Supplementary material

**SUPPLEMENTARY Table 1** Classification of drugs prescribed for Parkinson’s disease.

**SUPPLEMENTARY Table 2** Comorbidities included in this analysis.

**SUPPLEMENTARY Table 3** Prevalence of Parkinson’s disease by age group: All patients.

**SUPPLEMENTARY Table 4** Concomitant drug prescribing by ATC main category: All patients.

**Supplementary Table 5** Prescription of anti-PD drug by comorbidities: All patients.

**SUPPLEMENTARY Table 6** Demographics and clinical characteristics of patients who newly initiated PD treatment and who stayed on levodopa monotherapy during the observation period or switched to adjunct therapy.

**SUPPLEMENTARY Table 7** Factors associated with duration of levodopa monotherapy in patients who newly initiated PD treatment (*N* = 2,575).

**SUPPLEMENTARY Table 8** Factors associated with a prescription for non-ergot DA monotherapy in patients who newly initiated PD treatment (*N* = 3,467).

**SUPPLEMENTARY Table 9** Factors associated with duration of non-ergot DA monotherapy in patients who newly initiated PD treatment (*N* = 267).

**SUPPLEMENTARY TABLE 10** Demographics and clinical characteristics of elderly patients ≥75 years who newly initiated PD treatment and who stayed on levodopa monotherapy during the observation period or switched to levodopa and non-ergot DA adjunct therapy.

**SUPPLEMENTARY Table 11** Demographics and clinical characteristics of patients who increased levodopa dose from <300 mg to ≥300 mg during the observation period.

**SUPPLEMENTARY FIGURE 1** Flow diagram.

**SUPPLEMENTARY FIGURE 2** Maximum levodopa doses prescribed by age group during the observation period (All patients and those who newly initiated PD treatment).

**SUPPLEMENTARY FIGURE 3** Longitudinal analysis of the type and combinations of anti-PD drugs prescribed during the observation period: Patients Total (*N* = 39,731), patients 65–74 years (*N* = 5,312), and patients ≥85 years (*N* = 8,162).

**supplementary Figure 4** Duration of non-ergot DA monotherapy in patients who newly initiated PD treatment with a first prescription for non-ergot DA monotherapy (*N* = 267).

**SUPPLEMENTARY Figure 5** Treatment modalities and drug prescriptions when patients who increased their levodopa dose to ≥300 mg. (**A**) Total, (**B**) ≥75-year-group, and (**C**) <75-year-group.

