**Supplementary Material**

**Treatment Patterns in Patients with Incident Parkinson’s Disease in the United States**

**Supplementary Table 1 Attrition table for selection of patients for study cohort**

|  |  |
| --- | --- |
| **Inclusion/exclusion rule** | **Remaining number of patients eligible** |
| Patients with at least one PD diagnosis code during 2007-2016 | 269,649 |
| Patients with at least two PD diagnosis codes (and not on the same day) during 2007-2016 | 209,046 |
| Patients with at least 1 year ‘Parkinson’s disease-free’ period of continuous enrollment in database prior to first PD diagnosis code | 84,104 |
| Patients with medical and drug coverage on first PD diagnosis date\* | 68,532 |

Each row is a further criterion applied to the preceding row.

PD, Parkinson’s disease.

**Supplementary Table 2. Charlson comorbidities in newly diagnosed Parkinson’s disease (n=84,104)**

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Score for severity** | **Overall**  **(N=84,104)** | | **<50 years**  **(n=2,508)** | | **50-70 years**  **(n=28,670)** | | **70+ years**  **(n=52,926)** | |
|  |  | **n** | **%** | **n** | **%** | **n** | **%** | **n** | **%** |
| **AIDS/HIV** | 6 | 69 | 0.1 | 10 | 0.4 | 45 | 0.2 | 14 | <0.1 |
| **Cancer** | 2 | 10,163 | 12.1 | 72 | 2.9 | 2,298 | 8.0 | 7,793 | 14.7 |
| **Cerebrovascular disease** | 1 | 18,370 | 21.8 | 157 | 6.3 | 4,032 | 14.1 | 14,181 | 26.8 |
| **Chronic pulmonary disease** | 1 | 10,171 | 12.1 | 38 | 1.5 | 1,577 | 5.5 | 8556 | 16.2 |
| **Congestive heart disease** | 1 | 14,797 | 17.6 | 253 | 10.1 | 3,871 | 13.5 | 10,673 | 20.2 |
| **Dementia** | 1 | 8,132 | 9.7 | 13 | 0.5 | 883 | 3.1 | 7,236 | 13.7 |
| **Diabetes** | 1 | 20,829 | 24.8 | 240 | 9.6 | 6,609 | 23.1 | 13,980 | 26.4 |
| **Diabetes with complications** | 2 | 7,357 | 8.7 | 48 | 1.9 | 2,041 | 7.1 | 5,268 | 10.0 |
| **Hemiplegia** | 2 | 1,858 | 2.2 | 113 | 4.5 | 670 | 2.3 | 1,075 | 2.0 |
| **Metastatic tumor** | 6 | 892 | 1.1 | 14 | 0.6 | 276 | 1.0 | 602 | 1.1 |
| **Mild liver disease** | 1 | 2,573 | 3.1 | 91 | 3.6 | 1,167 | 4.1 | 1,315 | 2.5 |
| **Moderate/severe liver disease** | 3 | 280 | 0.3 | 9 | 0.4 | 134 | 0.5 | 137 | 0.3 |
| **Myocardial infarction** | 1 | 3,376 | 4.0 | 18 | 0.7 | 693 | 2.4 | 2,665 | 5.0 |
| **Peptic ulcer disease** | 1 | 1,048 | 1.2 | 20 | 0.8 | 296 | 1.0 | 732 | 1.4 |
| **Peripheral vascular disease** | 1 | 12,454 | 14.8 | 46 | 1.8 | 2,113 | 7.4 | 10,295 | 19.5 |
| **Renal disease** | 2 | 7,959 | 9.5 | 45 | 1.8 | 1,635 | 5.7 | 6,279 | 11.9 |
| **Rheumatological disease** | 1 | 2,749 | 3.3 | 55 | 2.2 | 843 | 2.9 | 1,851 | 3.5 |
| **CCI score: 0** | - | 29,694 | 35.3 | 1,710 | 68.2 | 14,030 | 48.9 | 13,954 | 26.4 |
| **CCI score: 1+** | - | 54,410 | 64.7 | 798 | 31.8 | 14,640 | 51.1 | 38,972 | 73.6 |
| **CCI score: 1** | - | 17,694 | 21.0 | 417 | 16.6 | 5,988 | 20.9 | 11,289 | 21.3 |
| **CCI score: 2** | - | 12,596 | 15.0 | 191 | 7.6 | 3,333 | 11.6 | 9,072 | 17.1 |
| **CCI score: 3+** | - | 24,120 | 28.7 | 190 | 7.6 | 5,319 | 18.6 | 18,611 | 35.2 |
| **CCI score: mean (SD) [median]** | - | 1.85 (2.20) [1.0] | | 0.66 (1.37) [0.0] | | 1.31 (1.98) [1.0] | | 2.20 (2.27) [2.0] | |

Scores for severity of present comorbidities make up the CCI score. Higher scores represent greater severity of comorbidity burden.

