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Potentially inappropriate prescribing for prostatic hyperplasia in older persons

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In our study, treatments for benign prostatic hyperplasia potentially inappropriate prescribing for elderly was close to 72%, mainly from α 1-blockers (90%), and was associated with a three-fold higher frequency of falls.

Keywords: Aging, elderly, benign prostatic hyperplasia, α 1-blockers, 5 α -reductase inhibitors, inappropriate prescribing, deprescribing.

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1 **ABSTRACT**

2

3 Objectives: In the context of improved medication management of elderly patients, we wished
4 to evaluate the over-prescription of potentially inappropriate drugs (α 1-blockers and 5 α -
5 reductase inhibitors [5-ARI]) for benign prostate hyperplasia (BPH). These drugs are
6 considered by geriatricians to increase the risk of falls and pharmacodynamic interactions but
7 these properties have not yet been proven. Design: This was a descriptive study of drug
8 prescriptions in a geriatric academic center. Setting and Participants: We included all patients
9 over 75 years of age who received a prescription for α 1-blockers or 5-ARIs for two weeks in
10 our hospital. Methods: We evaluated the prevalence of the potentially inappropriate
11 prescription of α 1-blockers and 5-ARI in the elderly during hospitalization using a new tool
12 consisting of an eight-item list of explicit indicators developed using the most recent
13 summary of product characteristics (SmPC) and latest European Association of Urology
14 (EAU) guidelines. Results: A population of 117 patients (\geq 75 years) was included in the
15 study. The median age was 84.5 (\pm 6.3) years. The average time since urological medication
16 prescription was 1.2 ± 1.6 years. According to explicit criteria, 84 patients (71.8%) received
17 at least one potentially inappropriate urological medication, 77 (91.7%) related to α 1-
18 blockers. Patients with a potentially inappropriate prescription for α 1-blockers and/or 5-ARIs
19 more frequently had urological assessments ($p = 0.026$), more frequently showed
20 pharmacological interactions, with the risk of orthostatic hypotension ($p = 0.005$) or
21 arrhythmia ($p = 0.028$), and experienced more falls in their history ($p = 0.043$). The misuse
22 group was associated with an increased risk of falls, with an OR of 3.22 ($p = 0.039$, 95%CI
23 [1.08-10.2]).

24 Conclusions and implications: In our study, potentially inappropriate prescriptions for the
25 elderly for BPH was close to 72% and mainly involved α 1-blockers. Potentially inappropriate
26 prescriptions for BPH were associated with a three-fold higher frequency of falls.

27 **INTRODUCTION**

28 Monitoring potentially inappropriate medication (PIM) use in an elderly population is
29 crucial because of their frailty due to multi-morbidity and associated polypharmacy. Such
30 errors in medication management can affect health outcomes of older patients and are
31 associated with higher hospitalization rates and mortality^{1,2}. Several assessment tools have
32 been created to identify and avoid PIM in the elderly^{3,4}.

33 Most common medication classes reported in PIM lists do not provide any specific
34 consideration to the over-prescription of benign prostatic hyperplasia (BPH) treatment⁴,
35 whereas geriatricians consider them as PIM because they likely increase the risk of falls and
36 pharmacodynamic interactions. BPH and prostatic enlargement are one of the most common
37 diseases in aging men and can lead to lower urinary-tract symptoms (LUTS)^{5,6,7}. With a
38 changing demographic profile and an increasingly aging population in almost all societies,
39 α 1-blockers and 5 α -reductase inhibitors (5-ARIs) have been widely used. However, strict and
40 citable evidence, such as that from typically derived from randomized control trials (RCTs), is
41 the exception rather than the rule for the elderly population. The recognition of older patients
42 as frequent recipients of pharmacological treatment for LUTS has increased in recent years,
43 leading to a focus on the need for data specific to this population. Prostate-specific
44 α 1-blockers are associated with a small but significant increased risk of falls, probably as a
45 result of induced hypotension⁸.

46 In the context of improved medication management of elderly patients, we evaluated
47 the prevalence of potentially inappropriate prescribing of α 1-blockers and 5-ARIs in the
48 elderly during hospitalization. The subject of such research should empower clinicians in
49 “deprescribing”.