**SUPPLEMENTARY Table 1** Classification of drugs prescribed for Parkinson’s disease.

| **Drug** | **Receipt code from computerized processing system** | **ATC code** |
| --- | --- | --- |
| Levodopa LevodopaLevodopa carbidopa hydrate Levodopa benserazide hydrochlorideLevodopa carbidopa hydrate entacapone   | 620006042, 620006043, 620008660, 620008661, 620008662, 620008889, 620008890 | N04BA01 |
| 620123601, 620123701, 620123801, 620123901, 620124001, 620124101, 620124201, 620124301, 620124401, 620124501, 620124601, 621865201, 622050801, 622051301, 622067101, 622080201, 622509401, 622711600, 622711800 | N04BA02 |
|  | 620008030, 620008659, 622325500, 622711700 |  N04BA02  |
|  | 622375701, 622375801 | N04BA03 |
| Dopamine agonist – ergotBromocriptine mesilatePergolide mesilateCabergoline | 610422106, 620005063, 620005096, 620006069, 620006743, 620008579, 620008688, 620009237, 620120902, 620121001, 620121101, 620121102, 620121401, 620121701, 620121802, 620121902, 620121904, 620122001 | N04BC01 |
| 620121801 | NA |
| 610406392, 610406393, 620002124, 620002125, 620002823, 620002857, 620002858, 620004067, 620004068, 621642002, 621642103, 621690101 | N04BC02 |
|  | 620006684, 620006685, 622711100, 622711200 | NA |
|  | 610432023, 610432024, 620005369, 620005370, 620005371, 620005372, 620005375, 620005376, 620005377, 620005378, 620005379, 620008002, 622711400, 622711500 | N04BC06 |
|  | 620005373, 620006667, 620006668, 620008001 | NA |
| Dopamine agonist – non-ergotTalipexole hydrochlorideRopinirole Pramipexole hydrochloride hydrateApomorphine hydrochloride hydrateRotigotine | 610409337 | N04BC |
| 620004415, 620004416, 620004417, 622183601, 622183701, 622492301, 622492401, 622492501, 622500001, 622500101, 622500201, 622582201, 622582301, 622583401, 622583501, 622656201, 622656301, 622687201, 622687301, 622687401, 622687501, 622687601 | N04BC04 |
|  | 620000435, 620000436, 622069601, 622069701, 622226701, 622226801, 622228701, 622228801, 622229801622229901, 622231601, 622231701, 622233901, 622234001, 622235901, 622236001, 622238001, 622238101, 622239601, 622239701, 622245201, 622245301, 622247301, 622247401, 622249201, 622249301, 622253101, 622253201, 622253501, 622253601, 622254501, 622254601, 622256401, 622256501, 622257401, 622257501, 622272601, 622272701, 622511201, 622511301, 622513801, 622513901, 622520201, 622520301, 622524801, 622524901, 622528201, 622528301, 622530001, 622530101, 622691900 | N04BC05 |
|  | 622263001, 622263101, 622263201, 622263301, 622692000 | NA |
|  | 622149301 | N04BC07 |
|  | 622163501, 622163601, 622163701, 622163801, 622478301 | N04BC09 |
| Monoamine oxidase type B inhibitorSelegiline hydrochlorideRasagiline mesilateSafinamide mesilate | 610421338, 620003975, 620005364, 620005511, 620008494, 622711300 | N04BD01 |
| 622624401, 622624501 | N04BD02 |
|  | 622696101 | N04BD03 |
| Catechol-*O*-methyltransferase inhibitorEntacaponeOpicapone | 620004853, 622478401, 622490101, 622498501, 622503001 | N04BX02 |
| 622845500, 622878901 | NA |
|  | 622821701 | N04BX04 |
| Anticholinergic agent Trihexyphenidyl hydrochloride Biperiden hydrochloride Biperiden lactateProfenamine hydrochlorideProfenamine hibenzate | 610454002, 611240304, 611240415, 611240423, 611240425, 620003078, 620004382, 620004384, 620004548, 620006589, 620008311, 620008663, 620119903, 620119906, 620119907, 620119919, 620119923, 620119927, 620120303 | N04AA01 |
| 620004556, 620005847, 622319200 | NA |
|  | 610444006, 610444007, 620000066, 620000067, 620000243, 620004893, 620004894, 620005147, 620117802, 620118102, 620118203, 620118402, 621218501, 621392101 | N04AA02 |
|  | 620006075 | NA |
|  | 611240172, 611240173 | N04AA05 |
|  | 610463153 |  |
| Zonisamide  | 611130087, 620001972, 620009098, 621390801, 621390901, 622400401, 622589801, 622673201, 622709200, 622709300 | N03AX15 |
| Istradefylline  | 622245801 | N04CX01 |
| Amantadine  | 610461044, 610461047, 611240079, 611240080, 620002335, 620004505, 620008286, 620116802, 620116809, 620117101, 620117103, 620117110, 620117112, 620117114, 620117401, 620117402, 620117404, 620117412, 620117413, 620117414, 622710800 | N04BB01 |
|  | 610461046, 611240122, 611240123, 620003077, 620003267, 620003268, 620005903, 620006587, 620008280, 620116701, 620117107, 620117410, 620116702, 622309500, 620116805 | NA |
| Droxidopa  | 620004007, 620004008, 620004009, 620004010, 620005044, 620005045, 620005046, 620006676, 620006677, 620006678, 622061101, 622061201 | C01CA27 |
|  | 622710900, 622711000 |  |

ATC, Anatomical Therapeutic Chemical; NA, not applicable.

