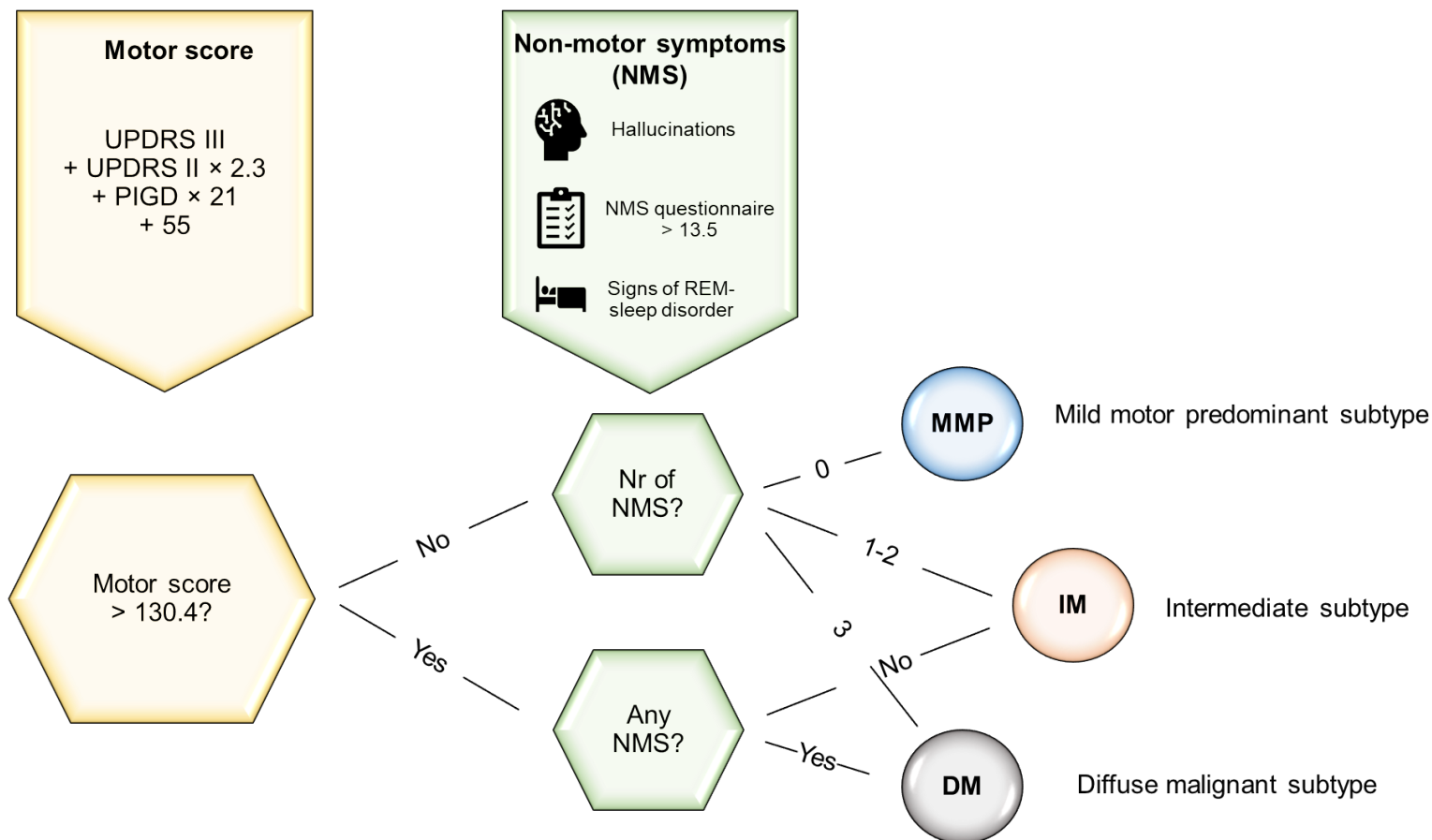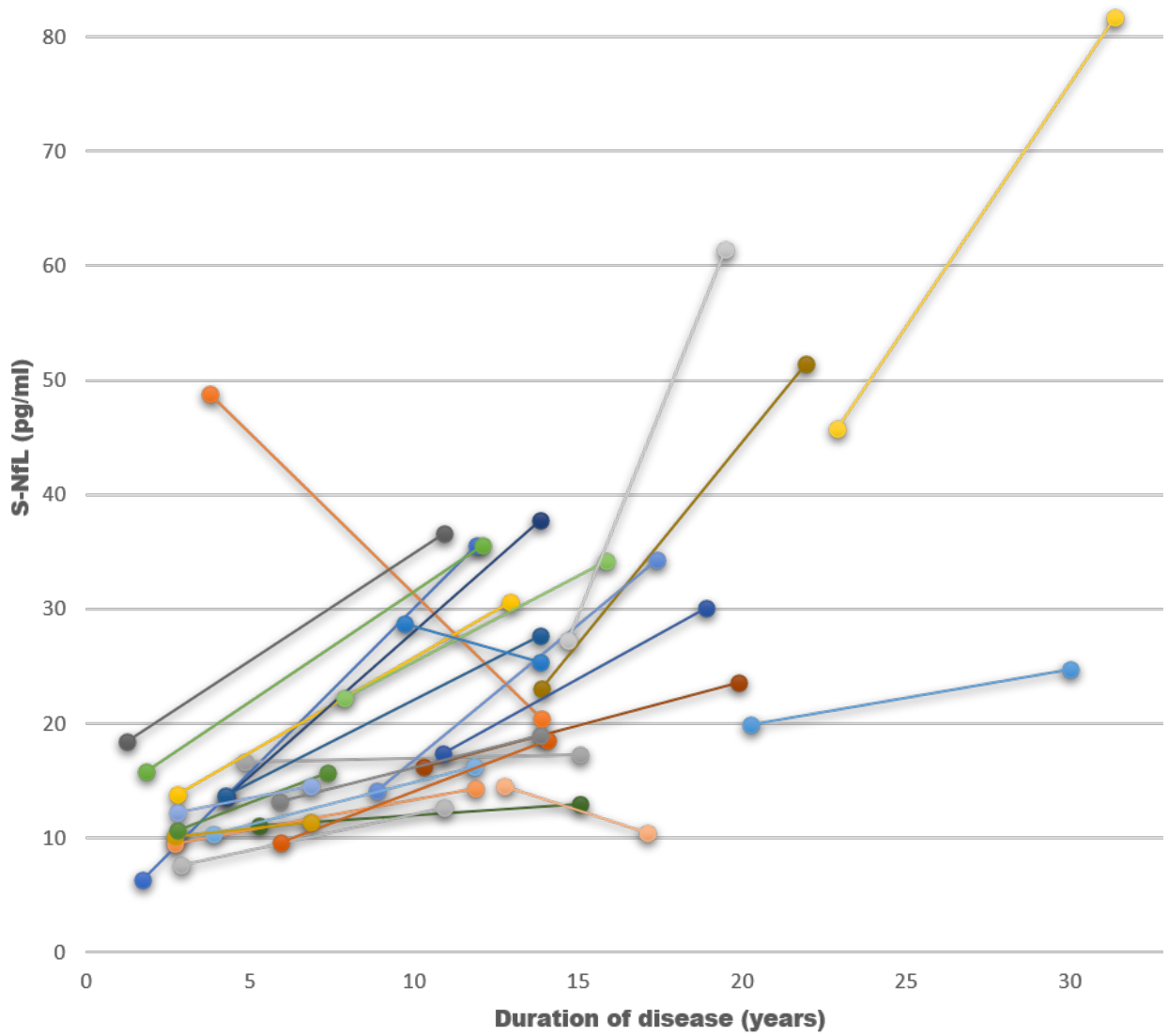# Supplementary Material

