

Running head: Stratifying QoL outcomes in STN-DBS for PD

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Supplementary Table 1: Baseline clinical parameters in non-motor, motor progression, and levodopa response strata

| | Non-motor Symptom Scale | | | | | | | | | p |
|--------------------------------------|----------------------------------|--------|-------|----------------------|--------|-------|----------------------|--------|-------|-----------|
| | 'mild to moderate' (≤ 40) | | | 'severe' (41 – 70) | | | 'very severe' (≥ 71) | | | |
| | n | mean | SD | n | mean | SD | n | mean | SD | |
| PDQ-8 SI | 56 | 26.2 | 12.3 | 50 | 33.7 | 13.3 | 60 | 41.4 | 15.5 | <0.001*** |
| NMSS total | 56 | 27.3 | 10.1 | 50 | 53.8 | 8.0 | 60 | 102.4 | 28.5 | <0.001*** |
| Hoehn & Yahr | 56 | 2.4 | 0.8 | 47 | 2.4 | 0.8 | 60 | 2.8 | 0.8 | 0.041* |
| Levodopa challenge test response (%) | 54 | 46.0 | 20.0 | 49 | 48.5 | 19.0 | 60 | 47.1 | 18.0 | 0.809 |
| UPDRS-III | 56 | 24.4 | 12.6 | 50 | 21.3 | 9.0 | 60 | 31.7 | 14.1 | <0.001*** |
| SCOPA-M ADL | 53 | 6.0 | 2.9 | 49 | 7.0 | 2.9 | 58 | 8.7 | 3.2 | <0.001*** |
| Motor complications | 53 | 4.2 | 3.0 | 49 | 4.7 | 2.6 | 58 | 6.1 | 2.7 | <0.001*** |
| LEDD | 56 | 1082.2 | 426.3 | 49 | 1125.7 | 510.9 | 60 | 1128.3 | 591.8 | 0.983 |
| | Hoehn and Yahr Scale | | | | | | | | | p |
| | 'minimal to mild' (≤ 2.5) | | | 'moderate' (3) | | | 'severe' (≥ 4) | | | |
| | n | mean | SD | n | mean | SD | n | mean | SD | |
| PDQ-8 SI | 96 | 31.3 | 14.5 | 48 | 37.2 | 14.7 | 19 | 37.3 | 16.7 | 0.112 |
| NMSS total | 96 | 55.9 | 34.5 | 48 | 69.6 | 37.4 | 19 | 78.9 | 43.4 | 0.020* |
| Hoehn & Yahr | 96 | 2.0 | 0.5 | 48 | 3.0 | 0.0 | 19 | 4.1 | 0.2 | <0.001*** |
| Levodopa challenge test response (%) | 94 | 44.3 | 18.0 | 48 | 48.2 | 18.5 | 18 | 58.7 | 21.0 | 0.030* |
| UPDRS-III | 96 | 21.4 | 9.6 | 48 | 31.6 | 13.6 | 19 | 36.5 | 15.7 | <0.001*** |
| SCOPA-M ADL | 93 | 6.8 | 3.2 | 46 | 7.3 | 3.2 | 18 | 9.6 | 2.0 | <0.001*** |
| Motor complications | 93 | 4.4 | 2.7 | 46 | 5.2 | 2.8 | 18 | 8.0 | 1.6 | <0.001*** |
| LEDD | 96 | 1120.6 | 505.4 | 48 | 1085.1 | 522.0 | 18 | 1207.5 | 555.3 | 0.809 |
| | Levodopa challenge test response | | | | | | | | | p |
| | 'low' (< 33%) | | | 'partial' (33 – 50%) | | | 'full' (> 50%) | | | |
| | n | mean | SD | n | mean | SD | n | mean | SD | |
| PDQ-8 SI | 43 | 34.2 | 14.1 | 55 | 34.1 | 15.5 | 66 | 33.7 | 15.8 | 0.983 |
| NMSS total | 42 | 62.5 | 32.2 | 55 | 62.6 | 45.2 | 66 | 63.0 | 32.9 | 0.809 |
| Hoehn & Yahr | 41 | 2.5 | 0.6 | 55 | 2.5 | 0.7 | 64 | 2.6 | 0.9 | 0.484 |
| Levodopa challenge test response (%) | 43 | 24.0 | 5.5 | 55 | 42.3 | 5.0 | 66 | 65.9 | 11.2 | <0.001*** |
| UPDRS-III | 43 | 26.9 | 11.8 | 55 | 25.6 | 12.8 | 66 | 26.1 | 13.9 | 0.917 |
| SCOPA-M ADL | 40 | 7.5 | 2.6 | 54 | 6.9 | 3.1 | 64 | 7.4 | 3.6 | 0.640 |
| Motor complications | 40 | 4.8 | 3.1 | 54 | 4.2 | 2.4 | 64 | 5.9 | 2.9 | 0.004** |
| LEDD | 43 | 957.5 | 501.2 | 54 | 1183.8 | 482.6 | 66 | 1151.2 | 546.1 | 0.135 |