50 **PATIENTS AND METHODS**

51 Study population and data collection

52 This retrospective observational study was carried out by the Department of Geriatric
53 Medicine of our university hospital. All male patients aged ≥ 75 years admitted to the
54 structure over two one-week periods (from 2/25/2019 to 3/3/2019 and from 3/25/2019 to
55 3/31/2019) and treated with $\alpha 1$ -blockers and/or 5-ARIs were enrolled. There was an interval
56 of more than two weeks between each collection of data to limit the number of duplicates.

57 The information needed to evaluate the clinical profile of patients and the
58 appropriateness of their prescriptions was obtained from electronic clinical records
59 (DxCare[®]) and collected in an anonymized Excel database.

60 The demographic characteristics, date of admission and discharge, medical history
61 (diagnoses and co-morbidities, surgical interventions, chronology of treatment), past
62 urological evaluations (symptom score, physical examination, including rectal examination,
63 creatinine measurement, urinalysis, flow rate, post-void residual volume, endoscopy, imaging
64 of upper urinary tract and/or prostate, and voiding chart [diaries]), as well as drug therapy and
65 dosage on admission and during the hospital stay by the generic name and the Anatomical
66 Therapeutic Chemical (ATC) classification system (ATC G04CA [$\alpha 1$ -blockers] and ATC
67 G04 CB [5-ARIs]), were recorded for each patient. Classical geriatric parameters were
68 individualized: activity of daily living (ADL) [9], visual disturbances, incontinence, hearing
69 impairment¹⁰, orthostatic hypotension¹¹, serum albumin¹² and vitamin D¹³ levels, and history
70 of falls. Falls were identified from medical observations and nurses' and hospital reports.
71 Only falls under treatment were counted to potentially incriminate treatment with $\alpha 1$ -blockers
72 and 5-ARIs.

73 Definition of potentially inappropriate prescriptions

74 The prevalence of potentially inappropriate prescription of α 1-blockers and 5-ARIs in
75 the elderly during hospitalization was assessed using an eight-item list of explicit indicators
76 developed and used to assess the appropriateness of drug therapies (Table 1). We developed
77 this composite tool using the most recent summary of product characteristics (SmPC)
78 (downloaded for all drugs from the National Drug Health Agency [ANSM] website source
79 [<https://www.anism.sante.fr/Produits-de-sante/Medicaments>]), the latest EAU guidelines for
80 the management of non-neurogenic male LUTS¹⁴, and data from a number of studies relevant
81 to BPH in consultation with geriatricians and urological specialists^{15,16,17,18}. Pharmacological
82 interactions were analyzed using Diane[®] prescription and kidney guide (GPR) software.
83 Economic appraisal of the potentially inappropriate prescription of α 1-blockers and 5-ARIs
84 was performed using Theriaque[®] software and extended to the National level using the French
85 National Health system tool, called open medic ([http://open-data-assurance-](http://open-data-assurance-maladie.ameli.fr/medicaments/index.php#Open_MEDIC)
86 [maladie.ameli.fr/medicaments/index.php#Open_MEDIC](http://open-data-assurance-maladie.ameli.fr/medicaments/index.php#Open_MEDIC)).

87 Each patient was classified into either a "misuse group" or "non-misuse group" using
88 the composite tool and the two groups compared to each other.

89 Ethical approval

90 The local ethics committee approved this study (N°. PI2020_843_0083). As the study
91 was retrospective, formal consent by patients was not required.

92 Statistical analysis

93 All values are expressed as means or medians, with the standard deviation, or minima
94 and maxima, with interquartile ranges. The Chi² test was used to compare frequencies (or
95 Fischer's F test, if necessary) and the Student t test to compare the means (or the Mann-
96 Whitney test, if necessary). P values < 0.05 were considered statistically significant. The
97 frequency of the potentially inappropriate prescription of α -blockers and 5-ARIs are

98 expressed as percentages. Multivariate logistic regression analysis was performed for factors
99 relevant to falls and those statistically associated with falls in univariate analyses. The number
100 of adjustment variables was limited due to the small number of patients included in the study.
101 We therefore selected the following most relevant variables for the logistic regression: taking
102 combined treatments (α -blocker with 5-ARI), neurocognitive disorders, and heart failure. We
103 estimated the odds ratios (ORs) with a 95% confidence interval (CI). Statistical analyses were
104 performed using Statistical Package for the Social Sciences (SPSS) software (version 26.0,
105 SPSS Inc., Armonk, NY, USA).