Serum Neurofilament Light Chain as a Marker of Progression in Parkinson's Disease: Long-Term Observation and Implications of Clinical Subtypes

Supplementary Figure 1. SCS algorithm

SCS classification algorithm. Modified from Ygland Rödström E, Puschmann A (2021) Clinical classification systems and long-term outcome in mid- and late-stage Parkinson's disease. *NPJ Parkinsons Dis* **7**, 66. NMS, non-motor symptoms; SCS, Simplified Clinical Subtype; UPDRS, Unified Parkinson's Disease Rating Scale

Supplementary Figure 2. Parallel coordinates plot of individual S-NfL levels at baseline and re-examination

Supplementary Table 1. Proportionality of the hazards

Walker unadjusted models

NfL-model	p	NfL + SCS model	p	NfL + PIGD score model	p
Ln(NfL)	0.680	Ln(NfL)	0.700	Ln(NfL)	0.750
		SCS	0.200	PIGDscore	0.180
		Global	0.370	Global	0.370

Walker adjusted models

NfL-model	p	NfL + SCS model	p	NfL + PIGD score model	p
Ln(NfL)	0.490	Ln(NfL)	0.483	Ln(NfL)	0.45
AaO	0.300	AaO	0.261	AaO	0.33
Duration	0.790	Sex	0.971	Sex	0.94
Sex	0.990	Duration	0.722	Duration	0.70
Global	0.620	SCS	0.097	PIGDscore	0.20
		Global	0.388	Global	0.50

Nursing-home unadjusted models

NfL-model	p	NfL + SCS model	p	NfL + PIGD score model	p
Ln(NfL)	0.095	Ln(NfL)	0.240	Ln(NfL)	0.21
		SCS	0.820	PIGDscore	0.66
		Global	0.490	Global	0.41

Nursing-home adjusted models

NfL-model	p	NfL + SCS model	p	NfL + PIGD score model	p
Ln(NfL)	0.490	Ln(NfL)	0.635	Ln(NfL)	0.62
AaO	0.290	AaO	0.676	AaO	0.51
Duration	0.580	Sex	0.426	Sex	0.55
Sex	0.320	Duration	0.952	Duration	0.82
Global	0.730	SCS	0.052	PIGDscore	0.65
		Global	0.402	Global	0.96

HY5 unadjusted models

NfL-model	p	NfL + SCS model	p	NfL + PIGD score model	p
Ln(NfL)	0.170	Ln(NfL)	0.24	Ln(NfL)	0.34
		SCS	0.820	PIGDscore	0.78
		Global	0.490	Global	0.56

HY5 adjusted models

NfL-model	p	NfL + SCS model	p	NfL + PIGD score model	p
Ln(NfL)	0.351	Ln(NfL)	0.44	Ln(NfL)	0.40
AaO	0.611	AaO	0.88	AaO	0.87

Duration	0.198	Sex	0.18	Sex	0.18
Sex	0.084	Duration	0.35	Duration	0.45
Global	0.068	SCS	0.99	PIGDscore	0.80
		Global	0.34	Global	0.30

Dementia unadjusted models

NfL-model	p	NfL + SCS model	p	NfL + PIGD score model	p
Ln(NfL)	0.370	Ln(NfL)	0.600	Ln(NfL)	0.54
		SCS	**0.014**	PIGDscore	0.72
		Global	**0.039**	Global	0.8

Dementia adjusted models

NfL-model	p	NfL + SCS model	p	NfL + PIGD score model	p
Ln(NfL)	0.430	Ln(NfL)	0.536	Ln(NfL)	0.54
AaO	0.930	AaO	0.621	AaO	0.67
Duration	0.830	Sex	0.293	Sex	0.28
Sex	0.210	Duration	0.761	Duration	0.92
Global	0.640	SCS	**0.015**	PIGDscore	0.64
		Global	0.123	Global	0.80