CCI, Charlson Comorbidity Index; SD, standard deviation.

**Supplementary Table 3. Cox proportional-hazards models for time to first treatment and switch/add-on including year of first PD claim as a covariate**

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Hazard ratios for time between PD diagnosis and first treatment with:** | | | | | | | | | | | | | |
|  |  | **Any treatment** | | **Levodopa/**  **combination** | | **Dopamine agonists** | | **MAO-Bi** | | **Amantadine** | | **Other dopaminergic agent** | | | |
| **Gender** | Female | 0.93 (0.92, 0.95) | | 0.91 (0.90, 0.93) | | 0.99 (0.96, 1.02) | | 0.81 (0.78, 0.84) | | 0.99 (0.94, 1.05) | | 0.79 (0.72, 0.86) | | | |
| **Age, years\*** | 50–70 | 1.37 (1.30, 1.45) | | 1.55 (1.45, 1.66) | | 0.93 (0.87, 1.00) | | 0.89 (0.82, 0.97) | | 0.78 (0.70, 0.88) | | 0.84 (0.68, 1.03) | | | |
|  | >70 | 1.21 (1.14, 1.27) | | 1.92 (1.79, 2.05) | | 0.39 (0.36, 0.42) | | 0.30 (0.27, 0.33) | | 0.33 (0.29, 0.37) | | 0.62 (0.50, 0.76) | | | |
| **CCI $** | 1 | 0.94 (0.92, 0.96) | | 0.98 (0.96, 1.01) | | 0.83 (0.80, 0.87) | | 0.70 (0.67, 0.74) | | 0.84 (0.78, 0.90) | | 0.81 (0.72, 0.90) | | | |
|  | 2 | 0.88 (0.86, 0.91) | | 0.93 (0.91, 0.96) | | 0.79 (0.75, 0.82) | | 0.63 (0.59, 0.67) | | 0.78 (0.72, 0.85) | | 0.71 (0.62, 0.82) | | | |
|  | 3 | 0.79 (0.77, 0.81) | | 0.86 (0.84, 0.88) | | 0.68 (0.65, 0.70) | | 0.41 (0.39, 0.44) | | 0.67 (0.62, 0.73) | | 0.65 (0.57, 0.73) | | | |
| **Year of first PD claim #** | 2011-2013 | 1.00 (0.98, 1.02) | | 1.00 (0.98, 1.03) | | 0.88 (0.85, 0.91) | | 1.01 (0.96, 1.05) | | 0.93 (0.87, 0.98) | | 0.71 (0.65, 0.79) | | | |
|  | 2014-2016 | 0.93 (0.91, 0.95) | | 0.97 (0.95, 0.99) | | 0.76 (0.73, 0.80) | | 0.84 (0.79, 0.88) | | 0.76 (0.70, 0.82) | | 0.57 (0.49, 0.66) | | | |
| **Hazard ratios for time to switch/add-on of another treatment class, following first-line treatment with:** | | | | | | | | | | | | | | | | |
|  |  | **Any treatment** | | **Levodopa/**  **combination** | | **Dopamine agonists** | | **MAO-Bi** | | **Amantadine** | | **Other dopaminergic agent** | | | |
| **Gender** | Female | 0.92 (0.90, 0.95) | | 0.93 (0.90, 0.97) | | 0.85 (0.81, 0.90) | | 0.95 (0.88, 1.01) | | 0.92 (0.82, 1.04) | | 0.97 (0.72, 1.29) | | | |
| **Age, years\*** | 50–70 | 0.82 (0.77, 0.88) | | 0.75 (0.66, 0.84) | | 0.97 (0.86, 1.10) | | 0.95 (0.83, 1.09) | | 1.10 (0.85, 1.42) | | 0.91 (0.13, 6.62) | | | |
|  | >70 | 0.40 (0.37, 0.42) | | 0.36 (0.32, 0.41) | | 0.87 (0.77, 0.99) | | 0.91 (0.78, 1.05) | | 1.03 (0.79, 1.34) | | 0.86 (0.12, 6.20) | | | |
| **CCI$** | 1 | 0.81 (0.78, 0.84) | | 0.83 (0.79, 0.87) | | 0.83 (0.77, 0.89) | | 0.90 (0.82, 0.99) | | 0.82 (0.71, 0.95) | | 0.70 (0.49, 1.01) | | | |
|  | 2 | 0.77 (0.73, 0.80) | | 0.80 (0.76, 0.85) | | 0.75 (0.69, 0.83) | | 0.93 (0.83, 1.04) | | 0.69 (0.57, 0.83) | | 0.84 (0.55, 1.30) | | | |
|  | 3 | 0.66 (0.63, 0.68) | | 0.71 (0.67, 0.75) | | 0.66 (0.61, 0.71) | | 0.85 (0.76, 0.95) | | 0.63 (0.53, 0.75) | | 0.79 (0.55, 1.13) | | | |
| **Time to first treatment start, in years** | | | 0.81 (0.79, 0.84) | | 0.79 (0.76, 0.83) | | 0.78 (0.73, 0.83) | | 0.82 (0.75, 0.89) | | 0.69 (0.60, 0.79) | | 0.85 (0.63, 1.14) | |
| **Year of first PD claim#** | 2011-2013 | 0.90 (0.87, 0.93) | | 0.88 (0.84, 0.92) | | 0.90 (0.84, 0.95) | | 0.95 (0.88, 1.02) | | 0.95 (0.84, 1.08) | | 0.91 (0.66, 1.26) | | | |
|  | 2014-2016 | 0.80 (0.77, 0.83) | | 0.77 (0.73, 0.81) | | 0.86 (0.80, 0.93) | | 0.93 (0.84, 1.02) | | 0.84 (0.72, 0.98) | | 0.82 (0.52, 1.29) | | | |