**SUPPLEMENTARY Table 2** Comorbidities included in this analysis.

|  |  |
| --- | --- |
| **Comorbidity** | **Disease code** |
|
| Constipation | 8850626, 8847697, 8833027, 8834176, 5640018, 5640016, 8847705, 8837133, 5640007, 8837785, 5640011, 8840042, 8849551, 8849481  |
| Insomnia | 8839792 |
| Pain | 8838060, 8846220, 8849544, 7213016, 8845840, 7153018, 8850089 |
| Cognitive disorder | 8831737, 7809004, 7809005, 7809006, 7809007, 7809026, 8833248, 7809021, 8842548, 8842549, 8842550, 8842551, 3310002, 8842308, 8849974, 8847912, 8847913, 8842565, 8842571, 8842608, 8842625, 8842626, 8845840, 8842575, 2901004, 8842591, 2902001, 8842615, 8842618, 2902006, 8842637, 8842638, 8842639, 2902008, 2902012 |
| Depression and anxiety | 3004001, 2961003, 2961005, 8832914, 8850416, 2961017, 2961020, 8835867, 8835868, 2961023, 8837202, 8837626, 2980001, 2961027, 8831486, 8832918, 2961024, 8837627, 2961025, 8839033, 2961026, 8839040, 8839041, 8832574, 8833458, 8843724, 8834492, 8842740, 8845669, 8836029, 3002024, 8836934, 8837086, 8837121, 3002018, 8839428, 8839939, 8833894, 8836575, 8836634, 3000003, 8844095, 8844096, 3004024, 3000004, 8839596, 3000010, 8839600 |
| Hallucination | 2989002, 7801001, 2971002, 2971003, 2979001, 3009003, 8833547, 2971005, 8834119, 2971007, 2971009, 3002009, 3002010, 8835222, 2972002, 2971001, 2971012, 8840579, 8840580, 7800001 |

**SUPPLEMENTARY Table 3** Prevalence of Parkinson’s disease by age group: All patients.

|  |  |  |
| --- | --- | --- |
|  | **≥75 years** | **<75 years** |
| **Elderly database*****N* = 29,130** | **NHI database (self-employed/unemployed)*****N* = 5,364** | **JMDC database (company/government employees and their dependents)*****N* = 5,237** |
| Prevalence (June 2016 to May 2021), (%) | 1.14 | 0.31 | 0.07 |
| Prevalence (June 2020 to May 2021), (%) | 1.21 | 0.37 | 0.07 |
| ≤54 years | NA | 0.10 | 0.03 |
| 55–64 years | NA | 0.30 | 0.13 |
| 65–74 years | NA | 0.58 | 0.32 |
| 75–84 years | 1.13 | NA | NA |
| ≥85 years | 1.36 | NA | NA |

NA, not applicable; NHI, National Health Insurance.