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Abbreviations: **ADL** = activities of daily living, **SD** = standard deviation, **LEDD** = levodopa-equivalent daily dose, **NMSS** = Non-motor Symptom Scale, **PDQ-8** = Parkinson's Disease Questionnaire-8, **SCOPA** = Scales for Outcomes in Parkinson's Disease, **UPDRS-III** = Unified Parkinson's Disease Rating Scale-motor examination.

Legend: Kruskal-Wallis tests were performed for independent samples for between-strata analyses of baseline parameters. Multiple comparisons (multiple scales and three stratifications) were corrected with the Benjamini-Hochberg method.

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

Bold font highlights significant results.

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Supplementary Table 2: Relative and change and effect size of Parkinson's Disease Questionnaire-8 domains at follow-up

| | Non-motor Symptom Scale | | | | | |
|-----------------------------|----------------------------------|-------------|-------------------------|-------------|-------------------------|-------------|
| | 'mild to moderate' (≤ 40) | | 'severe' (41 – 70) | | 'very severe' (≥ 71) | |
| | Relative change [%] | Effect size | Relative change [%] | Effect size | Relative change [%] | Effect size |
| Mobility | -23.0 | 0.31 | -19.8 | 0.36 | -25.2 | 0.42 |
| ADL | -27.5 | 0.30 | -26.9 | 0.40 | -36.6 | 0.54 |
| Emotional well-being | -30.3 | 0.30 | 9.3 | 0.10 | -25.6 | 0.37 |
| Social support | -18.7 | 0.16 | 17.9 | 0.18 | -21.7 | 0.25 |
| Cognition | -41.5 | 0.58 | 5.0 | 0.07 | -35.0 | 0.54 |
| Communication | -19.5 | 0.17 | 10.5 | 0.12 | -26.7 | 0.40 |
| Bodily discomfort | -15.2 | 0.15 | -16.5 | 0.25 | -37.9 | 0.70 |
| Stigma | -28.2 | 0.22 | -17.9 | 0.16 | -37.1 | 0.45 |
| | Hoehn and Yahr Scale | | | | | |
| | 'minimal to mild' (≤ 2.5) | | 'moderate' -3 | | 'severe' (≥ 4) | |
| | Relative change [%] | Effect size | Relative change [%] | Effect size | Relative change [%] | Effect size |
| Mobility | -22.7 | 0.34 | -28.1 | 0.49 | -6.2 | 0.10 |
| ADL | -35.9 | 0.43 | -24.9 | 0.38 | -30.6 | 0.47 |
| Emotional well-being | -22.9 | 0.27 | -8.3 | 0.10 | -15.6 | 0.18 |
| Social support | 3.4 | 0.03 | -12.2 | 0.13 | -47.2 | 0.45 |
| Cognition | -25.1 | 0.37 | -23.0 | 0.31 | -29.6 | 0.37 |
| Communication | -9.1 | 0.10 | -16.4 | 0.21 | -22.0 | 0.23 |
| Bodily discomfort | -24.3 | 0.32 | -22.0 | 0.33 | -37.2 | 0.66 |
| Stigma | -34.2 | 0.31 | -19.3 | 0.20 | -35.9 | 0.41 |
| | Levodopa challenge test response | | | | | |
| | 'low' (< 33%) | | 'partial' (33 – 50%) | | 'full' (> 50%) | |
| | Relative change [%] | Effect size | Relative change [%] | Effect size | Relative change [%] | Effect size |
| Mobility | -6.2 | 0.10 | -25.3 | 0.39 | -17.8 | 0.29 |
| ADL | -30.6 | 0.47 | -40.3 | 0.58 | -28.4 | 0.37 |

