

Supplemental Online Content

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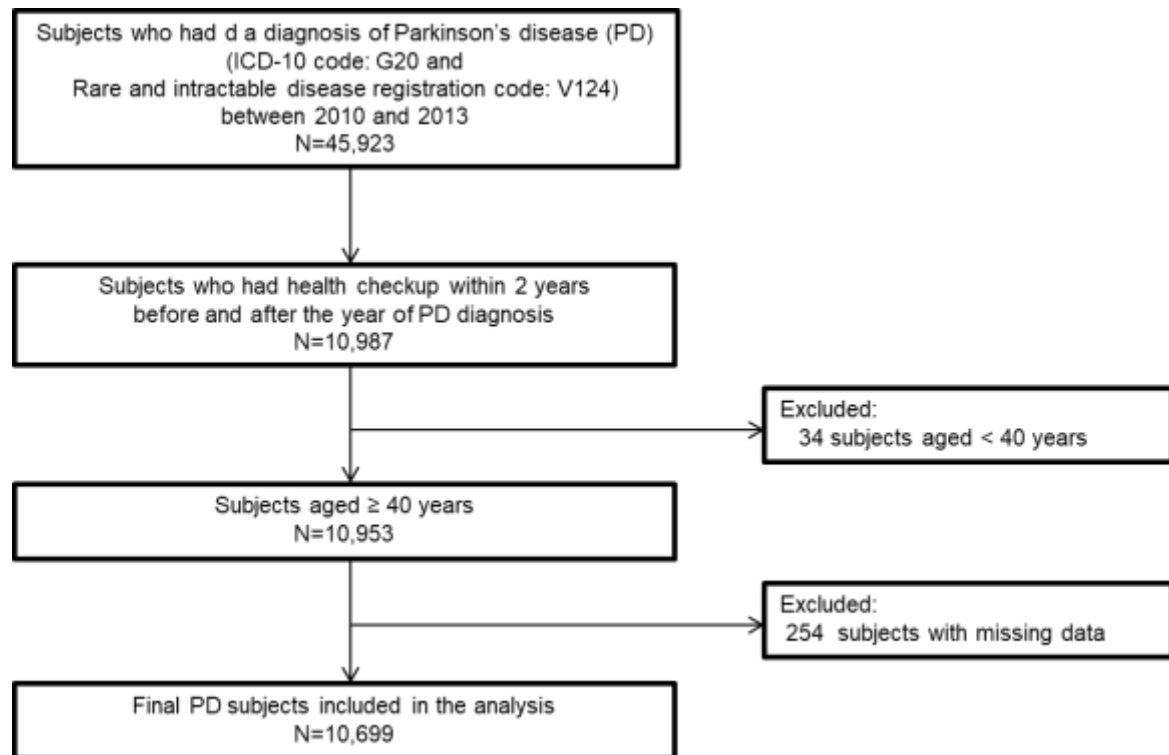
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This supplemental material has been provided by the authors to give readers additional information about their work.

eAppendix 1. Criteria for Parkinson's disease in the Registration Program for Rare Intractable Diseases

- (1) bradykinesia (a score of at least 2 in the bradykinesia items of the Unified Parkinson's Disease Rating Scale) with at least one of the following features: muscle rigidity, rest tremor, and postural instability
- (2) exclusion of secondary parkinsonism such as stroke, head injury, encephalitis, hypoxic brain injury, and adverse effects of medication
- (3) three or more of the following: unilateral onset, rest tremor, disease progression, persistent asymmetry affecting the side of onset, excellent response (70–100%) to levodopa, severe levodopa-induced chorea, levodopa response for 5 years or more, and a clinical course of ten years or more

eFigure 1. Flowchart of the subject selection process



eTable 1. Physical Activity Status Before and After Diagnosis of Parkinson’s Disease stratified by Mortality