**SUPPLEMENTARY Table** **4** Concomitant drug prescribing by ATC main category: All patients.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **ATC main category** | **Total*****N* = 39,731** | **≥75 years*****N* = 29,130** | **<75 years*****N* = 10,601** | **Group Difference*****P*-value** |
| Alimentary tract and metabolism | 36,887 (92.8) | 27,567 (94.6) | 9,320 (87.9) | 0.000 |
| Blood and blood forming organs | 19,947 (50.2) | 15,529 (53.3) | 4,418 (41.7) | 0.000 |
| Cardiovascular system | 28,668 (72.2) | 22,496 (77.2) | 6,172 (58.2) | 0.000 |
| Dermatologicals | 3,025 (7.6) | 2,419 (8.3) | 606 (5.7) | 0.000 |
| Genito urinary system and sex hormones | 11,716 (29.5) | 9,205 (31.6) | 2,511 (23.7) | 0.000 |
| Systemic hormonal preparations, excluding sex hormones and insulins | 4,013 (10.1) | 2,985 (10.2) | 1,028 (9.7) | 0.112 |
| Antiinfectives for systemic use | 13,778 (34.7) | 10,283 (35.3) | 3,495 (33.0) | 0.000 |
| Antineoplastic and immunomodulating agents | 1,322 (3.3) | 952 (3.3) | 370 (3.5) | 0.289 |
| Musculo-skeletal system | 16,119 (40.6) | 10,966 (37.6) | 5,153 (48.6) | 0.000 |
| Nervous system | 31,295 (78.8) | 23,402 (80.3) | 7,893 (74.5) | 0.000 |
| Antiparasitic products, insecticides, and repellents | 1,274 (3.2) | 946 (3.2) | 328 (3.1) | 0.462 |
| Respiratory system | 19,558 (49.2) | 14,207 (48.8) | 5,351 (50.5) | 0.003 |
| Sensory organs | 2,230 (5.6) | 1,872 (6.4) | 358 (3.4) | 0.000 |
| Various | 3,222 (8.1) | 810 (2.8) | 2,412 (22.8) | 0.000 |

Data are n (%).

ATC, Anatomical Therapeutic Chemical.

**Supplementary Table 5** Prescription of anti-PD drug by comorbidities: All patients.

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Characteristic | **Constipation** | **Insomnia** | **Pain** | **Cognitive Disorders** | **Depression and anxiety** | **Hallucination** | **Orthostatic hypotension** |
|  | ***N = 32,909*** | ***N = 21,607*** | ***N = 20,777*** | ***N = 15,871*** | ***N = 14,195*** | ***N = 2,114*** | ***N = 2,659*** |
| Male, *n* (%) | 11,779 (35.8) | 7,331 (33.9) | 6,776 (32.6) | 5,953 (37.5) | 4,191 (29.5) | 762 (36.0) | 1,276 (48.0) |
| Age (years), mean ± SD (range) | 77.2 ± 9.9(30–104) | 76.4 ± 11.1(30–102) | 77.7 ± 9.1(30–102) | 80.4 ± 7.2(34–102) | 75.2 ± 12.0(30–102) | 78.4 ± 9.4(30–101) | 76.6±9.9(30–97) |
| Age, *n* (%) |  |  |  |  |  |  |  |
| ≤54 | 1,206 (3.7) | 1,272 (5.9) | 557 (2.7) | 91 (0.6) | 1,100 (7.7) | 71 (3.4) | 113 (4.2) |
| 55–64 | 2,199 (6.7) | 1,509 (7.0) | 1,224 (5.9) | 415 (2.6) | 1,185 (8.3) | 84 (4.0) | 190 (7.1) |
| 65–74 | 3,792 (11.5) | 2,335 (10.8) | 2,293 (11.0) | 1,102 (6.9) | 1,660 (11.7) | 200 (9.5) | 290 (10.9) |
| 75–84 | 18,921 (57.5) | 12,217 (56.5) | 12,531 (60.3) | 9,815 (61.8) | 7,677 (54.1) | 1,261 (59.6) | 1,596 (60.0) |
| ≥85 | 6,791 (20.6) | 4,274 (19.8) | 4,172 (20.1) | 4,448 (28.0) | 2,573 (18.1) | 498 (23.6) | 470 (17.7) |
| Prescribing patten, *n* (%) |  |  |  |  |  |  |  |
| Levodopa | 16,163 (49.1) | 10,322 (47.8) | 10,596 (51.0) | 8,681 (54.7) | 6,899 (48.6) | 1,091 (51.6) | 1,000 (37.6) |
| DA – non-ergot | 1,905 (5.8) | 1,743 (8.1) | 1,517 (7.3) | 689 (4.3) | 1,222 (8.6%) | 99 (4.7) | 100 (3.8) |
| MAOBI | 404 (1.2) | 244 (1.1) | 296 (1.4) | 151 (1.0) | 159 (1.1) | 15 (0.7) | 24 (0.9) |
| Anticholinergic agent | 1,671 (5.1) | 1,638 (7.6) | 928 (4.5) | 611 (3.8) | 1,302 (9.2) | 161 (7.6) | 66 (2.5) |
| Levodopa + MAOBI | 2,435 (7.4) | 1,448 (6.7) | 1,597 (7.7) | 870 (5.5) | 852 (6.0) | 108 (5.1) | 195 (7.3) |
| Levodopa + DA – non-ergot | 3,601 (10.9) | 2,336 (10.8) | 2,358 (11.3) | 1,383 (8.7) | 1,517 (10.7) | 207 (9.8%) | 238 (9.0%) |
| Levodopa + Zonisamide | 2,740 (8.3) | 1,752 (8.1) | 1,908 (9.2) | 1,329 (8.4) | 1,181 (8.3) | 195 (9.2) | 207 (7.8) |
| Levodopa + COMTI | 1,742 (5.3) | 1,173 (5.4) | 1,106 (5.3) | 923 (5.8) | 809 (5.7) | 172 (8.1) | 150 (5.6) |
| Levodopa + Droxidopa | 1,455 (4.4) | 922 (4.3) | 931 (4.5) | 873 (5.5) | 607 (4.3) | 100 (4.7) | 539 (20.3) |
| Levodopa + Amantadine | 1,660 (5.0) | 998 (4.6) | 1,033 (5.0) | 890 (5.6) | 697 (4.9) | 104 (4.9) | 100 (3.8) |
| Levodopa + Anticholinergic agent | 858 (2.6) | 573 (2.7) | 531 (2.6) | 348 (2.2) | 439 (3.1) | 64 (3.0) | 51 (1.9) |