Death unadjusted models

NfL-model	p	NfL + SCS model	p	NfL + PIGD score model	p
Ln(NfL)	0.790	Ln(NfL)	0.790	Ln(NfL)	0.95
		SCS	0.450	PIGDscore	0.5
		Global	0.670	Global	0.78

Death adjusted models

NfL-model	p	NfL + SCS model	p	NfL + PIGD score model	p
Ln(NfL)	0.370	Ln(NfL)	0.27	Ln(NfL)	0.41
AaO	0.250	AaO	0.42	AaO	0.37
Duration	0.900	Sex	0.15	Sex	0.19
Sex	0.130	Duration	0.85	Duration	0.94
Global	0.460	SCS	0.37	PIGDscore	0.30
		Global	0.34	Global	0.51

Results from test of proportional hazards. p-values < 0.05 indicate non-proportional hazards. Results of unadjusted analyses are found in Supplementary Table 2. Results of adjusted analyses are found in Table 3 and Supplementary Table 4. PIGD, postural instability and gait disorder; SCS, simplified clinical subtype; S-NfL, serum neurofilament light chain levels (Ln-transformed)

Supplementary Table 2. Cox regression results for all covariates and unadjusted analyses.
Complete results from Cox regression analyses summarized in Table 3 in the article. HY5,
Hoehn and Yahr stage 5; UPDRS, Unified Parkinson Disease Rating Scale; PIGD, Postural
instability and gait disorder; SCS, simplified clinical subtype; S-NfL, Serum neurofilament light
chain levels (Ln-transformed); S-NfL + SCS, model including both S-NfL (Ln-transformed) and
SCS; S-NfL + PIGD, model including both S-NfL (Ln-transformed) and PIGD score

S-NfL

Walking aid unadjusted

	B	SE	Wald	df	p	HR	95.0% CI for HR	
							Lower	Upper
Baseline_NfL_Ln	1.156	0.330	12.254	1	0.000	3.177	1.663	6.069

Walking aid adjusted

	B	SE	Wald	df	p	HR	95.0% CI for HR	
							Lower	Upper
Baseline_NfL_Ln	1.247	0.456	7.493	1	0.006	3.481	1.425	8.502
Male	-0.126	0.357	0.125	1	0.723	0.881	0.438	1.774
Age@Onset	0.091	0.023	15.112	1	0.000	1.095	1.046	1.146
Duration@Baseline	0.181	0.044	16.858	1	0.000	1.198	1.099	1.306

Nursing home unadjusted

	B	SE	Wald	df	p	HR	95.0% CI for HR	
							Lower	Upper
Baseline_NfL_Ln	1.657	0.365	20.590	1	0.000	5.244	2.563	10.727

Nursing home adjusted

	B	SE	Wald	df	p	HR	95.0% CI for HR	
							Lower	Upper
Baseline_NfL_Ln	1.626	0.457	12.635	1	0.000	5.082	2.074	12.457
Male	-0.383	0.399	0.923	1	0.337	0.682	0.312	1.490
Age@Onset	0.103	0.028	13.761	1	0.000	1.108	1.050	1.170
Duration@Baseline	0.106	0.047	5.066	1	0.024	1.111	1.014	1.219

HY5 unadjusted

	B	SE	Wald	df	p	HR	95.0% CI for HR	
							Lower	Upper
Baseline_NfL_Ln	2.052	0.396	26.787	1	0.000	7.781	3.578	16.923

HY5 unadjusted

	B	SE	Wald	df	p	HR	95.0% CI for HR	
							Lower	Upper
Baseline_NfL_Ln	1.818	0.541	11.274	1	0.001	6.158	2.131	17.792
Male	-0.509	0.439	1.345	1	0.246	0.601	0.255	1.420
Age@Onset	0.117	0.032	13.173	1	0.000	1.124	1.055	1.197
Duration@Baseline	0.132	0.055	5.773	1	0.016	1.141	1.025	1.271

Dementia unadjusted

	B	SE	Wald	df	p	HR	95.0% CI for HR	
							Lower	Upper
Baseline_NfL_Ln	1.287	0.463	7.721	1	0.005	3.623	1.461	8.982

Dementia adjusted

	B	SE	Wald	df	p	HR	95.0% CI for HR	
							Lower	Upper
Baseline_NfL_Ln	1.017	0.628	2.627	1	0.105	2.766	0.808	9.465
Male	-1.589	0.645	6.067	1	0.014	0.204	0.058	0.723
Age@Onset	0.119	0.037	10.308	1	0.001	1.126	1.047	1.211
Duration@Baseline	0.170	0.072	5.538	1	0.019	1.186	1.029	1.366

Death unadjusted

	B	SE	Wald	df	p	HR	95.0% CI for HR	
							Lower	Upper
Baseline_NfL_Ln	1.605	0.306	27.427	1	0.000	4.978	2.730	9.078

Death adjusted

	B	SE	Wald	df	p	HR	95.0% CI for HR	
							Lower	Upper
Baseline_NfL_Ln	1.405	0.440	10.170	1	0.001	4.074	1.718	9.661
Male	-1.538	0.450	11.671	1	0.001	0.215	0.089	0.519
Age@Onset	0.135	0.028	23.777	1	0.000	1.145	1.084	1.209
Duration@Baseline	0.129	0.047	7.643	1	0.006	1.138	1.038	1.247

S-NfL + SCS
Walking aid unadjusted

	B	SE	Wald	df	p	HR	95.0% CI for HR	
							Lower	Upper
Baseline_NfL_Ln	1.281	0.353	13.165	1	0.000	3.599	1.802	7.187

| | | | | | | | 95.0% CI for HR | |
| SCS-group at baseline | 0.462 | 0.241 | 3.674 | 1 | 0.055 | 1.587 | 0.990 | 2.545 |