		Mortality							
		No (n=8876)				Yes (n=1823)			
		Group 1	Group 2	Group 3	Group 4	Group 1	Group 2	Group 3	Group 4
	No.	2536	1867	1599	2874	690	306	398	429
Pre-diagnosis	Physically active subjects	250 (9.86)	237 (12.69)	1049 (65.6)	2111(73.45)	51 (7.39)	43 (14.05)	232 (58.29)	287 (66.9)
	MET-min/week (Quartiles)								
	Q1	1613 (63.6)	988 (52.92)	0 (0)	0(0)	471 (68.26)	177 (57.84)	0 (0)	0 (0)
	Q2	923 (36.4)	879 (47.08)	0 (0)	0(0)	219 (31.74)	129 (42.16)	0 (0)	0 (0)
	Q3	0(0)	0 (0)	893 (55.85)	1306 (45.44)	0 (0)	0 (0)	229 (57.54)	200 (46.62)
	Q4	0(0)	0 (0)	706 (44.15)	1568 (54.56)	0 (0)	0 (0)	169 (42.46)	229 (53.38)
	MET-min/week, median (IQR)	0 (0-180)	0 (0-270)	680 (600-1200)	835 (630-1400)	0 (0-180)	0 (0-270)	630 (630-1140)	800 (630-1360)
Post-diagnosis	Physically active subjects	230 (9.07)	1213 (64.97)	197 (12.32)	2059 (71.64)	42 (6.09)	176 (57.52)	39 (9.8)	258 (60.14)
	MET-min/week (Quartiles)								
	Q1	1578 (62.22)	0(0)	841 (52.6)	0 (0)	502 (72.75)	0 (0)	242 (60.8)	0 (0)
	Q2	958 (37.78)	0(0)	758 (47.4)	0 (0)	188 (27.25)	0 (0)	156 (39.2)	0 (0)
	Q3	0 (0)	1053 (56.4)	0 (0)	1316 (45.79)	0 (0)	193 (63.07)	0 (0)	243 (56.64)
	Q4	0 (0)	814 (43.6)	0 (0)	1558 (54.21)	0 (0)	113 (36.93)	0 (0)	186 (43.36)
	MET-min/week, median (IQR)	0 (0-180)	760 (630-1230)	0 (0-270)	930 (630-1510)	0 (0-90)	630 (600-1180)	0 (0-240)	750 (630-1440)

The median values of MET-min/week were 400 (90-800) and 450 (90-820) at pre-diagnosis and post-diagnosis, respectively. Subjects with PD were divided into four groups according to the median values at pre- and post-diagnosis (Group 1; <400/<450, Group 2; <400/≥450, Group 3; ≥400/<450, Group 4; ≥400/≥450).

eTable 2. Cox Proportional Hazard Regression Analysis of the Risk of All-Cause Mortality in Patients with Parkinson’s Disease Stratified by Intensity

Intensity	PD (n)	Mortality (n)	Person-Years	Mortality Rate	Model 1	P Value	Model 2	P Value	Model 3	P Value
Vigorous										
Active	8927	1616	39810.21	40.5926	1 (Ref.)		1 (Ref.)		1 (Ref.)	
Inactive	1772	207	8151.69	25.3935	0.62 (0.54-0.72)	<0.001	0.74 (0.64-0.86)	<0.001	0.80 (0.69-0.93)	0.004
Moderate										
Active	9445	1686	42090.96	40.0561	1 (Ref.)		1 (Ref.)		1 (Ref.)	
Inactive	1254	137	5870.93	23.3353	0.57 (0.48-0.68)	<0.001	0.63 (0.53-0.75)	<0.001	0.66 (0.55-0.78)	<0.001
Light										
Active	7142	1311	31892.5	41.1068	1 (Ref.)		1 (Ref.)		1 (Ref.)	
Inactive	3557	512	16069.39	31.8618	0.78 (0.70-0.86)	<0.001	0.80 (0.72-0.88)	<0.001	0.81 (0.73-0.90)	<0.001

PD, Parkinson’s disease

Mortality rate is the incidence of mortality per 1000 person-years

Model 1: unadjusted

Model 2: adjusted for age, sex, income level, and residential area

Model 3: adjusted for age, sex, income level, residential area, comorbidities, smoking, alcohol consumption, body mass index, and disability registration

eTable 3. Subgroup Analyses of Age, Sex, Smoking, Alcohol, Comorbidities, Body Mass Index, and Disability Registration