106

107 **RESULTS**

108 A population of 117 patients (≥ 75 years of age) was included in the study.

109 Geriatric characteristics

110 The median age of the patients was 84.5 (± 6.3) years [75-97]. The median Charlson
111 score was 7 (± 0.5) [3-15]. Among comorbidities, hypertension and neurocognitive disorders
112 were the most prevalent (71.8% and 57.3%, respectively). The median number of co-
113 morbidities per patient was seven. The patients' characteristics and diseases registered at
114 admission are shown in Table 2. Medication used at home was reported at admission in the
115 electronic clinical record for all patients. The number of drugs consumed at admission was 6
116 ± 2 . A history of falls was found for 53.8% of patients (n = 63). Among those who fell, 70.6%
117 of the tests for orthostatic hypotension were positive. The activity of daily living (ADL) was
118 homogeneously distributed (35% not dependent, 35% slightly dependent, 30% highly
119 dependent).

120 Urological characteristics:

121 At least one urological evaluation was performed in the past for 41% of patients. The
122 initial therapeutic indication was found for 75% of patients (symptomatic BPH [35%], acute
123 urinary retention [AUR] [30.8%], obstructive LUTS [36.8%], irritative LUTS [10.3%], or
124 both [obstructive and irritative] LUTS [9.8%]). BPH was present in the medical history for
125 57.3% of patients, among whom 1/3 had a positive clinical or imaging assessment. At least
126 one instance of AUR in the medical history was found for 49.6% of patients, among which
127 79.5% were precipitated AUR (likely due to pharmacological causes e.g., pain relievers,
128 antiparkinsonian drugs, anxiolytics, urological agents [anticholinergic drugs]). The most
129 frequently used medical therapy consisted of alfuzosin (58.1%), finastéride (23.1%), or
130 bitherapy (18.8%). Two concomitant α 1-blockers were used for two patients and midodrine
131 was associated with α 1-blockers for one. The time since the prescription was 1.2 ± 1.6 years
132 for a well characterized urological prescription history and 4.5 [2-7] years for those that were
133 undetermined. The urological characteristics and diseases recorded at admission are shown in
134 Table 3.

135 Potentially inappropriate medication prescribing for BPH

136 In total, 84 patients (71.8%) had at least one potentially inappropriate urological
137 medication at admission and during hospitalization according to our eight-item composite tool
138 of explicit indicators (1 to 8), 77 (91.7%) related to α 1-blockers. We distinguished and
139 compared two groups: group 1 (n = 84; who received a potentially inappropriate prescription
140 [one or more criteria]) and Group 2 (n = 33, who received no inappropriate prescriptions [no
141 criteria]) (Table 2 and 3). Members of Group 1 more frequently received a urological
142 assessment (p = 0.026), and they were more frequently on α 1-blockers (p < 0.001) or bi-
143 therapy (p = 0.004) and less frequently on 5-ARIs (p = 0.014). Group 1 showed a more
144 frequent history of falls (p = 0.043) and more pharmacological interactions with a risk of
145 orthostatic hypotension (p = 0.005) or arrhythmia (p = 0.028). Falling patients were more

146 frequently treated with α 1-blockers ($p = 0.041$) and were more frequently dependent based on
147 the ADL assessment.

148 After multivariate analysis by logistic regression, with adjustment for the intake of
149 combined treatments (α -blocker with I5AR), neurocognitive disorders, and heart failure, the
150 misuse group was associated with an increased risk of falls with an OR of 3.22 ($p = 0.039$,
151 95%CI [1.08-10.2]).

