**Additional file 4** Summary of patient characteristics of included studies

**Table d** Summary of patient characteristics of included interventional studies

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Authors (Year)** | **Recruitment** | **Sample size and age profile** | **Race/ethnicity in %** | **Men in %** | **BPH related scores (mean values)** | **Co-medication** | **Co-morbidities** |
| ALLHAT (2003) [43]1 | Practice based setting in the US only through (e.g.):* Universities or medical centers
* Veterans Hospitals
* Practices
* Primary care
* Specialty clinics
 | Doxazosin:* n=9,061
* ≥70 y: 3,092

Chlorthalidone:* n=15,255
* ≥70 y: 5,410
 | Chlorthalidone:* White: 47.2%
* Black: 31.9%
* Hispanic: 15.8%
* Other: 5.1%

Doxazosin:* White: 46.5%
* Black: 32.9%
* Hispanic: 16%
* Other: 4.6%
 | Chlorthalidone: 53.0%Doxazosin: 53.6% | N.a. | Additional treatment for hypertension was allowed with:* Atenolol
* Reserpine
* Clonidine
* Hydralazine
 | Comorbidities such as atherosclerotic cardiovascular disease, type 2 diabetes and unfavourable cholesterol levels were matched between the chlorthalidone and doxazosin group |
| Gotoh et al. (2005) [44]2 | Multicenter trial in JP through 17 urologists in 16 sites | Tamsulosin:* n=75
* mean age: 68.5 y
* 95% CI: 67.0 – 70.1 y

Naftopidil:* n=69
* mean age: 68.0 y
* 95% CI: 66.4 – 69.8 y
 | N.a. | 100% | Tamsulosin:* Vprostate: 33.6 ml
* IPSS: 17.1
* QoL: 4.4
* PVR: 42.5 ml

Naftopidil:* Vprostate: 29 ml
* IPSS: 15.5
* QoL: 4.5
* PVR: 46.6 ml
 | Patients were excluded if they were currently in treatment with:* Antiandrogens
* α1-antagonists
* Anticholinergic drugs
 | Patients were excluded if they had (a history of) one or more of the following diseases:* Orthostatic hypertension
* Neurological disease incl. bladder dysfunction
* Carcinoma of bladder or prostate
* Surgery for BPH or bladder neck obstruction
* Urinary tract infections
 |
| Nishino et al. (2006) [45]3 | Patients of the Department of Urology at Gifu University (JP) | Tamsulosin/ naftopidil: * n=17

Naftopidil/ tamsulosin:* n=17
 | N.a. | 100% | * Vprostate: 19.8 ml
* IPSS: 20.4
* QoL: 4.9
* PVR: 54.1 ml
* Qmax: 9.9 ml/s
 | Patients were excluded if they had ever been medically treated for BPH | Patients were excluded if they had (a history of) one or more of the following diseases (e.g.):* Neurogenic disorders
* Urinary retention
* Carcinoma of bladder
* Urinary tract infections
 |
| Oelke et al. (2014) [46]4 | Patients were recruited internationally in 44 urology sites in Europe (71%), Mexico and Australia  | Tamsulosin:* n=168
* ≥66 y: 72

Tadalafil:* n=171
* ≥66 y: 75

Placebo:* n=172
* ≥66 y: 77
 | Tamsulosin:* White: 78%
* Black/African American: 0%
* American Indian/Alaska Native: 22%

Tadalafil:* White: 76%
* Black/African American: 0.6%
* American Indian/Alaska Native: 23.4%

Placebo:* White: 76.2%
* Black/African American: 0%
* American Indian/Alaska Native: 23.8%
 | 100% | Tamsulosin:* IPSS: 16.8
* Erectile dysfunction (ED): 69%
* BMI: 27.9 kg/m²

Tadalafil:* IPSS: 17.2
* ED: 70.8%
* BMI: 27.1 kg/m²

Placebo:* IPSS: 17.4
* ED: 69.8%
* BMI: 28.1 kg/m²
 | Previous therapies within 12 mo prior to screening:Tamsulosin:* α-blockers: 25.6%
* Other LUTS/BPH therapy: 5.4%
* ED therapy: 12.5%

Tadalafil:* α-blockers: 24%
* Other LUTS/BPH therapy: 3.5%
* ED therapy: 12.3%

Placebo:* α-blockers: 26.2%
* Other LUTS/BPH therapy: 4.7%
* ED therapy: 13.4%
 | Patients excluded if they had (had) prostate cancer |
| Roehrborn (2006) [47]5 | Patients were recruited internationally in 148 urology sites in North America, Europe, Australia, Middle East and South-Africa | Alfuzosin:* n=759
* ≥65 y: 449