Subgroup		Quartile (MET-Min/Week)	PD (n)	Mortality (n)	Person-Years	Mortality Rate	HR (95% CI)	P Value	P value for Interaction
Age	<65	Q1 (<90)	603	62	2821.32	21.9755	1 (Ref.)	0.42	0.32
		Q2 (<450)	534	37	2578.35	14.3503	0.87 (0.58-1.32)	0.51	
		Q3 (<820)	814	75	3846.17	19.4999	1.07 (0.76-1.51)	0.70	
		Q4 (820≤)	1081	70	5153.51	13.583	0.82 (0.58-1.17)	0.28	
	65≤	Q1 (<90)	2560	682	10995.69	62.0243	1 (Ref.)	<0.001	
		Q2 (<450)	1526	307	6672.2	46.0118	0.81 (0.71-0.92)	<0.001	
		Q3 (<820)	1991	361	8697.25	41.5074	0.72 (0.63-0.82)	<0.001	
		Q4 (820≤)	1590	229	7197.41	31.817	0.59 (0.50-0.69)	<0.001	
Sex	Male	Q1 (<90)	1243	399	5211.62	76.5597	1 (Ref.)	<0.001	0.56
		Q2 (<450)	867	204	3745.55	54.4646	0.85 (0.72-1.01)	0.06	
		Q3 (<820)	1335	288	5790.54	49.7363	0.80 (0.68-0.93)	0.004	
		Q4 (820≤)	1480	211	6821.5	30.9316	0.61 (0.52-0.73)	<0.001	
	Female	Q1 (<90)	1920	345	8605.4	40.0911	1 (Ref.)	<0.001	
		Q2 (<450)	1193	140	5504.99	25.4315	0.75 (0.62-0.92)	0.005	
		Q3 (<820)	1470	148	6752.88	21.9166	0.69 (0.57-0.84)	<0.001	
		Q4 (820≤)	1191	88	5529.41	15.9149	0.60 (0.48-0.77)	<0.001	
Heavy drinker	No	Q1 (<90)	3125	733	13650.45	53.6979	1 (Ref.)	<0.001	0.40
		Q2 (<450)	2048	340	9198.33	36.9632	0.80 (0.70-0.91)	<0.001	
		Q3 (<820)	2782	432	12435.62	34.7389	0.76 (0.67-0.86)	<0.001	
		Q4 (820≤)	2632	292	12174.01	23.9855	0.60 (0.52-0.69)	<0.001	
	Yes	Q1 (<90)	38	11	166.57	66.0394	1 (Ref.)	0.47	
		Q2 (<450)	12	4	52.21	76.6163	3.02 (0.70-13.15)	0.14	
		Q3 (<820)	23	4	107.81	37.1039	0.95 (0.28-3.24)	0.93	
		Q4 (820≤)	39	7	176.91	39.5688	1.27 (0.43-3.72)	0.66	

Current smoker	No	Q1 (<90)	2994	700	13077.26	53.528	1 (Ref.)	<0.001	0.21
		Q2 (<450)	1943	326	8714.32	37.4097	0.82 (0.71-0.93)	0.002	
		Q3 (<820)	2652	403	11894.71	33.8806	0.74 (0.65-0.84)	<0.001	
		Q4 (820≤)	2545	278	11761.27	23.6369	0.60 (0.52-0.69)	<0.001	
	Yes	Q1 (<90)	169	44	739.75	59.4793	1 (Ref.)	0.33	
		Q2 (<450)	117	18	536.22	33.568	0.64 (0.36-1.13)	0.12	
		Q3 (<820)	153	33	648.71	50.8702	1.02 (0.64-1.64)	0.92	
		Q4 (820≤)	126	21	589.64	35.6147	0.77 (0.45-1.33)	0.35	
Diabetes mellitus	No	Q1 (<90)	2008	421	8951.65	47.0305	1 (Ref.)	<0.001	0.92
		Q2 (<450)	1352	197	6167.27	31.9428	0.82 (0.70-0.97)	0.02	
		Q3 (<820)	1847	246	8356.12	29.4395	0.75 (0.64-0.88)	<0.001	
		Q4 (820≤)	1921	185	8987.57	20.584	0.60 (0.50-0.72)	<0.001	
	Yes	Q1 (<90)	1155	323	4865.37	66.3876	1 (Ref.)	<0.001	
		Q2 (<450)	708	147	3083.27	47.6766	0.80 (0.65-0.97)	0.02	
		Q3 (<820)	958	190	4187.31	45.3752	0.77 (0.64-0.92)	0.004	
		Q4 (820≤)	750	114	3363.34	33.8949	0.61 (0.49-0.76)	<0.001	
Hypertension	No	Q1 (<90)	1325	306	5742.88	53.2834	1 (Ref.)	<0.001	0.08
		Q2 (<450)	894	145	4010.04	36.1593	0.82 (0.67-1.00)	0.05	
		Q3 (<820)	1277	187	5768.14	32.4195	0.73 (0.61-0.88)	0.001	
		Q4 (820≤)	1345	120	6227.53	19.2693	0.49 (0.39-0.61)	<0.001	
	Yes	Q1 (<90)	1838	438	8074.14	54.2473	1 (Ref.)	<0.001	
		Q2 (<450)	1166	199	5240.51	37.9734	0.79 (0.67-0.94)	0.007	
		Q3 (<820)	1528	249	6775.28	36.7512	0.78 (0.67-0.91)	0.002	
		Q4 (820≤)	1326	179	6123.38	29.2322	0.71 (0.59-0.85)	<0.001	
Dyslipidemia	No	Q1 (<90)	1619	416	7110.37	58.5061	1 (Ref.)	<0.001	0.69
		Q2 (<450)	1027	188	4637.23	40.5415	0.83 (0.69-0.98)	0.03	