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|-----------------------------|-------|------|-------|------|-------|------|
| Emotional well-being | -15.6 | 0.18 | -9.7 | 0.12 | -23.5 | 0.26 |
| Social support | -47.2 | 0.45 | -13.9 | 0.15 | -7.7 | 0.06 |
| Cognition | -29.6 | 0.37 | -23.2 | 0.36 | -34.9 | 0.45 |
| Communication | -22.0 | 0.23 | -25.9 | 0.36 | -11.7 | 0.12 |
| Bodily discomfort | -37.2 | 0.66 | -18.4 | 0.25 | -32.8 | 0.53 |
| Stigma | -35.9 | 0.41 | -17.1 | 0.15 | -29.1 | 0.31 |

Abbreviations: ADL = activities of daily living

Legend: We calculate relative change from baseline to follow-up [$(\text{mean Test}_{\text{baseline}} - \text{mean Test}_{\text{follow-up}}) / \text{mean Test}_{\text{baseline}} \times 100$] and quantified effect size with Cohen's *d*.

Supplementary Table 3: Changes of clinical parameters at 6-month follow-up in non-motor, motor progression, and levodopa response strata

| | Non-motor Symptom Scale | | | | | | | | | | | | |
|----------------------------|------------------------------|-------|-------|----------------|-----------------------|-------|-------|----------------|-------------------------|-------|-------|----------------|----------------|
| | 'mild to moderate' (≤ 40) | | | | 'severe' (41 – 70) | | | | 'very severe' (≥ 71) | | | | p ^b |
| | n | mean | SD | p ^a | n | mean | SD | p ^a | n | mean | SD | p ^a | |
| PDQ-8 Summary Index | 52 | 7.9 | 12.5 | <0.001*** | 49 | 2.7 | 16.7 | 0.173 | 60 | 13.0 | 16.3 | <0.001*** | 0.003** |
| NMSS total | 53 | 3.0 | 17.1 | 0.063 | 48 | 12.4 | 24.4 | 0.001** | 60 | 44.3 | 39.4 | <0.001*** | <0.001*** |
| Hoehn & Yahr | 52 | 0.3 | 0.8 | 0.030* | 45 | 0.2 | 0.8 | 0.087 | 59 | 0.3 | 0.9 | 0.012* | 0.841 |
| UPDRS-III | 42 | -17.4 | 10.6 | <0.001*** | 37 | -19.4 | 8.8 | 0.054 | 35 | -18.5 | 8.8 | <0.001*** | 0.26 |
| SCOPA-M ADL | 49 | 1.7 | 2.9 | <0.001*** | 47 | 1.6 | 3.1 | 0.001** | 57 | 2.3 | 3.7 | <0.001*** | 0.247 |
| Motor complications | 49 | 1.8 | 3.0 | <0.001*** | 47 | 2.4 | 2.5 | <0.001*** | 56 | 2.9 | 2.6 | <0.001*** | 0.032* |
| LEDD | 51 | 515.4 | 451.3 | <0.001*** | 49 | 569.4 | 525.3 | <0.001*** | 60 | 521.7 | 598.8 | <0.001*** | 0.727 |