152 Criterion 1 from the eight-item list was found for 16 patients (13.7%). No differences
153 were observed concerning polypharmacy but these patients were more exposed to
154 pharmacological interactions with a risk of arrhythmia ($p < 0.001$) or neutropenia ($p = 0.018$).
155 Among geriatric parameters, only albumin was associated with this criterion ($p = 0.003$ [mean
156 25.3 g/L]). Criterion 2 was found for 28 patients (23.9%). Urological surgical therapies
157 performed before prescription included transurethral incision of the prostate ($n = 2$),
158 transurethral resection of the prostate ($n = 14$), open prostatectomy ($n = 6$), transurethral laser
159 enucleation or vaporization ($n = 2$), radical prostatectomy ($n = 2$), and cystoprostatectomy (n
160 $= 1$). Criterion 3 was found for 59 patients (50.4%). Criteria 3 and 4 were associated ($p =$
161 0.014). Criterion 4 was found for 15 patients (12.8%). No general, urological or geriatric
162 parameters were associated with this criterion. Criterion 5 was found for three patients (2.6%)
163 and was associated with bitherapy ($p = 0.007$), obstructif LUTS ($p = 0.03$), younger age ($p =$
164 0.047), and fewer co-morbidies ($p = 0.041$). Criterion 6 was found for one patient (0.9%).
165 One bitherapy prescription was given for AUR and maintained while the patient was under
166 palliative care. Criterion 7 was found for eight patients (6.8%) and was associated with
167 obstructive LUTS ($p = 0.021$). Criterion 8 was found for 10 patients (8.5%) and was
168 associated with bitherapy ($p < 0.001$) and 5-ARI prescriptions ($p = 0.051$).

169 We estimated the annual excess cost of PIM prescription for the 84 patients in the
170 study by taking the sum of the known prices for one month of treatment for each of the drugs

171 used according to their selling price in France in 2019 and then translated it to one year of
172 treatment. We considered the excess cost to be the portion reimbursed by French social
173 security, i.e., 30% of the total sum, which makes an annual additional cost of 3,500€ for these
174 84 patients.

175 The French database ([http://open-data-assurance-](http://open-data-assurance-maladie.ameli.fr/medicaments/index.php#Open_MEDIC)
176 [maladie.ameli.fr/medicaments/index.php#Open_MEDIC](http://open-data-assurance-maladie.ameli.fr/medicaments/index.php#Open_MEDIC)) allowed extraction of the number of
177 consumers of α -blockers and 5-ARI over 60 years of age, as well as the reimbursement by
178 French social security. The number of male patients over 60 years of age in 2018 who
179 consumed α -blockers and 5-ARI was 1,244,091 and 344,773, respectively, representing a total
180 reimbursement from the French social security of € 44,070,480 for α -blockers and €
181 16,202,107 for 5-ARIs.

182 Extrapolation of the results of our study to French social security figures results in an
183 estimated annual excess cost of PIM prescriptions linked to misuse in 2018 of € 30,000,000 for
184 α -blockers and € 3,000,000 for 5-ARI, for a total of approximately € 33,000,000,
185 notwithstanding the costs related to hospitalizations and adverse events.

186 **DISCUSSION**

187 This study determined that 72% of frail elderly patients hospitalized in our geriatric
188 academic center were taking PIM for BPH using a formal eight-item composite tool of
189 explicit indicators. International research shows that polypharmacy and PIM use is significant
190 among the hospitalized elderly population^{19,20,21}. The prevalence of PIM use varies from 18.5
191 to 82.6% for the elderly based on Beers general criteria²². A strongly varying prevalence of
192 PIM use has been observed in the institutionalized care setting for the elderly, and does not
193 appear to correlate with the extent of the assessment or the set of instruments (e.g., Beer's
194 criteria, STOPP and START, the PRISCUS list)^{22,23,24,25}.

195 Our geriatric population was associated with multiple comorbidities (the median
196 Charlson index was 7), polypharmacy (half of patients taking more than 7 medications), and a
197 high frequency of dependence (60%), as classically reported^{26,27}. Well-known risks of
198 polypharmacy have been heightened in the elderly and are related to age, physiological
199 changes, complex comorbid conditions, and the efficacy and safety of the medications
200 themselves. Even worse, misuse can be identified, irrespective of drug marketing
201 authorization, the summary of product characteristics, and scientific panel guidelines, as
202 observed in our study²⁸. The number of medications was a predictor of unnecessary drug use:
203 the higher the number of medications added to a regimen, the higher the likelihood of a drug
204 being nonessential²⁶.