Walking aid adjusted

	B	SE	Wald	df	p	HR	95.0% CI for HR Lower	Upper
Baseline_NfL_Ln	1.409	0.485	8.448	1	0.004	4.093	1.583	10.588
Male	-0.184	0.364	0.255	1	0.613	0.832	0.408	1.697
Age@Onset	0.093	0.024	15.153	1	0.000	1.098	1.047	1.151
Duration@Baseline	0.184	0.044	17.159	1	0.000	1.202	1.102	1.312
SCS-group at baseline	0.487	0.250	3.804	1	0.051	1.628	0.998	2.656

Nursing home unadjusted

	B	SE	Wald	df	p	HR	95.0% CI for HR Lower	Upper
Baseline_NfL_Ln	1.477	0.390	14.370	1	0.000	4.379	2.041	9.398
SCS-group at baseline	0.730	0.245	8.865	1	0.003	2.076	1.283	3.357

Nursing home adjusted

	B	SE	Wald	df	p	HR	95.0% CI for HR Lower	Upper
Baseline_NfL_Ln	1.606	0.500	10.301	1	0.001	4.981	1.868	13.277
Male	-0.285	0.422	0.457	1	0.499	0.752	0.329	1.719
Age@Onset	0.103	0.031	11.022	1	0.001	1.109	1.043	1.178
Duration@Baseline	0.071	0.051	1.902	1	0.168	1.073	0.971	1.187
SCS-group at baseline	0.623	0.254	6.007	1	0.014	1.864	1.133	3.068

HY5 unadjusted

	B	SE	Wald	df	p	HR	95.0% CI for HR Lower	Upper
Baseline_NfL_Ln	1.639	0.443	13.714	1	0.000	5.152	2.164	12.269
SCS-group at baseline	0.973	0.276	12.458	1	0.000	2.645	1.541	4.538

HY5 adjusted

	B	SE	Wald	df	p	HR	95.0% CI for HR Lower	Upper
Baseline_NfL_Ln	1.779	0.612	8.450	1	0.004	5.925	1.785	19.661
Male	-0.278	0.461	0.362	1	0.547	0.758	0.307	1.871
Age@Onset	0.123	0.039	9.931	1	0.002	1.131	1.048	1.222
Duration@Baseline	0.072	0.063	1.298	1	0.255	1.074	0.950	1.215
SCS-group at baseline	0.923	0.285	10.474	1	0.001	2.518	1.439	4.405

Dementia unadjusted

	B	SE	Wald	df	p	HR	95.0% CI for HR	
							Lower	Upper
Baseline_NfL_Ln	1.230	0.518	5.645	1	0.018	3.420	1.240	9.433
SCS-group at baseline	0.798	0.317	6.357	1	0.012	2.222	1.195	4.132

Dementia adjusted

	B	SE	Wald	df	p	HR	95.0% CI for HR	
							Lower	Upper
Baseline_NfL_Ln	0.698	0.705	0.980	1	0.322	2.010	0.504	8.006
Male	-2.000	0.779	6.600	1	0.010	0.135	0.029	0.622
Age@Onset	0.114	0.040	7.960	1	0.005	1.121	1.035	1.213
Duration@Baseline	0.156	0.075	4.264	1	0.039	1.168	1.008	1.354
SCS-group at baseline	0.749	0.322	5.402	1	0.020	2.115	1.125	3.979

Death unadjusted

	B	SE	Wald	df	p	HR	95.0% CI for HR	
							Lower	Upper
Baseline_NfL_Ln	1.391	0.360	14.938	1	0.000	4.020	1.985	8.141
SCS-group at baseline	0.527	0.227	5.418	1	0.020	1.694	1.087	2.641

Death adjusted

	B	SE	Wald	df	p	HR	95.0% CI for HR	
							Lower	Upper
Baseline_NfL_Ln	1.134	0.502	5.106	1	0.024	3.108	1.162	8.310
Male	-1.527	0.485	9.900	1	0.002	0.217	0.084	0.562
Age@Onset	0.132	0.029	20.608	1	0.000	1.141	1.078	1.207
Duration@Baseline	0.108	0.053	4.084	1	0.043	1.114	1.003	1.237
SCS-group at baseline	0.390	0.243	2.565	1	0.109	1.477	0.916	2.379

S-NfL + PIGD

Walking aid unadjusted

	B	SE	Wald	df	p	HR	95.0% CI for HR	
							Lower	Upper
Baseline_NfL_Ln	1.201	0.343	12.233	1	0.000	3.324	1.696	6.515
Baseline_PIGD_total	0.138	0.091	2.302	1	0.129	1.148	0.961	1.372

Walking aid adjusted

	B	SE	Wald	df	p	HR	95.0% CI for HR	
							Lower	Upper
Baseline_NfL_Ln	1.216	0.462	6.930	1	0.008	3.375	1.364	8.350

	B	SE	Wald	df	p	HR	Lower	Upper
Male	-0.077	0.361	0.046	1	0.831	0.926	0.456	1.880
Age@Onset	0.092	0.024	14.705	1	0.000	1.096	1.046	1.149
Duration@Baseline	0.175	0.044	15.641	1	0.000	1.191	1.092	1.299
Baseline_PIGD_total	0.096	0.101	0.899	1	0.343	1.100	0.903	1.341

Nursing home unadjusted

							95.0% CI for HR	
	B	SE	Wald	df	p	HR	Lower	Upper
Baseline_NfL_Ln	1.456	0.392	13.780	1	0.000	4.291	1.989	9.257
Baseline_PIGD_total	0.139	0.061	5.194	1	0.023	1.149	1.020	1.294

Nursing home adjusted

							95.0% CI for HR	
	B	SE	Wald	df	p	HR	Lower	Upper
Baseline_NfL_Ln	1.543	0.490	9.923	1	0.002	4.679	1.791	12.222
Male	-0.196	0.419	0.217	1	0.641	0.822	0.361	1.871
Age@Onset	0.105	0.031	11.828	1	0.001	1.111	1.046	1.179
Duration@Baseline	0.081	0.051	2.547	1	0.111	1.085	0.982	1.198
Baseline_PIGD_total	0.109	0.071	2.362	1	0.124	1.115	0.970	1.282