| | Hoehn and Yahr Scale | | | | | | | | | | | | |
|----------------------------|------------------------------|-------|-------|----------------|-------------------|-------|-------|----------------|-------------------|-------|-------|----------------|----------------|
| | 'minimal to mild' (≤ 2.5) | | | | 'moderate' (3) | | | | 'severe' (≥ 4) | | | | p ^b |
| | n | mean | SD | p ^a | n | mean | SD | p ^a | n | mean | SD | p ^a | |
| PDQ-8 Summary Index | 93 | 7.9 | 13.3 | <0.001*** | 47 | 7.6 | 19.9 | 0.010* | 18 | 10.9 | 16.3 | 0.006** | 0.961 |
| NMSS total | 92 | 19.6 | 35.6 | <0.001*** | 47 | 24.8 | 28.6 | <0.001*** | 19 | 21.7 | 43.6 | 0.068 | 0.377 |
| Hoehn & Yahr | 91 | -0.1 | 0.7 | <0.001*** | 46 | 0.6 | 0.7 | <0.001*** | 19 | 1.3 | 0.8 | 0.003** | <0.001*** |
| UPDRS-III | 77 | -17.2 | 8.9 | <0.001*** | 28 | -20.7 | 9.7 | <0.001*** | 6 | -20.0 | 11.9 | <0.001*** | 0.157 |
| SCOPA-M ADL | 88 | 2.0 | 2.8 | <0.001*** | 44 | 1.1 | 3.9 | <0.001*** | 18 | 3.2 | 3.2 | 0.001** | 0.083 |
| Motor complications | 87 | 2.3 | 2.9 | <0.001*** | 44 | 2.3 | 2.6 | <0.001*** | 18 | 3.0 | 2.4 | 0.012* | 0.466 |
| LEDD | 92 | 605.8 | 542.3 | 0.151 | 47 | 436.8 | 414.1 | <0.001*** | 18 | 473.2 | 689.3 | <0.001*** | 0.251 |

| | Levodopa challenge test response | | | | | | | | | | | | |
|----------------------------|----------------------------------|-------|-------|----------------|-------------------------|-------|-------|----------------|-------------------|-------|-------|----------------|----------------|
| | 'low' (< 33%) | | | | 'partial' (33 – 50%) | | | | 'full' (> 50%) | | | | p ^b |
| | n | mean | SD | p ^a | n | mean | SD | p ^a | n | mean | SD | p ^a | |
| PDQ-8 Summary Index | 42 | 8.2 | 16.0 | 0.007** | 51 | 8.0 | 16.7 | 0.001** | 66 | 8.9 | 15.2 | <0.001*** | 0.993 |
| NMSS total | 42 | 18.4 | 29.0 | 0.001** | 52 | 23.9 | 42.6 | <0.001*** | 64 | 21.6 | 30.7 | <0.001*** | 0.841 |
| Hoehn & Yahr | 41 | 0.2 | 0.6 | 0.122 | 50 | 0.2 | 0.8 | 0.057 | 62 | 0.4 | 1.0 | 0.004** | 0.294 |
| UPDRS-III | 36 | -19.2 | 9.4 | <0.001*** | 45 | -19.0 | 9.0 | <0.001*** | 30 | -17.0 | 10.5 | <0.001*** | 0.468 |
| SCOPA-M ADL | 40 | 2.3 | 3.2 | <0.001*** | 51 | 1.6 | 3.2 | 0.001** | 60 | 1.9 | 3.4 | <0.001*** | 0.564 |
| Motor complications | 39 | 2.8 | 3.0 | <0.001*** | 51 | 1.9 | 2.8 | <0.001*** | 60 | 2.6 | 2.5 | <0.001*** | 0.346 |
| LEDD | 43 | 529.1 | 506.7 | <0.001*** | 51 | 542.5 | 490.3 | <0.001*** | 64 | 525.1 | 585.2 | <0.001*** | 0.993 |

Abbreviations: ADL = activities of daily living, SD = standard deviation, LEDD = levodopa-equivalent daily dose, NMSS = Non-motor Symptom Scale, PDQ-8 =

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Parkinson's Disease Questionnaire-8, **SCOPA** = Scales for Outcomes in Parkinson's Disease, **UPDRS-III** = Unified Parkinson's Disease Rating Scale-motor examination.