COMTI, catechol-*O*-methyltransferase inhibitor; DA, dopamine agonist; MAOBI, monoamine oxidase type B inhibitor; PD, Parkinson’s disease; SD, standard deviation.

**SUPPLEMENTARY Table 6** Demographics and clinical characteristics of patients who newly initiated PD treatment and who stayed on levodopa monotherapy during the observation period or switched to adjunct therapy.

|  |  |  |  |
| --- | --- | --- | --- |
| **Characteristic** | **Levodopa****monotherapy*****N* = 1,398** | **Levodopa adjunct therapy****†*****N* = 1,092** | **Group Difference*****P*-value** |
| Male, *n* (%) | 607 (43.4) | 551 (50.5) | 0.001 |
| Age (years) | 76.4 ± 9.6 | 70.3 ± 10.9 | 0.000 |
| Age, *n* (%) |  |  |  |
| ≤54 years | 41 (2.9) | 96 (8.8) | 0.000 |
| 55–64 years | 128 (9.2) | 212 (19.4) | 0.000 |
| 65–74 years | 278 (19.9) | 305 (27.9) | 0.000 |
| 75–84 years | 690 (49.4) | 409 (37.5) | 0.000 |
| ≥85 years | 261 (18.7) | 70 (6.4) | 0.000 |
| Observation period (year) | 3.5 ± 0.9 | 3.9 ± 1.0 | 0.000 |
| Duration of PD treatment (days) | 545.0 ± 287.0 | 732.8 ± 364.6 | 0.000 |
| Charlson Comorbidity Index | 1.4 ± 1.7 | 1.1 ± 1.6 | 0.000 |
| Number of anti-PD drug types | 1.0 ± 0.1 | 2.5 ± 0.9 | 0.000 |
| Number of drugs by ATC (major category),  | 2.5 ± 1.9 | 2.2 ± 1.8 | 0.000 |
| Comorbidities, *n* (%) |  |  |  |
| Constipation | 636 (45.5) | 397 (36.4) | 0.000 |
| Pain | 408 (29.2) | 288 (26.4) | 0.132 |
| Insomnia | 363 (26.0) | 214 (19.6) | 0.000 |
| Depression and anxiety | 231 (16.5) | 160 (14.7) | 0.223 |
| Cognitive disorder | 179 (12.8) | 51 (4.7) | 0.000 |
| Hallucination | 7 (0.5) | 8 (0.7) | 0.630 |

Data are mean ± SD unless otherwise stated.