\*Reference category for age is <50 years.

$CCI, with reference category of CCI=0.

#Reference category for year of first PD claim is 2008-2010.

‘Switch/add-on’ means the initiation of another treatment class (those listed) different to the first (regardless if first line is discontinued or not).

CCI, Charlson Comorbidity Index; PD, Parkinson’s disease.

**Supplementary Table 4. Cox proportional-hazards models for time to first treatment and switch/add-on including region as a covariate**

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Hazard ratios for time between PD diagnosis and first treatment with:** | | | | | | | | | | | | | | |
|  |  | | **Any treatment** | | **Levodopa/**  **combination** | | **Dopamine agonists** | | **MAO-Bi** | | **Amantadine** | | **Other dopaminergic agent** | | |
| **Gender** | Female | | 0.93 (0.92, 0.95) | | 0.91 (0.90, 0.93) | | 0.99 (0.96, 1.02) | | 0.81 (0.78, 0.85) | | 0.99 (0.94, 1.04) | | 0.79 (0.72, 0.86) | | |
| **Age, years\*** | 50–70 | | 1.38 (1.30, 1.45) | | 1.56 (1.45, 1.66) | | 0.93 (0.87, 1.00) | | 0.91 (0.84, 0.99) | | 0.78 (0.69, 0.88) | | 0.84 (0.69, 1.04) | | |
|  | >70 | | 1.21 (1.15, 1.28) | | 1.92 (1.80, 2.05) | | 0.40 (0.37, 0.43) | | 0.31 (0.29, 0.34) | | 0.33 (0.30, 0.38) | | 0.64 (0.52, 0.79) | | |
| **CCI $** | 1 | | 0.94 (0.92, 0.96) | | 0.98 (0.96, 1.01) | | 0.84 (0.80, 0.87) | | 0.71 (0.68, 0.75) | | 0.84 (0.78, 0.90) | | 0.81 (0.73, 0.91) | | |
|  | 2 | | 0.88 (0.86, 0.91) | | 0.93 (0.91, 0.96) | | 0.79 (0.75, 0.82) | | 0.63 (0.60, 0.68) | | 0.78 (0.71, 0.85) | | 0.71 (0.62, 0.81) | | |
|  | 3 | | 0.79 (0.77, 0.81) | | 0.86 (0.84, 0.88) | | 0.67 (0.64, 0.70) | | 0.42 (0.39, 0.44) | | 0.66 (0.61, 0.71) | | 0.64 (0.56, 0.72) | | |
| **Region &** | North Central | | 1.04 (1.01, 1.06) | | 1.03 (1.01, 1.06) | | 1.17 (1.11, 1.22) | | 0.56 (0.53, 0.60) | | 0.96 (0.89, 1.04) | | 0.95 (0.83, 1.09) | | |
|  | South | | 1.09 (1.06, 1.12) | | 1.04 (1.01, 1.07) | | 1.43 (1.37, 1.50) | | 0.82 (0.78, 0.87) | | 0.95 (0.87, 1.03) | | 1.06 (0.93, 1.21) | | |
|  | West | | 1.09 (1.06, 1.12) | | 1.06 (1.03, 1.10) | | 1.32 (1.25, 1.39) | | 1.06 (1.00, 1.12) | | 0.94 (0.86, 1.03) | | 1.33 (1.15, 1.53) | | |