HY5 unadjusted

							95.0% CI for HR	
	B	SE	Wald	df	p	HR	Lower	Upper
Baseline_NfL_Ln	1.669	0.436	14.629	1	0.000	5.309	2.257	12.488
Baseline_PIGD_total	0.226	0.065	11.931	1	0.001	1.254	1.103	1.425

HY5 adjusted

							95.0% CI for HR	
	B	SE	Wald	df	p	HR	Lower	Upper
Baseline_NfL_Ln	1.552	0.591	6.901	1	0.009	4.719	1.483	15.019
Male	-0.164	0.458	0.129	1	0.720	0.848	0.346	2.083
Age@Onset	0.122	0.038	10.349	1	0.001	1.130	1.049	1.218
Duration@Baseline	0.091	0.061	2.249	1	0.134	1.096	0.972	1.234
Baseline_PIGD_total	0.211	0.077	7.624	1	0.006	1.236	1.063	1.436

Dementia unadjusted

							95.0% CI for HR	
	B	SE	Wald	df	p	HR	Lower	Upper
Baseline_NfL_Ln	0.986	0.515	3.666	1	0.056	2.679	0.977	7.347
Baseline_PIGD_total	0.120	0.064	3.541	1	0.060	1.128	0.995	1.278

Dementia adjusted

	B	SE	Wald	df	p	HR	95.0% CI for HR	
							Lower	Upper
Baseline_NfL_Ln	0.536	0.748	0.514	1	0.474	1.709	0.395	7.405
Male	-1.880	0.770	5.969	1	0.015	0.153	0.034	0.690
Age@Onset	0.110	0.039	8.007	1	0.005	1.116	1.034	1.205
Duration@Baseline	0.161	0.075	4.598	1	0.032	1.175	1.014	1.362
Baseline_PIGD_total	0.069	0.071	0.950	1	0.330	1.071	0.933	1.230

Death unadjusted

	B	SE	Wald	df	p	HR	95.0% CI for HR	
							Lower	Upper
Baseline_NfL_Ln	1.475	0.362	16.634	1	0.000	4.371	2.152	8.881
Baseline_PIGD_total	0.071	0.051	1.942	1	0.163	1.074	0.971	1.187

Death adjusted

	B	SE	Wald	df	p	HR	95.0% CI for HR	
							Lower	Upper
Baseline_NfL_Ln	1.200	0.519	5.344	1	0.021	3.320	1.200	9.182
Male	-1.492	0.483	9.535	1	0.002	0.225	0.087	0.580
Age@Onset	0.138	0.029	22.732	1	0.000	1.148	1.085	1.215
Duration@Baseline	0.128	0.051	6.169	1	0.013	1.136	1.027	1.257
Baseline_PIGD_total	0.032	0.059	0.294	1	0.588	1.032	0.920	1.159

Supplementary Table 3. Sensitivity analysis

a) General linear regression at baseline and re-examination, corresponding to table 2 in the paper

	Sensitivity analysis Baseline S-NfL		*Re-examination S-NfL*			*Re-examination change in S-NfL*	
	B (95%CI)	p	Slope (S-NfL)	p		Slope (change in S-NfL)	p
Age (unadjusted)	9.10 (5.30 – 12.90)	**0.000**	6.50 (0.00–13.00)	**0.050**	**Δ-age (unadjusted)**	0.07 (-0.02 – 0.16)	0.118
UPDRS-2	3.36 (0.36–6.36)	**0.028**	4.60 (-0.94–10.14)	0.099	**Δ-UPDRS2**	0.19 (-0.00–0.37)	0.051
UPDRS-3	2.75 (-3.22–8.72)	0.362	7.16 (-2.45–16.77)	0.138	**Δ-UPDRS3**	0.37 (-0.35–0.78)	0.071
UPDRS-total	5.88 (-2.64–14.40)	0.173	15.87 (-0.20–31.93)	0.053	**Δ-UPDRStotal**	0.73 (0.19–1.26)	**0.010**
PIGD-score	1.55 (-0.05–3.16)	0.058	4.31 (1.19–7.44)	**0.009**	**Δ-PIGD-score**	0.18 (0.07–0.30)	**0.003**
HY-stage	0.21 (-0.23 – 0,64)	0.347	0,96 (0,26 – 1,66)	**0.009**	**Δ-HY-stage**	0.03 (0,00 – 0,06)	**0.036**
S&E	-14.80 (-30.01–0.40)	0.056	-25.75 (-46.20– -5.29)	**0.016**	**Δ-S&E (n=14)**	-0.73 (-2.10–0.64)	0.259
ACER	n/a	n/a	-14.75 (-30.41–0.91)	0.064	**ACER**	-0.88 (-1.45– -0.31)	**0.004**

Results from general linear regression models when removing any individual with S-NfL level outside 1½ interquartile range from cohort quartiles. Baseline S-NfL-values (left column n=76), NfL values at re-examination (middle column, n=30), or NfL change between examinations (right column, n=25). All analyses but the age model were adjusted for age at onset, duration at re-examination or baseline and sex. p-values < 0.05 highlighted in bold. UPDRS, Unified Parkinson disease rating scale; PIGD, Postural instability and gait disorder; S-NfL, Serum neurofilament light chain levels (Ln-transformed) S&E, Schwab and England activity of daily living score

b) Cox regression of predefined outcomes during the observation period, corresponding to table 3 in the paper