†Patients who switched to monotherapy with other drug(s) were not included.

ATC, Anatomical Therapeutic Chemical; PD, Parkinson’s disease; SD, standard deviation.

**SUPPLEMENTARY Table 7** Factors associated with duration of levodopa monotherapy in patients who newly initiated PD treatment (*N* = 2,575).

|  |  |  |  |
| --- | --- | --- | --- |
| **Variable** | **Hazard ratio** | **95% CI** | ***p*-value** |
| Age (years) | 0.97 | 0.961–0.979 | 0.000 |
| Sex (ref. female) | 1.138 | 1.013–1.279 | 0.030 |
| Comorbidities†, middle category (ref. no comorbidity) |  |  |
| Depression and anxiety | 0.929 | 0.784–1.102 | 0.399 |
| Hallucination | 2.048 | 1.018–4.122 | 0.045 |
| Cognitive disorder | 0.569 | 0.433–0.747 | 0.000 |
| Number of concomitant drugs† | 1.010 | 0.994–1.027 | 0.223 |
| Charlson Comorbidity Index†  | 0.978 | 0.938–1.019 | 0.290 |
| Database (ref. JMDC database) |  |  |  |
| Elderly | 0.942 | 0.734–1.210 | 0.641 |
| NHI | 1.033 | 0.867–1.230 | 0.717 |

†Within 3 months of starting the second prescription pattern.

CI, confidence interval; NHI, National Health Insurance; PD, Parkinson’s disease; ref, reference.

**SUPPLEMENTARY Table** **8** Factors associated with a prescription for non-ergot DA monotherapy in patients who newly initiated PD treatment (*N* = 3,467).

|  |  |  |  |
| --- | --- | --- | --- |
| **Variable** | **Odds ratio** | **95% CI** | ***p*-value** |
| Age (years) | 0.971 | 0.955–0.987 | 0.001 |
| Sex (ref. female) | 0.812 | 0.624–1.054 | 0.118 |
| Comorbidities†, middle category (ref. no comorbidity) |  |  |
| Depression and anxiety | 1.250 | 0.883–1.753 | 0.201 |
| Hallucination | 0.509 | 0.028–2.627 | 0.520 |
| Cognitive disorder | 0.642 | 0.296–1.234 | 0.219 |
| Number of concomitant drugs† | 1.061 | 1.026–1.096 | 0.001 |
| Charlson Comorbidity Index†  | 0.994 | 0.903–1.086 | 0.895 |
| Database (ref. JMDC database) |  |  |  |
| Elderly | 0.335 | 0.197–0.570 | 0.000 |
| NHI | 0.710 | 0.497–1.010 | 0.058 |

†During3 months before the index date.

CI, confidence interval; DA, dopamine agonist; NHI, National Health Insurance; PD, Parkinson’s disease; ref, reference.