205 The American Geriatrics Society updated Beer's Criteria for PIM use in the elderly in
206 2019, but didn't specifically report α 1-blockers and/or 5-ARIs (to treat LUTS) as PIM²⁵.
207 However, older patients still receive such pharmaceutical treatment for LUTS, for which the
208 number of prescriptions has increased over recent years. Only strong recommendations
209 against the use of α 1-blockers as routine treatment for hypertension (doxazonin, prazosin, and
210 terazosin) have been made for this indication for older adults²⁵. The STOPP criteria are more

211 precise, as they specify the need to cease treatment in the event of orthostatic hypotension²⁴.
212 In this study, the prescription of PIM for BPH in the elderly was essentially related to the
213 continuation of α 1-blockers for more than six months after trials without a catheter for AUR
214 (50.4%). A systematic review, including randomized controlled trials (RCTs) and prospective
215 comparative studies, showed there to be evidence that alfuzosin and tamsulosin may increase
216 the success rates after a trial without a catheter²⁹. However, although a number of studies
217 have clearly demonstrated that α 1-blockers, used once daily, are effective for improving the
218 chance of success after a trial without a catheter after a first episode of AUR, there is no
219 strong evidence that they decrease the need for BPH surgery after six months of treatment^{15,16}.
220 Furthermore, in close to 30% of cases, AUR follows a triggering event (also called a
221 precipitated AUR), such as a procedure with locoregional or general anesthesia not related to
222 BPH^{17,18}.

223 An international interdisciplinary group of experts evaluated drugs to treat LUTS for
224 their efficacy, safety, and overall age adequacy profiles in older adults, classifying them in a
225 category called Fit for The Aged (FORTA), from level A (essential) to D (avoid). The use of
226 α -blockers for the elderly or the frail elderly appears to be questionable (FORTA C) or should
227 be avoided, such as for alfuzosin, doxazosin, or terazosin (FORTA D). Only dutasteride and
228 finasteride were classified as being beneficial for elderly patients (FORTA B)³⁰.

229 Falls are associated with increased morbidity and mortality in older adults and may be
230 precipitated by α 1-blockers. Moreover, the number of medications has been shown to be
231 associated with an increased risk of falls^{21,31}.

232 Observational data on the association between the use of α 1-blockers by older adults
233 (men over 66 years of age) and serious adverse drug events (probably as a result of induced
234 hypotension), including falls and fall-related injuries, has failed to demonstrate a consistent
235 association concerning the risk. Studies have both demonstrated^{8,32,33,34} and failed to

236 demonstrate such a risk^{35,36,37}. However, as a class, all α 1-blockers have been shown to be
237 associated with side effects, such as hypotension³⁸, suggesting that orthostatic hypotension
238 must be systematically sought in the elderly³⁹, and among α 1-blockers, silodosin (which
239 exhibits true α 1A receptor selectivity) should be the α 1-blocker of choice among older men³⁹.

240 “Deprescribing” for older patients likely results in reduced medication usage and costs
241 and is unlikely to cause harm⁴⁰. In our experience, potentially inappropriate prescriptions for
242 BPH is associated with a large increase in the frequency of falls, suggesting the need for a full
243 understanding of “deprescribing” barriers and the development of targeted interventions to
244 reduce iatrogenic harm⁴¹. Such interventions have generally been of insufficient duration to
245 determine the long-term clinically significant benefit (reduced hospitalization, improved
246 functionality), even if some trials demonstrated a reduced fall risk⁴².

247 We performed an economic appraisal of PIM by α 1-blockers and 5-ARI at the patient
248 level and calculated a potential extra cost of millions of euros for the French Health System in
249 2018 (notwithstanding the extra cost due to hospitalizations and adverse events related to
250 misuse). Several other studies have calculated the cost of PIM at the patient⁴³ or National
251 level^{44,45,46} and assessed the economic relevance of “deprescribing”.

252 Despite these findings, our study had certain limitations. The retrospective and
253 monocentric nature of the study inherently results in a low level of evidence. The total sample
254 size was small and may not be representative of the entire population. Causal relationships
255 between the potentially inappropriate prescription of α 1-blockers and fall risk could not be
256 determined in this observational study. A number of non-reported urological evaluations
257 could have been made by primary care physicians and, thus, certain patients could have been
258 classified using the C8 criterion of potential inappropriateness. Chart reviews of information
259 primarily relied on the assessment of unnecessary BPH drug use using a formal non-validated
260 eight-item composite tool, which therefore may have overestimated the problem if the

261 information was not recorded or vaguely or erroneously recorded in the medical chart.
262 Potential associations with sociodemographic factors were not studied. Finally, the data came
263 from a relatively homogenous sample of frail patients from our institutional department of
264 geriatric medicine and therefore may not be generalizable to other patients.

