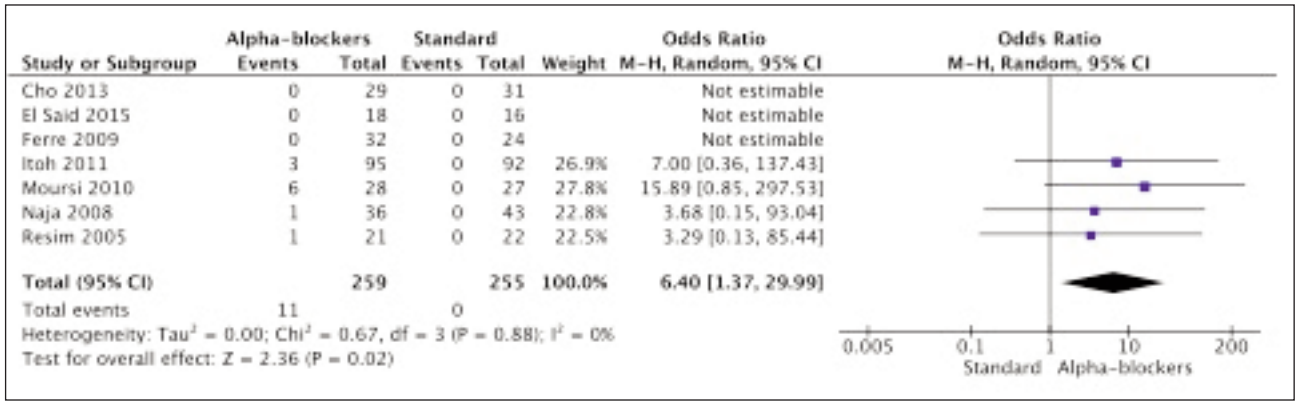


Figure 3.
Odds of erectile dysfunction in BPH patients. Data to the right of the vertical no-effect axis indicate higher odds for ejaculatory disorders in patients treated with uroselective alpha adrenoceptor blockers compared to placebo.

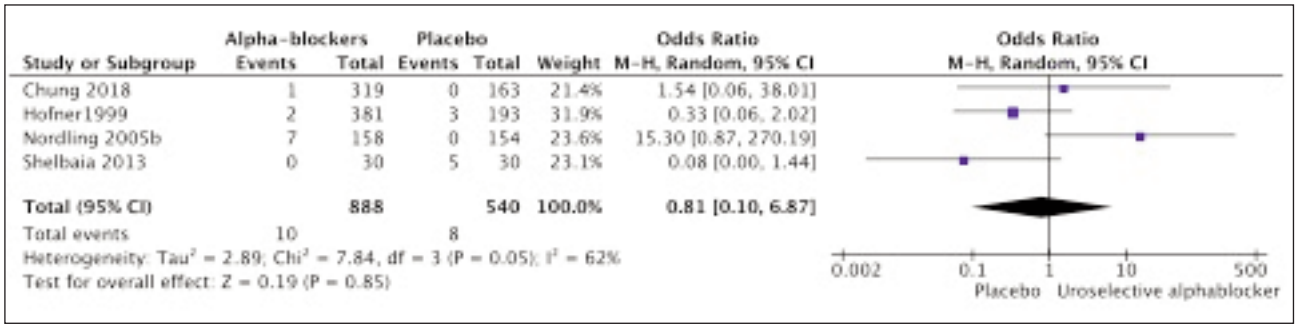
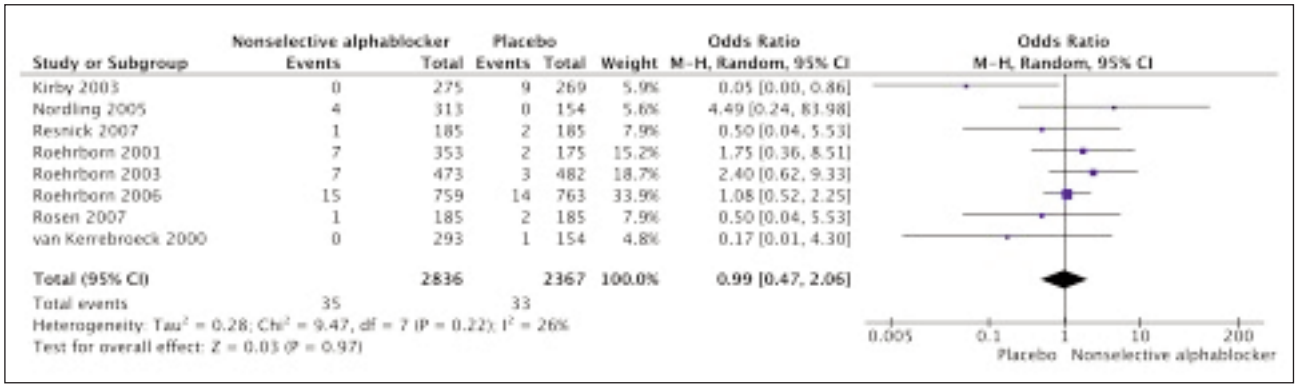