**SUPPLEMENTARY Table 9** Factors associated with duration of non-ergot DA monotherapy in patients who newly initiated PD treatment (*N* = 267).

|  |  |  |  |
| --- | --- | --- | --- |
| **Variable** | **Hazard ratio** | **95% CI** | ***p*-value** |
| Age (years) | 1.013 | 0.990–1.037 | 0.276 |
| Sex (ref. female) | 0.913 | 0.636–1.311 | 0.622 |
| Comorbidities†, middle category (ref. no comorbidity) |  |  |
| Depression and anxiety | 0.730 | 0.423–1.258 | 0.257 |
| Hallucination | 0.000 | 0.000–∞ | 0.996 |
| Cognitive disorder | 0.616 | 0.147–2.577 | 0.507 |
| Number of concomitant drugs† | 0.961 | 0.913–1.011 | 0.126 |
| Charlson Comorbidity Index†  | 0.861 | 0.726–1.021 | 0.085 |
| Database (ref. JMDC database) |  |  |  |
| Elderly | 0.518 | 0.224–1.199 | 0.125 |
| NHI | 0.939 | 0.586–1.502 | 0.792 |

†Within 3 months of starting the second prescription pattern.

CI, confidence interval; DA, dopamine agonist; ∞, infinity; NHI, National Health Insurance; PD, Parkinson’s disease; ref, reference.

**SUPPLEMENTARY Table 10** Demographics and clinical characteristics of elderly patients ≥75 years who newly initiated PD treatment and who stayed on levodopa monotherapy during the observation period or switched to levodopa and non-ergot DA adjunct therapy.

|  |  |  |  |
| --- | --- | --- | --- |
| **Characteristic** | **Levodopa****monotherapy*****N* = 951** | **DA adjunct therapy†*****N* = 96** | **Group Difference*****p*-value** |
| Male, *n* (%) | 385 (40.5) | 40 (41.7) | 0.908 |
| Age (years) | 81.8 ± 4.5 | 78.9 ± 3.5 | 0.000 |
| Age, *n* (%) |  |  |  |
| ≤54 years | NA | NA | NA |
| 55–64 years | NA | NA | NA |
| 65–74 years | NA | NA | NA |
| 75–84 years | 690 (72.6) | 88 (91.7) | 0.000 |
| ≥85 years | 261 (27.4) | 8 (8.3) | 0.000 |
| Observation period (year) | 3.2 ± 0.8 | 3.2 ± 0.7 | 0.256 |
| Duration of PD treatment (days) | 537.2 ± 272.2 | 657.3 ± 304.1 | 0.000 |
| Charlson Comorbidity Index | 1.6 ± 1.8 | 1.6 ± 2.1 | 0.209 |
| Number of anti-PD drug types | 1.0 ± 0.1 | 2.3 ± 0.6 | 0.000 |
| Number of drugs by ATC (major category) | 2.8 ± 1.9 | 2.8 ± 1.8 | 0.830 |
| Comorbidities, *n* (%) |  |  |  |
| Constipation | 514 (54.0) | 53 (55.2) | 0.912 |
| Pain | 323 (34.0) | 37 (38.5) | 0.431 |
| Insomnia | 289 (30.4) | 31 (32.3) | 0.788 |
| Depression and anxiety | 166 (17.5) | 20 (20.8) | 0.493 |
| Cognitive disorder | 157 (16.5) | 5 (5.2) | 0.006 |
| Hallucination | 5 (0.5) | 2 (2.1) | 0.129 |

Data are mean ± SD unless otherwise stated.

†Patients who switched to monotherapy with other drug(s) were not included.

ATC, Anatomical Therapeutic Chemical; DA, dopamine agonist; PD, Parkinson’s disease; SD, standard deviation.