265 **CONCLUSIONS AND IMPLICATIONS**

266 In our study, potentially inappropriate prescriptions for BPH for the elderly were close
267 to 72%, mainly for α 1-blockers (90%), and was associated with a three-fold higher likelihood
268 of prior falls. Empowering clinicians to “deprescribe” by collaboration between professionals
269 is essential to ensure optimal medication management. The elderly should be primary targets
270 for such intervention and a priority for health professionals.

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272 The authors declare that they have no conflict of interest.

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419 medication in the elderly in Germany: an economic appraisal of the PRISCUS list. *BMC*
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421 Table 1. Eight-item list for the prescription of potentially inappropriate medication (PIM) for
 422 benign prostatic hyperplasia (BPH).
 423

Criterion	Definition
1	Presence of an indwelling catheter with α 1-blocker prescription
2	Maintenance of α 1-blockers or a new prescription after prostate surgery (e.g., radical prostatectomy) without a new urological assessment
3	Continuation of α 1-blockers for more than six months after a trial without a catheter for AUR
4	α 1-blocker prescription despite contraindication
5	5-ARI for LUTS but BPH volume < 40 g
6	5-ARI for LUTS and BPH volume > 40 g but life expectancy < 6 months
7	No improvement in LUTS symptoms
8	Lack of documentation to evaluate the need for an α 1-blocker prescription

424 Abbreviations: AUR, acute urinary retention; 5-ARI, 5 α -reductase inhibitor; BPH, benign
 425 prostatic hyperplasia; LUTS, lower urinary tract symptoms.

426 Table 2. Characteristics of the 117 study patients taking medication for benign prostatic
 427 hyperplasia, overall and by the appropriateness of the medication prescription.
 428

Characteristics	Total	Inappropriate prescribing	No inappropriate prescribing	p
Patients	117 (100%)	84 (71.8%)	33 (28.2%)	-
Age	84.5 ± 6.3	84.5 ± 5.9	84.3 ± 7.2	0.906
Body-mass index	25.6 ± 5.0	25.5 ± 4.5	25.8 ± 6.1	0.797
Neurocognitive disorders	67 (57.3%)	49 (58.3%)	18 (54.5%)	0.913
High blood pressure	84 (71.8%)	60 (71.4%)	24 (72.7%)	0.888
Diabetes	31 (26.5%)	22 (26.2%)	9 (27.3%)	0.905
Atrial fibrillation	52 (44.4%)	37 (44%)	15 (45.5%)	0.890
Stroke	36 (30.8%)	27 (32.1%)	9 (27.3%)	0.608
Coronary artery disease	29 (24.8%)	19 (22.6%)	10 (30.3%)	0.386
Heart failure (*)	34 (29.1%)	24 (28.6%)	10 (30.3%)	0.853
reduced ejection fraction	19 (16.2%)	16 (19.0%)	3 (9.1%)	0.189
preserved ejection fraction	15 (12.8%)	8 (9.5%)	7 (21.2%)	0.123
Peripheral arterial disease	30 (25.6%)	20 (23.8%)	10 (30.3%)	0.469
Chronic renal failure (**)	52 (44.4%)	32 (38.1%)	20 (60.6%)	0.027
Staging 3A	23 (19.7%)	14 (16.7%)	9 (27.3%)	0.194
Staging 3B	20 (17.1%)	12 (4.3%)	8 (24.2%)	0.198
Staging 4	3 (2.6%)	2 (2.4%)	1 (3.0%)	1.000
Staging 5	6 (5.1%)	4 (4.8%)	2 (6.1%)	1.000
Sleep apnea syndrome	11 (9.4%)	9 (10.7%)	2 (6.1%)	0.726
Chronic obstructive pulmonary disease	17 (14.5%)	12 (14.3%)	5 (15.2%)	1.000
Parkinson disease	5 (4.3%)	3 (3.6%)	2 (6.1%)	0.620
Epilepsy	5 (4.3%)	3 (3.6%)	2 (6.1%)	0.620
Progressive cancer	29 (24.8%)	20 (23.8%)	9 (27.3%)	0.696
Cirrhosis	5 (4.3%)	4 (4.8%)	1 (3.0%)	1.000
Hypothyroidism	11 (9.4%)	8 (9.5%)	3 (9.1%)	1.000
Hyperthyroidism	2 (1.7%)	1 (1.2%)	1 (3.0%)	0.486
Depression	28 (23.9%)	17 (20.2%)	11 (33.3%)	1.000
Polymedication	6 ± 2.0	6 ± 2.0	7 ± 3.0	0.061
Fallers	63 (53.8%)	51 (60.7%)	12 (36.4%)	0.043
ADL(***)				
Independent	41 (35.0%)	27 (32.1%)	14 (42.4%)	0.294
Moderate handicap	41 (35.0%)	30 (35.7%)	11 (33.3%)	0.808
Severe handicap	35 (30.0%)	27 (32.1%)	8 (24.2%)	0.401
Constipation	55 (47.0%)	39 (46.4%)	16 (48.5%)	0.511
Orthostatic hypotension				
Positive test	12 (10.3%)	12 (14.3%)	0	0.007
Negative test	5 (4.3%)	3 (3.6%)	2 (6.0%)	0.074