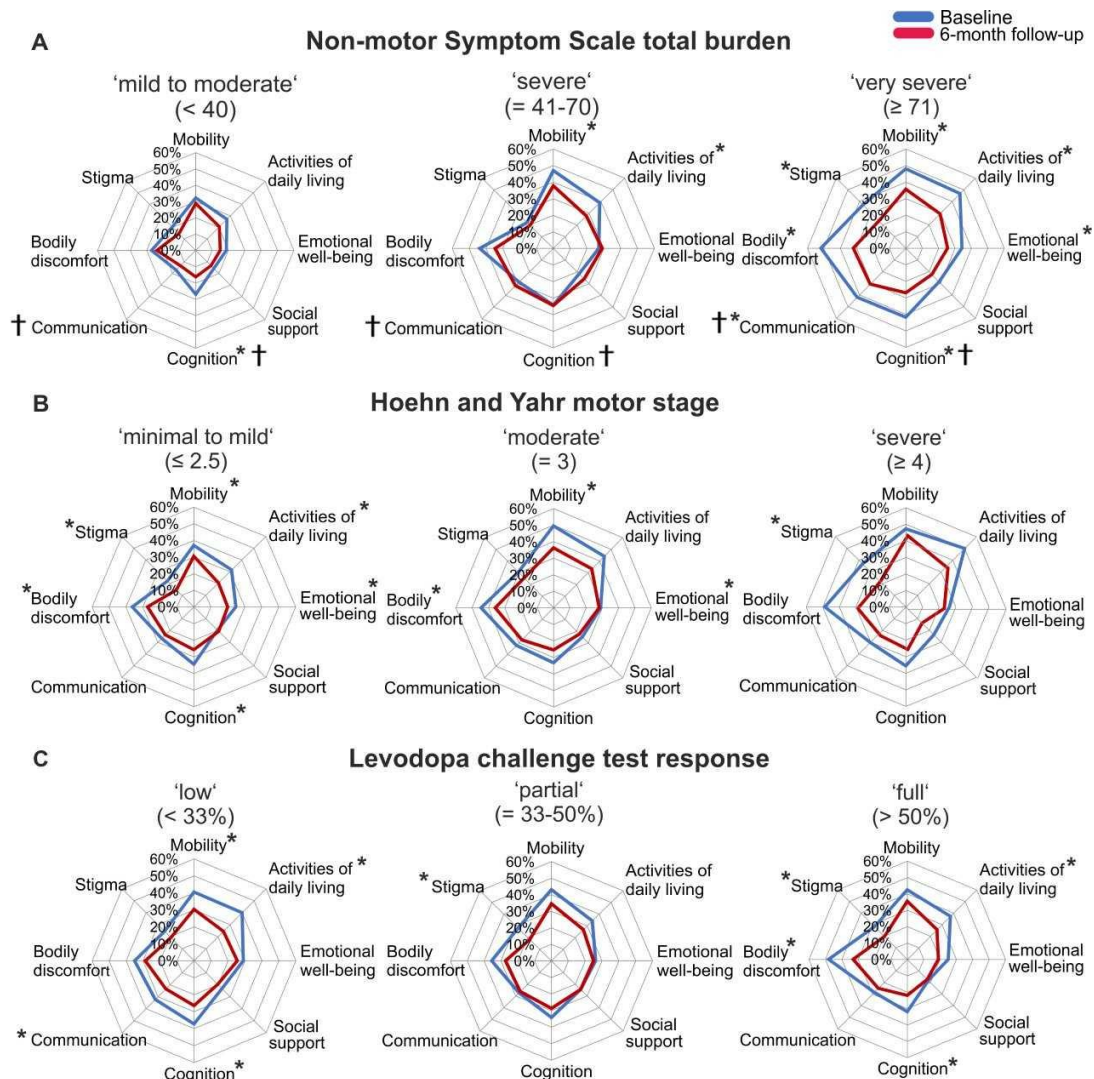
^a Wilcoxon signed-rank tests were used for within-group analyses of change scores between baseline and 6-month follow-up. Multiple comparisons (three strata and seven scales) were corrected with the Benjamini-Hochberg method.

^b Kruskal-Wallis tests were performed for independent samples for between-group analyses of change scores between baseline and 6-month follow-up.

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

Bold font highlights significant results.

Supplementary Figure 1: Domains of quality of life at baseline and 6-month follow-up stratified by Non-motor Symptom Scale total burden, Hoehn and Yahr motor stage, and levodopa challenge test response



Legend: Radar charts illustrate PDQ-8 domains at baseline (blue) and 6-month follow-up (red) stratified by (A) Non-motor Symptom Scale total burden, (B) Hoehn and Yahr motor stage, and (C) levodopa challenge test response. Domain scores are illustrated as the percentage of maximum scores and more extensive areas represent more severe impairment.

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* significant within-group differences of PDQ-8 domain outcomes from baseline to follow-up ($p < 0.05$)

† significant between-group outcome differences between strata ($p < 0.05$)