Figure 4.
Odds of erectile dysfunction in BPH patients. Data to the right of the vertical no-effect axis indicate higher odds for ejaculatory disorders in patients treated with non-uroselective alpha adrenoceptor blockers compared to placebo.



Summary of Findings

Effect of alpha-adrenoceptor blockers versus placebo (or standard care) on ejaculatory function

Patient or population: male patients with Benign Prostatic Hyperplasia (BPH) or with ureteral stones
Settings: outpatient
Intervention: uroselective or non-uroselective alpha blockers,
Comparison: placebo or standard care
Outcome: ejaculatory function

Comparisons (condition)	Illustrative comparative risks (95% CI)		Relative effect (95% CI)	No of Participants (studies or comparisons)	Quality of the evidence (GRADE)	Comments
	Assumed control risk	Corresponding intervention risk				
	Comparison	Intervention				
Alpha blockers (any) vs. placebo (BPH)	**4.06 per 1000**	**29.81 per 1000** (15.15 to 57,76)	**OR** 7.53 (3.77 to 15.02)	13006 (23)	⊕⊕⊕⊖ **Moderate**	*Reasons for upgrading:* -large magnitude of effect *Reasons for downgrading:* -publication bias -risk of bias
Uroselective alpha blockers vs. placebo (BPH)	**5.22 per 1000**	**56.77 per 1000** (28.47 to 110.03)	**OR** 11.46 (5.58 to 23.54)	8580 (16)	⊕⊕⊖⊖ **Low**	*Reasons for upgrading:* -large magnitude of effect *Reasons for downgrading:* -risk of bias -publication bias -inconsistency due to substantial heterogeneity
Non-uroselective alpha blockers vs. placebo (BPH)	**2.44 per 1000**	**5.40 per 1000** (1.75 to 16.45)	**OR** 2.22 (0.72 to 6.84)	4426 (7)	⊕⊕⊖⊖ **Low**	*Reasons for upgrading:* none *Reasons for downgrading:* -risk of bias -publication bias
Alpha blockers (any) vs. placebo or standard care (stones)	**37.48 per 1000**	**100.21 per 1000** (55.19 to 174.81)	**OR** 2.86 (1.50 to 5.44)	3192 (12)	⊕⊕⊕⊖ **Moderate**	*Reasons for upgrading:* -large magnitude of effect *Reasons for downgrading:* -risk of bias -publication bias
Alpha blockers (any) vs. placebo (stones)	**44.73 per 1000**	**108.53 per 1000** (53.20 to 209.21)	**OR** 2.60 (1.20 to 5.65)	2678 (5)	⊕⊕⊕⊖ **Moderate**	*Reasons for upgrading:* -large magnitude of effect *Reasons for downgrading:* -risk of bias
Alpha blockers (any) vs. standard care (stones)	**3.90 per 1000**	**24.48 per 1000** (5.34 to 105.23)	**OR** 6.40 (1.37 to 29.99)	514 (7)	⊕⊕⊖⊖ **Low**	*Reasons for upgrading:* -large magnitude of effect *Reasons for downgrading:* -risk of bias -publication bias -imprecision due to wide 95% CI