**SUPPLEMENTARY Table 11** Demographics and clinical characteristics of patients who increased levodopa dose from <300 mg to ≥300 mg during the observation period.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Characteristic** | **Total*****N* = 8,677** | **≥75 years*N* = 5,879** | **<75 years*****N* = 2,798** | ***p*-value** |
| Male, *n* (%) | 3,890 (44.8) | 2,443 (41.6) | 1,447 (51.7) | 0.000 |
| Age (years) | 75.9 ± 10.5 | 81.8 ± 4.8 | 63.5 ± 8.0 | 0.000 |
| Age, *n* (%) |  |  |  |  |
| ≤54 years | 403 (4.6) | NA | 403 (14.4) | NA |
| 55–64 years | 880 (10.1) | NA | 880 (31.5) | NA |
| 65–74 years | 1,515 (17.5) | NA | 1515 (54.1) | NA |
| 75–84 years | 4,234 (48.8) | 4,234 (72.0) | NA | NA |
| ≥85 years | 1,645 (28.0) | 1,645 (28.0) | NA | NA |
| Observation period (year) | 3.3 ± 1.1 | 2.9 ± 0.9 | 4.0 ± 1.2 | 0.000 |
| Duration of PD treatment (days) | 580.9 ± 398.3 | 520.0 ± 346.1 | 708.7 ± 465.0 | 0.000 |
| Duration from index date to levodopa prescription ≥300 mg (days) | 307.1 ± 287.5 | 297.9 ± 267.3 | 326.2 ± 325.1 | 0.612 |
| Charlson Comorbidity Index | 2.0 ± 2.0 | 2.4 ± 2.1 | 1.2 ± 1.6 | 0.000 |
| Number of anti-PD drug types | 1.5 ± 0.9 | 1.4 ± 0.8 | 1.7 ± 1.0 | 0.000 |
| Number of drugs, ATC major category | 3.0 ± 1.8 | 3.3 ± 1.7 | 2.2 ± 1.7 | 0.000 |
| Comorbidities, *n* (%)  |  |  |  |
| Constipation | 5,376 (62.0) | 4,160 (70.8) | 1,216 (43.5) | 0.000 |
| Insomnia | 3,105 (35.8) | 2,431 (41.4) | 674 (24.1) | 0.000 |
| Pain | 2,973 (34.3) | 2,429 (41.3) | 544 (19.4) | 0.000 |
| Cognitive disorder | 2,235 (25.8) | 2,015 (34.3) | 220 (7.9) | 0.000 |
| Depression and anxiety | 2,089 (24.1) | 1,491 (25.4) | 598 (21.4) | 0.000 |
| Hallucination | 165 (1.9) | 137 (2.3) | 28 (1.0) | 0.000 |

Data are mean ± SD unless otherwise stated.

ATC, Anatomical Therapeutic Chemical; NA, not applicable; PD, Parkinson’s disease; SD, standard deviation

**SUPPLEMENTARY FIGURE 1** Flow diagram.



NHI, National Health Insurance; PD, Parkinson’s disease.

**SUPPLEMENTARY FIGURE 2** Maximum levodopa doses prescribed by age group during the observation period (All patients and those who newly initiated PD treatment).



PD, Parkinson’s disease.

**SUPPLEMENTARY FIGURE 3** Longitudinal analysis of the type and combinations of anti-PD drugs prescribed during the observation period: Patients Total (*N* = 39,731), patients 65–74 years (*N* = 5,312), and patients ≥85 years (*N* = 8,162). The number of nodes and arrows in patients Total (11 and 15, respectively), 65–74 years (13 and 18, respectively), and ≥85 years (8 and 13, respectively).

 COMTI, catechol-O-methyltransferase inhibitor; DA, dopamine agonist; L-dopa, levodopa; MAOBI, monoamine oxidase type B inhibitor; NE, non-ergot; PD, Parkinson’s disease.

**SUPPLEMENTARY FIGURE 4** Duration of non-ergot DA monotherapy in patients who newly initiated PD treatment with a first prescription for non-ergot DA monotherapy (*N* = 267).



CI, confidence interval; DA, dopamine agonist; PD, Parkinson’s disease.

**SUPPLEMENTARY FIGURE 5** Treatment modalities and drug prescriptions when patients who increased their levodopa dose to ≥300 mg. (**A**) Total, (**B**) ≥75-year-group, and (**C**) <75-year-group.

 COMTI, catechol-O-methyltransferase inhibitor; DA, dopamine agonist; MAOBI, monoamine oxidase type B inhibitor; PD, Parkinson’s disease.