| **Hazard ratios for time to switch/add-on of another treatment class, following first-line treatment with:** | | | | | | | | | | | | | | |
|  |  | | **Any treatment** | | **Levodopa/**  **combination** | | **Dopamine agonists** | | **MAO-Bi** | | **Amantadine** | | **Other dopaminergic agent** | | |
| **Gender** | Female | | 0.92 (0.90, 0.95) | | 0.94 (0.90, 0.97) | | 0.85 (0.81, 0.90) | | 0.96 (0.89, 1.03) | | 0.92 (0.82, 1.03) | | 0.99 (0.74, 1.32) | | |
| **Age, years\*** | 50–70 | | 0.83 (0.77, 0.89) | | 0.75 (0.67, 0.85) | | 0.97 (0.86, 1.09) | | 0.96 (0.84, 1.10) | | 1.10 (0.85, 1.43) | | 0.90 (0.12, 6.54) | | |
|  | >70 | | 0.40 (0.38, 0.44) | | 0.37 (0.33, 0.42) | | 0.88 (0.78, 1.00) | | 0.92 (0.79, 1.07) | | 1.04 (0.80, 1.36) | | 0.85 (0.12, 6.19) | | |
| **CCI$** | 1 | | 0.81 (0.78, 0.84) | | 0.84 (0.79, 0.88) | | 0.83 (0.77, 0.89) | | 0.90 (0.82, 0.99) | | 0.82 (0.71, 0.95) | | 0.68 (0.47, 1.00) | | |
|  | 2 | | 0.77 (0.73, 0.80) | | 0.80 (0.76, 0.85) | | 0.75 (0.69, 0.83) | | 0.93 (0.83, 1.05) | | 0.68 (0.57, 0.82) | | 0.82 (0.53, 1.27) | | |
|  | 3 | | 0.65 (0.63, 0.68) | | 0.70 (0.67, 0.74) | | 0.65 (0.60, 0.70) | | 0.85 (0.76, 0.96) | | 0.61 (0.52, 0.73) | | 0.75 (0.52, 1.08) | | |
| **Time to first treatment start, in years** | | 0.83 (0.80, 0.86) | | 0.81 (0.77, 0.85) | | 0.79 (0.73, 0.84) | | 0.82 (0.76, 0.90) | | 0.69 (0.61, 0.79) | | 0.85 (0.63, 1.14) | |
| **Region &** | North Central | | 0.87 (0.83, 0.91) | | 0.89 (0.84, 0.94) | | 0.83 (0.76, 0.91) | | 1.10 (0.99, 1.22) | | 0.96 (0.81, 1.14) | | 1.00 (0.66, 1.50) | | |
|  | South | | 1.07 (1.02, 1.11) | | 1.11 (1.05, 1.17) | | 0.90 (0.83, 0.98) | | 1.18 (1.07, 1.30) | | 0.94 (0.79, 1.12) | | 0.99 (0.65, 1.51) | | |
|  | West | | 1.12 (1.07, 1.17) | | 1.15 (1.08, 1.23) | | 0.98 (0.89, 1.08) | | 1.16 (1.05, 1.29) | | 1.03 (0.84, 1.26) | | 0.93 (0.59, 1.46) | | |

\*Reference category for age is <50 years.

$CCI: with reference category of CCI=0.

&Reference for region is Northeast.

‘Switch/add-on’ means the initiation of another treatment class (those listed) different to the first (regardless if first line is discontinued or not).

CCI, Charlson Comorbidity Index; PD, Parkinson’s disease.

