**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.