	Walker	p	Nursing home	p	HY5	p	Dementia	p	Death	p
NfL only										
NfL HR	4.59 (1.69–12.49)	**0.003**	5.92 (2.02–17.37)	**0.001**	3.93 (1.17–13.24)	**0.027**	3.10 (0.84–11.37)	0.089	2.89 (0.92–9.11)[a]	0.070[a]
NfL + SCS										
NfL HR	5.14 (1.83–14.44)	**0.002**	5.58 (1.77–17.60)	**0.003**	3.51 (0.87–14.18)	0.078	2.15 (0.52–8.99)	0.293	2.57 (0.75–8.79)[a]	0.133[a]
SCS HR	1.58 (0.97–2.58)	0.066	1.78 (1.08–2.95)[a]	**0.025**	2.42 (1.38–4.25)	**0.002**	2.09 (1.11–3.94)[a]	**0.023**[a]	1.47 (0.91–2.38)	0.119
NfL + PIGD score										
NfL	4.34 (1.57–11.95)	**0.005**	5.00 (1.60–15.66)	**0.006**	2.50 (0.69–9.09)	0.165	1.92 (0.41–9.08)	0.412	2.46 (0.67–9.00)	0.174
PIGD score	1.08 (0.88–1.32)	0.464	1.12 (0.97–1.29)	0.131	1.27 (1.09–1.49)	**0.003**	1.06 (0.93–1.22)	0.378	1.04 (0.92–1.18)	0.555

Results from Cox regression models for predefined milestones of disease progression during the observation period when removing any individual with S-NfL level outside 1½ interquartile range from cohort quartiles. All models adjusted for age at onset, sex and disease duration plus that one of the two tested clinical classification systems were added as a covariate to the models (lower rows). For earlier assessment of SCS and PIGD-score HRs from the cohort, see reference [24] in the article. [a]Non-proportional hazard was indicated in the dementia and death models and the results should hence be considered inconclusive. HR, Hazard ratio; SCS, simplified clinical subtype; PIGD, postural instability and gait disorder score.

Supplementary Table 4. Results from all covariates in linear regressions

S-NfL at baseline

Age

Model	Unstandardized Coefficients B	Std. Error	Standardized Coefficients Beta	t	p	95.0% Confidence Interval for B Lower Bound	Upper Bound
(Constant)	47.684	4.969		9.597	0.000	37.793	57.576
Baseline_NfL_Ln	6.902	1.646	0.429	4.194	0.000	3.626	10.178

a. Dependent Variable: Baseline_age

UPDRS-2

Model	Unstandardized Coefficients B	Std. Error	Standardized Coefficients Beta	t	p	95.0% Confidence Interval for B Lower Bound	Upper Bound
(Constant)	-17.864	4.327		-4.128	0.000	-26.486	-9.242
Baseline_NfL_Ln	4.435	1.119	0.414	3.962	0.000	2.205	6.665
Age@Onset	0.176	0.065	0.272	2.698	0.009	0.046	0.307
Durationation@Baseline	0.339	0.124	0.301	2.743	0.008	0.093	0.586
Male	0.603	1.077	0.050	0.559	0.578	-1.544	2.749

a. Dependent Variable: Baseline_UPDRS2

UPDRS-3

Model	Unstandardized Coefficients B	Std. Error	Standardized Coefficients Beta	t	p	95.0% Confidence Interval for B Lower Bound	Upper Bound
(Constant)	-19.997	8.637		-2.315	0.023	-37.203	-2.792
Baseline_NfL_Ln	3.246	2.264	0.166	1.434	0.156	-1.263	7.756

Model	B	Std. Error	Beta	t	p	Lower Bound	Upper Bound
Age@Onset	0.408	0.131	0.348	3.108	0.003	0.146	0.670
Durationation@Baseline	0.802	0.252	0.385	3.185	0.002	0.301	1.304
Male	2.261	2.167	0.102	1.043	0.300	-2.056	6.579

a. Dependent Variable: Baseline_UPDRS3

UPDRS-total

Model	Unstandardized Coefficients		Standardized Coefficients			95.0% Confidence Interval for B	
	B	Std. Error	Beta	t	p	Lower Bound	Upper Bound
(Constant)	-26.347	12.559		-2.098	0.039	-51.377	-1.318
Baseline_NfL_Ln	5.442	3.235	0.190	1.682	0.097	-1.006	11.890
Age@Onset	0.545	0.189	0.318	2.885	0.005	0.168	0.921
Durationation@Baseline	1.260	0.367	0.405	3.437	0.001	0.529	1.991
Male	4.770	3.142	0.148	1.518	0.133	-1.493	11.032

a. Dependent Variable: Baseline_UPDRStotal

PIGD score

Model	Unstandardized Coefficients		Standardized Coefficients			95.0% Confidence Interval for B	
	B	Std. Error	Beta	t	p	Lower Bound	Upper Bound
(Constant)	-5.491	2.382		-2.305	0.024	-10.238	-0.743
Baseline_NfL_Ln	1.294	0.649	0.242	1.993	0.050	0.000	2.589
Age@Onset	0.064	0.035	0.208	1.828	0.072	-0.006	0.134
Durationation@Baseline	0.176	0.067	0.333	2.619	0.011	0.042	0.311
Male	0.429	0.591	0.075	0.727	0.470	-0.748	1.607

a. Dependent Variable: Baseline_PIGD-score

S&E

Model	Unstandardized Coefficients B	Std. Error	Standardized Coefficients Beta	t	p	95.0% Confidence Interval for B Lower Bound	Upper Bound
(Constant)	193.876	18.237		10.631	0.000	157.018	230.734
Baseline_NfL_Ln	-18.929	5.418	-0.440	-3.494	0.001	-29.879	-7.980
Age@Onset	-0.893	0.279	-0.351	-3.206	0.003	-1.456	-0.330
Durationation@Baseline	-1.675	0.517	-0.406	-3.241	0.002	-2.719	-0.630
Male	9.692	4.672	0.214	2.075	0.044	0.250	19.135