Placebo:* n=763
* ≥65 y: 439
 | N.a. | 100% | Alfuzosin:* Vprostate: 46.9 ml
* IPSS: 19.2
* PVR: 95.3 ml
* Qmax: 8.9 ml/s

Placebo:* Vprostate: 46.6 ml
* IPSS: 19.2
* PVR: 89 ml
* Qmax: 8.8 ml/s
 | Patients were excluded if they were taking medication which would eventually change the voiding pattern | Hypertension:* Alfuzosin: 36.1%
* Placebo: 35%

Patients were excluded if they had (a history of) one or more of the following diseases:* Postural hypotension or syncope
* Carcinoma of prostate
* Surgery of prostate
* AUR
 |
| Yokoyama et al. (2011) [48]6 | Department of Urology at Kawasaki Medical School, Japan | Tamsulosin:* n=45
* mean age: 71.5 y

Silodosin: * n=45
* mean age: 70.2 y

Naftopidil:* n=46
* mean age: 69.1 y
 | N.a. | 100% | Tamsulosin:* Vprostate: 32.5 ml
* IPSS: 18
* QoL: 4.49
* PVR: 29.7 ml
* Qmax: 8.56 ml/s

Silodosin: * Vprostate: 33.3 ml
* IPSS: 18.7
* QoL: 4.5
* PVR: 57.6 ml
* Qmax: 9.03 ml/s

Naftopidil:* Vprostate: 35 ml
* IPSS: 17.4
* QoL: 4.55
* PVR: 39.1 ml
* Qmax: 8.63 ml/s
 | N.a. | N.a. |

1 Patient characteristics refer to total study population including patients of all age groups ≥55 y.

2 Patient characteristics refer to total study population including patients of all age groups ≥50 y with mean age (95% CI) being 68.5 y (67.0 y – 70.1 y)

3 All patients are aged ≥66 y.

4 Patient characteristics refer to total study population including patients of all age groups ≥45 y.

5 Patient characteristics refer to total study population including patients of all age groups ≥55 y.

6 Patient characteristics refer to total study population including patients of all age groups ≥50 y with mean age (SD) being 70.2 y (0.9), 71.5 y (1.1) and 69 y (1.2) for the silodosin, tamsulosin or nifedipine group, respectively.

**Table e** Summary of patient characteristics of included observational studies

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Authors(Year) | Recruitment | Sample size and age profile | Race/ethnicity in % | Men in % | Co-medication(numbers represent mean values) | Co-morbidities |
| Retrospective Cohort Studies: |
| Chrischilles et al. (2001) [49]1 | Cohorts were created from information received through a medical claims database in the US (1995-1997) including:* Outpatient drug utilization
* Inpatient physician services
* Outpatient physician services
 | Users: * n=1,564
* Mean age: 73 y
* Prazosin=15
* Doxazosin=782
* Terazosin=839

Non-Users:* n=8,641
* Mean age: 72.5 y
 | N.a. | 100% | Use of additional antihypertensive drugs (α1-blocker users vs. non-users): * Any agent: 56.3 % vs. 26.2%
* ACE-inhibitors: 28.9% vs. 12.2%
* Beta-blockers: 15.4% vs. 6.6%
* Ca-Channel-blockers: 35.6% vs. 14.7%
* Diuretics: 33.7% vs. 13.4%

No. of agents used:* 0: 34.1% vs. 71.4%
* 1: 30.2% vs. 14.3%
* 2: 21.4% vs. 9.8%
* >3: 14.2% vs. 4.6%
 | α1-blocker users vs. non-users:* Hypertension: 23% vs. 20.4%
* Type 2 Diabetes: 8.2% vs. 7.1%
* Cardiac arrhythmia: 8.3% vs. 7.2%

No. of comorbidities:* 0: 62.7% vs. 66.3%
* 1: 28.8% vs. 27.6%
* 2: 7.4% vs. 5.0%
* >3: 1.2% vs. 1.1%
 |
| Duan et al. (2018) [50]2 | Cohorts were created from US Medicare data (2006-2012) including 100% US Medicare beneficiaries | Tamsulosin: * n=253,136