		Q3 (<820)	1456	244	6544.46	37.2835	0.76 (0.64-0.89)	<0.001	
		Q4 (820≤)	1522	168	7139.64	23.5306	0.58 (0.48-0.69)	<0.001	
	Yes	Q1 (<90)	1544	328	6706.65	48.9067	1 (Ref.)	<0.001	
		Q2 (<450)	1033	156	4613.32	33.8152	0.78 (0.64-0.94)	0.01	
		Q3 (<820)	1349	192	5998.96	32.0055	0.76 (0.63-0.91)	0.002	
		Q4 (820≤)	1149	131	5211.27	25.1378	0.65 (0.53-0.80)	<0.001	
Body mass index	<25	Q1 (<90)	2142	557	9195.75	60.5715	1 (Ref.)	<0.001	0.55
		Q2 (<450)	1362	262	6023.28	43.4979	0.85 (0.73-0.98)	0.03	
		Q3 (<820)	1845	310	8227.08	37.6804	0.76 (0.66-0.87)	<0.001	
		Q4 (820≤)	1789	218	8229.99	26.4885	0.64 (0.54-0.75)	<0.001	
	25≤	Q1 (<90)	1021	187	4621.26	40.4651	1 (Ref.)	<0.001	
		Q2 (<450)	698	82	3227.27	25.4085	0.70 (0.54-0.91)	0.008	
		Q3 (<820)	960	126	4316.34	29.1914	0.80 (0.64-1.01)	0.06	
		Q4 (820≤)	882	81	4120.93	19.6558	0.56 (0.43-0.74)	<0.001	
Disability registration	No	Q1 (<90)	2935	651	12873.21	50.5701	1(Ref.)	<.001	0.31
		Q2 (<450)	1942	302	8719.2	34.6362	0.79 (0.69-0.91)	<.001	
		Q3 (<820)	2676	405	11915.35	33.9898	0.77 (0.68-0.88)	<.001	
		Q4 (820≤)	2551	264	11784.88	22.4016	0.61 (0.52-0.70)	<.001	
	Yes	Q1 (<90)	228	93	943.81	98.5373	1(Ref.)	0.023	
		Q2 (<450)	118	42	531.34	79.0455	0.88 (0.61-1.29)	0.52	
		Q3 (<820)	129	31	628.07	49.3575	0.55 (0.36-0.84)	0.006	
		Q4 (820≤)	120	35	566.03	61.8342	0.66 (0.44-0.98)	0.041	

CI, confidence interval; HR, hazard ratio; MET, metabolic equivalent task; PD, Parkinson's disease

eTable 4. Multivariate Cox Proportional Hazard Analyses of Covariables for All-cause Mortality in Parkinson's disease

Variables	HR (95% CI)	P value
Age	1.07 (1.06-1.07)	<0.001
Sex (reference=male)	0.53 (0.48-0.58)	<0.001
Residential area (reference=urban)	1.09 (0.99-1.20)	0.08
Disability registration	1.92 (1.66-2.23)	<0.001
Comorbidities		
Charlson comorbidity index	1.13 (1.11-1.16)	<0.001
Diabetes mellitus	1.09 (0.96-1.23)	0.03
Hypertension	0.93 (0.85-1.03)	0.17
Dyslipidemia	0.82 (0.74-0.90)	<0.001
Current smoker	0.98 (0.81-1.19)	0.87
Heavy drinker	1.42 (0.96-2.10)	0.08
Body mass index (kg/m ²)	0.94 (0.92-0.95)	<0.001