a. Dependent Variable: Baseline_S&E

HY-stage

Model	Unstandardized Coefficients B	Std. Error	Standardized Coefficients Beta	t	Sig.	95.0% Confidence Interval for B Lower Bound	Upper Bound
(Constant)	-1.490	0.659		-2.262	0.027	-2.805	-0.176
Baseline_NfL_Ln	0.538	0.176	0.309	3.060	0.003	0.187	0.889
Age@Onset	0.027	0.010	0.268	2.741	0.008	0.007	0.047
Durationation@Baseline	0.093	0.020	0.492	4.722	0.000	0.054	0.132
Male	0.140	0.169	0.071	0.825	0.412	-0.198	0.477

a. Dependent Variable: BL_HY_ny

S-NfL at reexamination

Age

Model	Unstandardized Coefficients B	Std. Error	Standardized Coefficients Beta	t	p	95.0% Confidence Interval for B Lower Bound	Upper Bound
(Constant)	48.356	7.937		6.093	0.000	32.147	64.565
Reexamination_NfL_Ln	6.780	2.413	0.456	2.809	0.009	1.851	11.708

a. Dependent Variable: reexamination age

UPDRS-2

Model	Unstandardized Coefficients		Standardized Coefficients			95.0% Confidence Interval for B	
	B	Std. Error	Beta	t	p	Lower Bound	Upper Bound
(Constant)	-12.543	10.666		-1.176	0.250	-34.427	9.341
Reexamination_NfL_Ln	5.877	2.376	0.452	2.473	0.020	1.001	10.752
Age@Onset	0.062	0.158	0.072	0.392	0.698	-0.262	0.386
Duration@Baseline	0.319	0.265	0.235	1.204	0.239	-0.225	0.863
Male	4.674	2.344	0.326	1.994	0.056	-0.135	9.484

a. Dependent Variable: Reexamined UPDRS2

UPDRS-3

Model	Unstandardized Coefficients		Standardized Coefficients			95.0% Confidence Interval for B	
	B	Std. Error	Beta	t	p	Lower Bound	Upper Bound
(Constant)	-27.383	19.406		-1.411	0.170	-67.201	12.434
Reexamination_NfL_Ln	7.350	4.323	0.308	1.700	0.101	-1.521	16.220
Age@Onset	0.357	0.287	0.225	1.242	0.225	-0.233	0.947
Duration@Baseline	1.038	0.482	0.416	2.152	0.041	0.048	2.027
Male	8.338	4.265	0.316	1.955	0.061	-0.413	17.089

a. Dependent Variable: Reexamined UPDRS3

UPDRS-total

Model	Unstandardized Coefficients		Standardized Coefficients			95.0% Confidence Interval for B	
	B	Std. Error	Beta	t	p	Lower Bound	Upper Bound
(Constant)	-39.692	31.853		-1.246	0.223	-105.049	25.666
Reexamination_NfL_Ln	16.820	7.096	0.420	2.370	0.025	2.259	31.380
Age@Onset	0.357	0.472	0.134	0.757	0.456	-0.611	1.325

Duration@Baseline	1.433	0.791	0.342	1.811	0.081	-0.191	3.057
Male	12.782	7.000	0.289	1.826	0.079	-1.582	27.145

a. Dependent Variable: Reexamined UPDRStotal

PIGD-score

	Unstandardized Coefficients		Standardized Coefficients			95.0% Confidence Interval for B	
Model	B	Std. Error	Beta	t	p	Lower Bound	Upper Bound
(Constant)	-18.089	5.988		-3.021	0.005	-30.375	-5.802
Reexamination_NfL_Ln	3.731	1.334	0.477	2.797	0.009	0.994	6.469
Age@Onset	0.144	0.089	0.276	1.620	0.117	-0.038	0.326
Duration@Baseline	0.251	0.149	0.307	1.686	0.103	-0.054	0.556
Male	2.131	1.316	0.247	1.619	0.117	-0.570	4.831

a. Dependent Variable: Reexamined PIGD-score

S&E

	Unstandardized Coefficients		Standardized Coefficients			95.0% Confidence Interval for B	
Model	B	Std. Error	Beta	t	p	Lower Bound	Upper Bound
(Constant)	189.773	39.231		4.837	0.000	109.132	270.413
Reexamination_NfL_Ln	-20.244	8.475	-0.441	-2.389	0.024	-37.664	-2.823
Age@Onset	-0.596	0.604	-0.191	-0.987	0.333	-1.836	0.645
Duration@Baseline	-1.434	0.992	-0.296	-1.445	0.161	-3.474	0.606
Male	-18.661	8.478	-0.362	-2.201	0.037	-36.089	-1.234

a. Dependent Variable: Reexamined S&E

HY-stage

Model	Unstandardized Coefficients B	Std. Error	Standardized Coefficients Beta	t	Sig.	95.0% Confidence Interval for B Lower Bound	Upper Bound
(Constant)	-1.116	1.280		-0.872	0.391	-3.748	1.515
Reexamination_NfL_Ln	0.792	0.282	0.474	2.804	0.009	0.211	1.372
Age@Onset	0.012	0.019	0.104	0.636	0.530	-0.026	0.050
Duration@Baseline	0.067	0.031	0.381	2.151	0.041	0.003	0.131
Male	0.245	0.281	0.132	0.872	0.391	-0.333	0.824

a. Dependent Variable: H&Y

ACER

Model	Unstandardized Coefficients B	Std. Error	Standardized Coefficients Beta	t	p	95.0% Confidence Interval for B Lower Bound	Upper Bound
(Constant)	163.481	30.557		5.350	0.000	100.784	226.178
Reexamination_NfL_Ln	-12.260	6.808	-0.351	-1.801	0.083	-26.228	1.708
Age@Onset	-0.527	0.453	-0.227	-1.164	0.255	-1.455	0.402
Duration@Baseline	-0.975	0.759	-0.267	-1.284	0.210	-2.532	0.583
Male	-5.518	6.715	-0.143	-0.822	0.418	-19.297	8.261