**Supplementary Table 5. Cox proportional-hazards models for time to first treatment and switch/add-on including specialty of physician at first PD claim as a covariate**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Hazard ratios for time between PD diagnosis and first treatment with:** | | | | | | | |
|  |  | **Any treatment** | **Levodopa/**  **combination** | **Dopamine agonists** | **MAO-Bi** | **Amantadine** | **Other dopaminergic agent** |
| **Gender** | Female | 0.94 (0.92, 0.96) | 0.92 (0.90, 0.94) | 0.99 (0.96, 1.03) | 0.82 (0.78, 0.85) | 0.99 (0.94, 1.05) | 0.79 (0.72, 0.86) |
| **Age, years\*** | 50–70 | 1.37 (1.30, 1.45) | 1.56 (1.45, 1.66) | 0.93 (0.86, 1.00) | 0.89 (0.82, 0.97) | 0.78 (0.70, 0.88) | 0.84 (0.68, 1.03) |
|  | >70 | 1.31 (1.24, 1.38) | 2.06 (1.92, 2.20) | 0.41 (0.38, 0.44) | 0.33 (0.30, 0.36) | 0.35 (0.31, 0.40) | 0.66 (0.53, 0.81) |
| **CCI $** | 1 | 0.95 (0.93, 0.98) | 1.00 (0.97, 1.02) | 0.84 (0.81, 0.88) | 0.72 (0.68, 0.75) | 0.85 (0.79, 0.91) | 0.81 (0.72, 0.91) |
|  | 2 | 0.90 (0.88, 0.93) | 0.95 (0.92, 0.98) | 0.79 (0.76, 0.83) | 0.65 (0.61, 0.69) | 0.79 (0.72, 0.86) | 0.71 (0.62, 0.82) |
|  | 3 | 0.81 (0.79, 0.83) | 0.88 (0.86, 0.90) | 0.68 (0.65, 0.71) | 0.43 (0.40, 0.45) | 0.68 (0.62, 0.73) | 0.63 (0.56, 0.72) |
| **Specialty of physician at first PD claim** | Other | 0.66 (0.65, 0.67) | 0.73 (0.71, 0.74) | 0.73 (0.71, 0.76) | 0.58 (0.55, 0.60) | 0.76 (0.72, 0.80) | 0.75 (0.69, 0.82) |
| **Hazard ratios for time to switch/add-on of another treatment class, following first-line treatment with:** | | | | | | | |
|  |  | **Any treatment** | **Levodopa/**  **combination** | **Dopamine agonists** | **MAO-Bi** | **Amantadine** | **Other dopaminergic agent** |
| **Gender** | Female | 0.92 (0.90, 0.95) | 0.94 (0.90, 0.97) | 0.85 (0.81, 0.90) | 0.95 (0.88, 1.02) | 0.92 (0.82, 1.04) | 0.97 (0.73, 1.30) |
| **Age, years\*** | 50–70 | 0.83 (0.77, 0.89) | 0.75 (0.67, 0.84) | 0.97 (0.86, 1.09) | 0.96 (0.83, 1.10) | 1.10 (0.85, 1.43) | 0.94 (0.13, 6.85) |
|  | >70 | 0.41 (0.39, 0.45) | 0.38 (0.34, 0.43) | 0.91 (0.80, 1.03) | 0.91 (0.79, 1.06) | 1.07 (0.82, 1.40) | 0.91 (0.13, 6.66) |
| **CCI$** | 1 | 0.82 (0.79, 0.85) | 0.84 (0.80, 0.88) | 0.83 (0.78, 0.90) | 0.90 (0.82, 0.99) | 0.83 (0.71, 0.96) | 0.70 (0.49, 1.01) |
|  | 2 | 0.77 (0.73, 0.80) | 0.80 (0.76, 0.85) | 0.76 (0.69, 0.83) | 0.93 (0.83, 1.04) | 0.69 (0.57, 0.83) | 0.83 (0.54, 1.28) |
|  | 3 | 0.66 (0.63, 0.68) | 0.70 (0.67, 0.74) | 0.66 (0.61, 0.71) | 0.84 (0.75, 0.95) | 0.62 (0.53, 0.73) | 0.75 (0.53, 1.07) |
| **Time to first treatment start, in years** | | 0.84 (0.81, 0.87) | 0.82 (0.78, 0.86) | 0.79 (0.74, 0.85) | 0.82 (0.76, 0.09) | 0.70 (0.62, 0.80) | 0.84 (0.63, 1.13) |
| **Specialty of physician at first PD claim** | Other | 0.81 (0.78, 0.83) | 0.80 (0.77, 0.84) | 0.86 (0.81, 0.91) | 1.00 (0.93, 1.07) | 0.86 (0.77, 0.97) | 0.87 (0.66, 1.15) |

\*Reference category for age is <50 years.

$CCI: with reference category of CCI=0.

@Reference for specialty of first PD claim is Neurologist.

‘Switch/add-on’ means the initiation of another treatment class (those listed) different to the first (regardless if first line is discontinued or not).

CCI, Charlson Comorbidity Index; PD, Parkinson’s disease.