The **corresponding intervention risk** (and its 95% confidence interval) is based on the assumed control risk in the comparison group and the relative effect of the intervention (and its 95% CI). It is calculated from the odds ratio using the formula: OR x ACR/[1-ACR + (OR x ACR)]
CI: Confidence Interval; **OR:** Odds Ratio; **ACR:** Assumed Control Risk

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

Effect of alpha-adrenoceptor blockers versus placebo on erectile function

Patient or population: male patients with Benign Prostatic Hyperplasia (BPH)
Settings: outpatient
Intervention: uroselective or non-uroselective alpha blockers,
Comparison: placebo
Outcome: erectile function

Comparisons	Illustrative comparative risks (95% CI)		Relative effect (95% CI)	No of Participants (studies or comparisons)	Quality of the evidence (GRADE)	Comments
	Assumed control risk	Corresponding intervention risk				
	Comparison	Intervention				
Alpha blockers (any) vs. placebo	**13.72 per 1000**	**12.09 per 1000** (5.81 to 24.70)	**OR** 0.88 (0.42 to 1.82)	6631 (12)	⊕⊕⊖⊖ **Low**	*Reasons for upgrading:* None *Reasons for downgrading:* -risk of bias -indirectness of evidence due to outcome of secondary interest
Uroselective alpha blockers vs. placebo	**14.81 per 1000**	**12.03 per 1000** (1.50 to 93.63)	**OR** 0.81 (0.10 to 6.87)	1428 (4)	⊕⊖⊖⊖ **Very low**	*Reasons for upgrading:* none *Reasons for downgrading:* -risk of bias -inconsistency due to substantial heterogeneity -indirectness of evidence due to outcome of secondary interest
Non-uroselective alpha blockers vs. placebo	**13.94 per 1000**	**13.80 per 1000** (6.60 to 28.30)	**OR** 0.99 (0.47 to 2.06)	5203 (8)	⊕⊕⊖⊖ **Low**	*Reasons for upgrading:* -none *Reasons for downgrading:* -risk of bias -indirectness of evidence due to outcome of secondary interest

The **corresponding intervention risk** (and its 95% confidence interval) is based on the assumed control risk in the comparison group and the relative effect of the intervention (and its 95% CI). It is calculated from the odds ratio using the formula: OR/[1-ACR x (1-OR)]
CI: Confidence Interval; **OR:** Odds Ratio; **ACR:** Assumed Control Risk

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

Effect of different alpha-adrenoceptor blockers on ejaculatory function

Patient or population: male patients with Benign Prostatic Hyperplasia (BPH) or ureteral stones
Settings: outpatient
Intervention: Silodosin, naftopidil, alfuzosin
Comparison: Tamsulosin or uroselective alpha blockers
Outcome: ejaculatory function

Comparisons	Illustrative comparative risks (95% CI)		Relative effect (95% CI)	No of Participants (studies or comparisons)	Quality of the evidence (GRADE)	Comments
	Assumed control risk	Corresponding intervention risk				
	Comparison	Intervention				
Silodosin vs. tamsulosin	**31.95 per 1000**	**104.10 per 1000** (67.13 to 157.90)	**OR** 3.52 (2.18 to 5.68)	1512 (15)	⊕⊕⊕⊕ **High**	*Reasons for upgrading:* -large magnitude of effect *Reasons for downgrading:* -risk of bias
Naftopidil vs. uroselective alpha-blockers	**132.47 per 1000**	**42.40 per 1000** (19.46 to 89.03)	**OR** 0.29 (0.13 to 0.64)	474 (6)	⊕⊕⊕⊖ **Moderate**	*Reasons for upgrading:* none *Reasons for downgrading:* -risk of bias
Alfuzosin vs. uroselective alpha-blockers	**115.64 per 1000**	**21.74 per 1000** (9.07 to 47.33)	**OR** 0.17 (0.07 to 0.38)	877 (8)	⊕⊕⊕⊕ **High**	*Reasons for upgrading:* -large magnitude of effect *Reasons for downgrading:* -risk of bias

The **corresponding intervention risk** (and its 95% confidence interval) is based on the assumed control risk in the comparison group and the relative effect of the intervention (and its 95% CI). It is calculated from the odds ratio using the formula: OR/[1-ACR x (1-OR)]
CI: Confidence Interval; **OR:** Odds Ratio; **ACR:** Assumed Control Risk

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.