**Supplementary Table 1.** Effect of adding features to 953 PD cases with one or more of a family history of Parkinson’s, constipation, never-smoked

|  |  |  |
| --- | --- | --- |
|  | Proportion identified in cohort | |
| Non-motor features | AND  additional features | AND/OR  additional  features |
| One additional feature  Hyposmia  RBD  Depression | 43.5%  24.7%  10.9% | 88.5%  77.8%  68.9% |
| Two additional features |  |  |
| Hyposmia, RBD | 18.7% | 94.0% |
| Hyposmia, depression | 7.4% | 90.5% |
| RBD, depression | 6.3% | 80.6% |
| Three additional features |  |  |
| Hyposmia, RBD, depression | 4.3% | 94.5% |

RBD = rapid eye movement sleep behaviour disorder

**Supplementary Table 2.** Clinical correlates in 1719 recent onset Parkinson’s disease cases according to the presence of four key non-motor features. Analysis based on multiple imputation.

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | Number of non-motor features | | | | |  |  |
| Variable | None  12.1% | One  38.2% | Two  31.3% | Three  15.8% | Four  2.6% | Unadjusted p-value | Adjusted p-value |
| Age | 70.7 (7.7) | 68.7 (8.3) | 67.9 (7.8) | 68.1 (8.0) | 68.4 (7.9) | 0.002 | <0.001a |
| Male Sex | 65.6% | 63.4% | 66.0% | 67.1% | 76.5% | 0.44 | 0.40b |
| Disease duration | 1.3 (0.9) | 1.3 (0.9) | 1.4 (0.9) | 1.4 (1.0) | 1.5 (0.9) | 0.41 | 0.27c |
| UPDRS 3 | 20.8 (11.4) | 22.0 (12.2) | 21.9 (12.1) | 25.7 (12.6) | 31.4 (13.5) | <0.001 | <0.001d |
| Motor subtype | |  |  |  |  |  |  |
| TD | 55.8% | 52.5% | 43.9% | 36.6% | 32.2% |  |  |
| PIGD | 33.4% | 35.2% | 41.5% | 51.0% | 60.9% | <0.001 | <0.001d |
| Indeterminate | 10.8% | 12.3% | 14.6% | 12.3% | 6.9% | 0.13 | 0.10d |
| MoCA | | |  |  |  |  |  |
| Normal | 77.5% | 79.2% | 71.0% | 67.1% | 58.1% | <0.001 | <0.001d |
| MCI | 11.0% | 10.1% | 14.5% | 12.3% | 7.8% |  |  |
| Dementia | 11.5% | 10.7% | 14.5% | 20.5% | 34.1% |  |  |
| NMSSTotal | 17.4 (13.3) | 23.1 (18.0) | 32.5 (23.4) | 49.6 (32.1) | 65.3 (35.6) | <0.001 | <0.001d |
| Dopamine imaging  performed | 32.2% | 27.4% | 29.0% | 23.5% | 28.7% | 0.35 | 0.12d |

Data are mean (95% confidence intervals or SD) or number (percentage).

UPDRS 3= Movement Disorder Society unified Parkinson’s disease rating scale, TD = tremor dominant, PIGD = postural instability gait difficulty, MoCA = Montreal cognitive assessment, MCI = mild cognitive impairment, NMSS = non motor symptom scale.

a Adjusted for disease duration and sex, b Adjusted for age and disease duration, cAdjusted for age and sex, d Adjusted for age, sex and disease duration

**Supplementary Table 3.** Clinical correlates in recent onset Parkinson’s disease cases with only one non-motor feature. Analysis based on multiple imputation. Population size varies from 705 to 738 in the 10 imputed datasets.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Variable | Hyposmia only  71.9% | RBD only  17.5% | Constipation only  6.2% | Depression only  4.4% | Unadjusted p-value | Adjusted p-value |
| Age | 67.7 (8.0) | 71.1 (7.9) | 73.3 (8.9) | 70.0 (9.8) | <0.001 | <0.001a |
| Male Sex | 63.3% | 65.9% | 69.1% | 48.1% | 0.35 | 0.35b |
| Disease duration | 1.3 (0.9) | 1.4 (0.9) | 1.5 (0.9) | 1.1 (0.9) | 0.28 | 0.36c |
| UPDRS 3 | 21.2 (11.3) | 23.1 (13.2) | 25.2 (14.4) | 26.7 (15.9) | 0.033 | 0.20d |
| Motor subtype | |  |  |  |  |  |
| TD | 55.7% | 45.7% | 44.2% | 40.5% |  |  |
| PIGD | 31.9% | 41.9% | 50.4% | 41.3% | 0.042 | 0.20d |
| Indeterminate | 12.5% | 12.3% | 5.4% | 18.2% | 0.48 | 0.50d |
| MoCA | | |  |  |  |  |
| Normal | 80.0% | 79.9% | 82.8% | 58.6% | 0.038 | 0.009d |
| MCI | 10.6% | 6.9% | 11.3% | 13.0% |  |  |
| Dementia | 9.4% | 13.2% | 5.9% | 28.4% |  |  |
| NMSSTotal | 19.9 (14.8) | 26.5 (17.1) | 26.5 (15.7) | 55.1 (32.7) | <0.001 | <0.001d |
| Dopamine imaging  Performed | 26.6% | 25.0% | 37.1% | 35.6% | 0.43 | 0.25d |

Data are mean (standard deviation) or number (percentage).