No BPH-medication:* n=180,926

Doxazosin:* n=28,581

Terazosin:* n=23,858

Alfuzosin:* n=17,934

Dutasteride:* n=34,027

Finasteride:* n=38,767
 | Tamsulosin:* White: 86.7%
* Black: 5.7%
* Hispanic: 2.6%
* Other: 5.1%

No BPH medication:* White: 86.8%
* Black: 5.6%
* Hispanic: 2.5%
* Other: 5.1%
 | 100% | No. of drugs used (tamsulosin vs. no BPH medication):* 1-2: 29.2% vs. 29.2%
* 3-4: 31.3% vs. 31.3.%
* 5-6: 18.2% vs. 18.4%
* ≥7: 8.7% vs. 8.6%
 | Tamsulosin vs. no BPH medication:* CeVD: 7.7% vs. 7.7%
* PVD: 10.9% vs. 10.9%
* CHF: 10.3% vs. 10.1%
* Hypertension: 64.4% vs. 64.3%
* Diabetes: 26.7% vs. 26.7%
* Hyperlipidemia: 56.9% vs. 56.7%
* Depression: 4.9% vs. 4.8%
 |
| Welk et al. (2015) [51]3 | Cohorts were derived from administrative data provided by the province of Ontario, Canada | Alpha-blocker initiation:* n=147,084

No initiation:* n=147,084
 | n.a. | 100% | Matched cohorts: unexposed (no α1-blocker use) vs. exposed (α1-blocker use):* Cancer: 22% vs. 20.5%
* Cataract: 19.3% vs. 19%
* CKD: 9.8% vs. 9.1%
* Chronic lung disease: 28.1% vs. 28.1%
* CHF: 14.1% vs. 13.3%
* Coronary artery disease or angina: 42.9% vs. 42.4%
* Dementia: 9.9% vs. 10.5%
* Diabetes: 20.6% vs. 20.9%
* Glaucoma: 6.8% vs. 6.5%
* Hypertension: 69.8% vs. 69.4%
* Osteoporosis: 6.1% vs. 6.0%
* Prostate cancer: 13.0% vs. 11.7%
 | Matched cohorts: unexposed (no α1-blocker use) vs. exposed (α1-blocker use):* 5α-reductase inhibitors: 7.4% vs. 7.4%
* ACE-inhibitors: 49.5% vs. 49.3%
* Anti-inflammatory drugs: 15.8% vs. 16.8%
* Antibiotics: 37.3% vs. 38.3%
* Anticonvulsants: 5.0% vs. 5.1%
* Antidepressants: 7.2% vs. 7.4%
* Antineoplastic: 5.5% vs. 5.0%
* Antiplatelets: 7.3% vs. 7.2%
* Benzodiazepines: 14.2% vs. 14.4%
* Beta-blockers: 32.3% vs. 30.9%
* Bisphosphonates: 6.8% vs. 6.5%
* Ca-channel blockers: 26.9% vs. 27.3%
* Glucocorticoids: 9.6% vs. 9.5%
* Inhaled acetylcholine: 7.5% vs. 7.6%
* Inhaled beta-agonist: 13.3% vs. 12.8%
* Inhaled corticosteroids: 6.0% vs. 5.5%
* Narcotics: 19.2% vs. 19.4%
* Non-potassium sparing diuretics: 26.4% vs. 23.8%
* Potassium sparing diuretics: 4.2% vs. 3.6%
* PPI: 25.9% vs. 25.4%
* SSRI: 7.0% vs. 7.0%
* Statins: 48.8% vs. 48.6%
 |
| **Case-Control Studies:** |
| Hall and McMahon (2007) [52]4 | Cases and Controls were derived from data from the UK primary care records (THIN database) | Cases (fracture):* n=6,540
* Taking MR Doxazosin: 66
* Taking MR Doxazosin and ≥75y: 32

Controls (no fracture):* n=26,495
* Taking MR Doxazosin: 311
* Taking MR Doxazosin and ≥75y: 173
 | N.a. | 100% | Cases (fractures) vs. controls (no fractures):* Thiazide diuretics: 14.5% vs. 17.1%
* Other anti-hypertensives: 31.4% vs. 33.5%
* Other cardiac drugs: 22.1% vs. 19.9%
* Benzodiazepines: 9.8% vs. 7.3%
* Antipsychotics: 6.2% vs. 3.6%
* NSAIDs: 28.8% vs. 25.3%
* Antidepressants: 16.1% vs. 10.3%
* Oestrogen: 3.8% vs. 5.9%
* Other osteoporosis treatment: 12.3% vs. 7.7%
* Glucocorticoids: 8.4% vs. 6.0%
 | Cases (fractures) vs. controls (no fractures):* Arthritis (excl. rheumatoid arthritis): 27.6% vs. 26.8%
* Heart failure: 6.9% vs. 5.5%
* COPD: 20.2% vs. 27.6%
* Cerebrovascular accident: 10.9% vs. 8.6%
* Osteoporosis: 8.0% vs. 4.8%
* Type II diabetes: 8.9% vs. 7.9%
* Dementia: 5.4% vs. 2.2%
 |
| Testa et al. (2018) [53]5 | Cases and Controls were enrolled in different settings in Italy including outpatient departments, nursing homes and acute care units | Syncopal fall:* n=354
* Mean age: 83.3 y