a. Dependent Variable: Reexamined ACER

S-NfL change between examinations

Age

Model	Unstandardized Coefficients B	Std. Error	Standardized Coefficients Beta	t	p	95.0% Confidence Interval for B Lower Bound	Upper Bound
(Constant)	7.816	0.540		14.485	0.000	6.704	8.927
Reexamination_change_NfL	0.023	0.032	0.140	0.708	0.486	-0.043	0.088

a. Dependent Variable: years between exams

Δ-UPDRS-2

Model	Unstandardized Coefficients		Standardized Coefficients			95.0% Confidence Interval for B	
	B	Std. Error	Beta	t	p	Lower Bound	Upper Bound
(Constant)	1.708	9.112		0.187	0.853	-17.190	20.606
Reexamination_change_NfL	0.107	0.083	0.278	1.283	0.213	-0.066	0.279
Age@Onset	0.044	0.150	0.070	0.295	0.771	-0.266	0.355
Duration@Baseline	0.273	0.225	0.299	1.215	0.237	-0.193	0.739
Male	1.786	2.030	0.174	0.879	0.389	-2.425	5.996

a. Dependent Variable: Change in UPDRS2

Δ-UPDRS-3

Model	Unstandardized Coefficients		Standardized Coefficients			95.0% Confidence Interval for B	
	B	Std. Error	Beta	t	p	Lower Bound	Upper Bound
(Constant)	-12.066	21.425		-0.563	0.579	-56.500	32.367
Reexamination_change_NfL	0.177	0.196	0.191	0.904	0.376	-0.229	0.583
Age@Onset	0.239	0.352	0.156	0.679	0.504	-0.491	0.969
Duration@Baseline	0.991	0.528	0.450	1.877	0.074	-0.104	2.086
Male	3.007	4.774	0.121	0.630	0.535	-6.894	12.908

a. Dependent Variable: Change in UPDRS3

Δ-UPDRS-total

Model	Unstandardized Coefficients		Standardized Coefficients			95.0% Confidence Interval for B	
	B	Std. Error	Beta	t	p	Lower Bound	Upper Bound
(Constant)	-3.762	33.161		-0.113	0.911	-72.534	65.010
Reexamination_change_NfL	0.288	0.303	0.208	0.953	0.351	-0.339	0.916

Model	B	Std. Error	Beta	t	p	Lower Bound	Upper Bound
Age@Onset	0.248	0.545	0.109	0.456	0.653	-0.881	1.378
Duration@Baseline	1.218	0.817	0.369	1.491	0.150	-0.477	2.914
Male	3.477	7.389	0.093	0.470	0.643	-11.848	18.801

a. Dependent Variable: Change in UPDRStotal

Δ-PIGD score

Model	Unstandardized Coefficients		Standardized Coefficients			95.0% Confidence Interval for B	
	B	Std. Error	Beta	t	p	Lower Bound	Upper Bound
(Constant)	-2.062	5.607		-0.368	0.717	-13.690	9.567
Reexamination_change_NfL	0.132	0.051	0.521	2.572	0.017	0.026	0.238
Age@Onset	0.025	0.092	0.061	0.276	0.785	-0.166	0.216
Duration@Baseline	0.068	0.138	0.113	0.492	0.627	-0.219	0.355
Male	1.048	1.249	0.155	0.839	0.410	-1.543	3.639

a. Dependent Variable: Change in PIGD-score

Δ-S&E

Model	Unstandardized Coefficients		Standardized Coefficients			95.0% Confidence Interval for B	
	B	Std. Error	Beta	t	p	Lower Bound	Upper Bound
(Constant)	30.980	59.664		0.519	0.615	-101.960	163.920
Reexamination_change_NfL	-0.118	0.551	-0.076	-0.215	0.834	-1.345	1.108
Age@Onset	-0.557	0.981	-0.236	-0.568	0.582	-2.742	1.628
Duration@Baseline	-1.171	1.746	-0.277	-0.671	0.518	-5.061	2.719
Male	-12.300	14.663	-0.263	-0.839	0.421	-44.972	20.372

a. Dependent Variable: Change in S&E

HY-stage

Model	Unstandardized Coefficients B	Unstandardized Coefficients Std. Error	Standardized Coefficients Beta	t	Sig.	95.0% Confidence Interval for B Lower Bound	95.0% Confidence Interval for B Upper Bound
(Constant)	1.233	1.301		0.948	0.356	-1.500	3.967
Reexamination_change_NfL	0.021	0.012	0.392	1.752	0.097	-0.004	0.047
Age@Onset	-0.009	0.021	-0.103	-0.418	0.681	-0.054	0.036
Duration@Baseline	-0.038	0.037	-0.260	-1.032	0.316	-0.116	0.040
Male	-0.293	0.311	-0.202	-0.942	0.359	-0.946	0.360

a. Dependent Variable: FUP_HY_Change

ACER

Model	Unstandardized Coefficients B	Unstandardized Coefficients Std. Error	Standardized Coefficients Beta	t	p	95.0% Confidence Interval for B Lower Bound	95.0% Confidence Interval for B Upper Bound
(Constant)	90.723	29.710		3.054	0.006	29.109	152.338
Reexamination_change_NfL	-0.818	0.271	-0.588	-3.016	0.006	-1.381	-0.256
Age@Onset	0.173	0.488	0.076	0.355	0.726	-0.839	1.185
Duration@Baseline	-0.162	0.732	-0.049	-0.221	0.827	-1.681	1.357
Male	-9.058	6.620	-0.243	-1.368	0.185	-22.787	4.672

a. Dependent Variable: Reexamined ACER

Complete results from linear regression analyses summarized in Table 2 in the article. UPDRS, Unified Parkinson Disease Rating Scale; PIGD, Postural instability and gait disorder; S-NfL, Serum neurofilament light chain levels (Ln-transformed); S&E, Schwab and England activity of daily living score; ACER, Addenbrookes cognitive examination revised