UPDRS 3 = Movement Disorder Society unified Parkinson’s disease rating scale, TD = tremor dominant, PIGD = postural instability gait difficulty, MoCA = Montreal cognitive assessment, MCI = mild cognitive impairment, NMSS = non motor symptom scale.

a Adjusted for disease duration and sex, b Adjusted for age and disease duration, cAdjusted for age and sex, d Adjusted for age, sex and disease duration

**Supplementary Table 4.** Proportion and clinical characteristics of recent onset Parkinson’s disease patients identified by four different screening algorithms. Analysis based on multiple imputation.

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Hyposmia and/or  family history[3] | | | Hyposmia in enriched cohort  (50% family history) [4] | | | Hyposmia and/or RBD  and/or depression [6] | | | Hyposmia and RBD [5] | | |
|  | Yes  77.4% | No  22.6% | Adjusted p-value | Yes  70.2% | No  29.8% | Adjusted p-value | Yes  88.1% | No  11.9% | Adjusted p-value | Yes  31.5% | No  68.5% | Adjusted p-value |
| Age | 67.8 (7.9) | 71.3  (7.9) | <0.001a | 67.5 (7.9) | 69.8 (8.0) | 0.001a | 68.2 (8.0) | 71.4 (8.0) | <0.001a | 67.6 (7.8) | 69.0 (8.1) | <0.001a |
| Male Sex | 64.9% | 67.5% | 0.58b | 65.6% | 65.2% | 0.68b | 65.0% | 69.0% | 0.40b | 71.3% | 62.8% | <0.001b |
| Disease duration | 1.4 (0.9) | 1.3 (0.9) | 0.29c | 1.4 (0.9) | 1.3 (0.9) | 0.19c | 1.4 (0.9) | 1.3 (0.9) | 0.37c | 1.4 (0.9) | 1.3 (0.9) | 0.004c |
| UPDRS 3 | 22.7 (12.2) | 22.8 (12.6) | 0.20d | 21.8 (12.1) | 22.8 (12.8) | 0. 57d | 22.9 (12.4) | 21.4 (11.9) | 0.007d | 23.4 (12.5) | 22.3 (12.2) | 0.050d |
| Motor subtype | | |  |  |  |  |  |  |  |  |  |  |
| TD | 47.1% | 47.2% |  | 47.1% | 50.7% |  | 46.1% | 54.8% |  | 40.5% | 50.2% |  |
| PIGD | 39.9% | 41.1% | 0.47d | 39.8% | 39.4% | 0.45d | 40.8% | 35.2% | 0.008d | 44.9% | 37.9% | <0.001d |
| Indeterminate | 13.0% | 11.7% | 0.52d | 13.1% | 10.0% | 0.22d | 13.0% | 10.1% | 0.13d | 14.6% | 11.8% | 0.008d |
| MoCA | | |  |  |  |  |  |  |  |  |  |  |
| Normal | 73.9% | 74.4% | 0.067d | 75.7% | 76.8% | 0.28d | 73.6% | 76.9% | 0.010d | 68.9% | 76.3% | <0.001d |
| MCI | 12.4% | 10.2% |  | 11.9% | 12.1% |  | 11.9% | 12.0% |  | 13.5% | 11.1% |  |
| Dementia | 13.8% | 15.5% |  | 12.5% | 11.1% |  | 14.5% | 11.1% |  | 17.6% | 12.6% |  |
| NMSSTotal | 31.6 (26.1) | 27.4 (22.6) | 0.013d | 32.6 (25.9) | 31.0 (26.0) | 0.60d | 32.3 (26.1) | 18.4 (13.6) | <0.001d | 39.8 (29.7) | 26.4 (21.9) | <0.001d |
| Dopamine  Imaging performed | 27.1% | 30.6% | 0.034d | 30.0% | 29.5% | 0.66d | 27.2% | 33.2% | 0.005d | 26.9% | 28.4% | 0.23d |

Data are mean (standard deviation) or number (percentage).

UPDRS 3 = Movement Disorder Society unified Parkinson’s disease rating scale part 3, TD = tremor dominant, PIGD = postural instability gait difficulty, MoCA = Montreal cognitive assessment, MCI = mild cognitive impairment, NMSS = non motor symptom scale

a Adjusted for disease duration and sex, b Adjusted for age and disease duration, cAdjusted for age and sex, d Adjusted for age, sex and disease duration