Non-syncopal fall: * n=168
* Mean age: 83.9 y
 | N.a. | 37.9% | Cases (syncopal fall) vs. controls (non-syncopal fall):* No. of antihypertensives: 2.9 vs. 2.5
* < 2 antihypertensives: 50% vs. 56.4%
 | Cases (syncopal fall) vs. controls (non-syncopal fall):* Alzheimer’s: 31.9% vs. 35.1%
* Vascular dementia: 42.9% vs. 38.7%
* Mixed dementia: 15.5% vs. 15.5%
* Parkinson’s: 5.6% vs. 6.5%
* Hypertension: 74.3% vs. 75%
* CAD: 19.5% vs. 18.5%
* CHF: 8.5% vs. 10.1%
* Atrial fibrillation: 25.1% vs. 23.8%
* Stroke: 11.6% vs. 19.6%
* TIA: 7.6% vs. 7.1%
* Carotid atherosclerosis: 27.4% vs. 20.2%
* Psychiatric disease: 33.6% vs. 29.2%
* Diabetes: 20.9% vs. 24.4%
* Dysthyroidism: 10.9% vs. 10.9%
 |

1 All patients are aged ≥65 y.

2 Duan (2018) includes 6 cohort-pairs, all of which were prospensity-score-matched. The figures presented in this table only concern the biggest cohort with 161,729 people comparing tamsulosin-users vs. no BPH medication. All patients are aged ≥66 y.

3 All patients are aged ≥66 y.

4 Patient characteristics refer to total study population including patients of all age groups ≥50 y.

5 All patients are aged ≥65 y.

**Table f** Summary of patient characteristics of included meta-analyses

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Authors(Year) | Data used | Patients | Race/ethnicity in % | Men in % | BPH related scores (mean values) | Co-medication | Co-morbidities |
| Buzelin et al. (1997) [54]1 | Meta-analysis using raw data from two placebo-controlled studies conducted in 61 urological centers throughout Europe [56], 2nd study not published separately | SR alfzusosin:* n=292
* ≥65 y: 149

Placebo: * n=296
* ≥65 y: 153
 | N.a. | 100% | Alfuzosin:* Boyarsky score: 9.4
* Qmax: 9.3 ml/s

Placebo:* Boyarsky score: 9.6
* Qmax: 9.2 ml/s
 | Alfuzosin: * Antihypertensives: 30%

Placebo: * Antihypertensives: 30%
 | Alfuzosin: * CVD: 43%
* Hypertension: 29%

Placebo: * CVD: 43%
* Hypertension: 29%
 |
| Lowe (1994) [56]2 | Meta-analysis using raw data from six placebo-controlled trials, three conducted in the US (two of which two are unpublished) and three conducted in Europe [57-60] | Terazosin:* n=636
* ≥65 y: 285

Placebo: * n=360
* ≥65 y: 162
 | White: 94% | 100% | N.a. | N.a. | N.a. |
| Chapple et al. (1997) [55] | Retrospective analysis of data from a meta-analysis [61] using raw data from two European multinational, multicentre, double-blind, placebo-controlled, randomized trials [62], 2nd study not published separately | Tamsulosin:* <65 y: 190
* ≥65 y: 191

Placebo: * <65 y: 93
* ≥65 y: 100
 | N.a. | 100% | N.a. | Tamsulosin: * Antihypertensives/CV medication: 55/191 (29%)

Placebo: * Antihypertensives/CV medication: 25/100 (25%)
 | Tamsulosin: * CV disease: 69/191 (39%)
* Hypertension: 46/186 (25%)

Placebo: * CV disease: 23/100 (23%)

Hypertension: 22/97 (23%) |

1 Patient characteristics refer to total study population including patients of all age groups.

2 Patient characteristics refer to total study population including patients of all age groups.