Untested	100 (84.5%)	69 (82.1%)	31 (94.0%)	0.103
Visual disturbances	36 (30.8%)	26 (31%)	10 (30.3%)	0.556
Hearing impairment	19 (16.2%)	15 (17.9%)	4 (12.1%)	0.429
Nutritional parameters				
Albumin (g/L)	29.8 ± 6.1	30.2 ± 6.4	28.8 ± 5.2	0.308
Vitamin D (ng/mL)	22.9 ± 11.6	23.5 ± 12.0	20.9 ± 10.4	0.467

429 Abbreviations: ADL, activities of daily living.

430 Definitions:

431 (*) Heart failure with reduced ejection fraction was defined by an ejection fraction $\leq 45\%$.

432 (***) The glomerular filtration rate was estimated using the MDRD formula (ml/min/1.73 m²).

433 Patients with a glomerular filtration rate > 60 ml/min /1.73 m² were classified as having
434 normal kidney function.

435 (***) Patients were considered to be independent if the ADL was 6/6, to have a moderate
436 handicap if the ADL was 4/5 or 5/6, and a severe handicap if the was ADL $\leq 3/6$.

437 The p-value was determined using Student's t test for quantitative variables and the Chi² test
438 for qualitative variables. Groups with small numbers were compared using Fisher's F test.

439 Table 3. Characteristics and urological prescriptions.

Characteristic	Total	Inappropriate prescribing	No inappropriate prescribing	p
Urological assessment	48 (41.0%)	40 (47.6%)	8 (24.2%)	0.026
AUR	58 (49.6%)	41 (48.8%)	16 (48.5%)	0.883
Urinary incontinence				
Yes	28 (23.9%)	23 (27.4%)	5 (15.2%)	0.248
No	29 (24.8%)	20 (23.8%)	9 (27.3%)	0.248
Unknown	60 (51.3%)	41 (48.8%)	19 (57.6%)	0.393
BPH recorded in medical files	67 (57.3%)	56 (66.7%)	11 (33.3%)	0.983
LUTS related to BPH and documented	35 (29.9%)	30 (35.7%)	5 (15.2%)	1.000
Prostate size				
< 30 g	7 (6.0%)	7 (8.3%)	0	0.301
30-50 g	12 (10.3%)	10 (11.9%)	2 (6.1%)	1.000
> 50g	12 (10.3%)	10 (11.9%)	2 (6.1%)	1.000
Treatments potentially causing urinary problems	93 (79.5%)	67 (79.7%)	26 (78.8%)	0.907
Urological treatments				
α1-blockers	101(86.3%)	80 (95.2%)	21 (63.6%)	< 0.001
Alfuzosine	68 (58.1%)	54 (64.3%)	14 (42.4%)	0.026
Tamsulosine	25 (21.4%)	22 (26.2%)	3 (9.1%)	0.042
Silodosine	8 (6.8%)	7 (8.3%)	1 (3.0%)	0.437
5α-reductase inhibitors	37 (31.6%)	21 (25.0%)	16 (48.5%)	0.014
Dutasteride	10 (8.5%)	7 (8.3%)	3 (9.1%)	1.000
Finasteride	27 (23.1%)	14 (16.7%)	13 (39.4%)	0.010

440 Abbreviations: AUR, acute urinary retention; LUTS, lower urinary tract symptoms; BPH,

441 benign prostate hyperplasia.

442 The p-value was determined using the Chi² test for qualitative variables. Groups with small

443 numbers were compared using Fisher's F test.