

**eTable 1 Assessment of self-reported recreational physical activity in E3N questionnaires over the follow-up.**

<b>Activities</b>	<b>Unit</b>	<b>MET</b>	<b>Q1 (1990)</b>	<b>Q3 (1993)</b>	<b>Q5 (1997)</b>	<b>Q7 (2002)</b>	<b>Q8 (2005)</b>	<b>Q11 (2014)</b>	<b>Total number of measures</b>
Heavy cleaning	Hours per week	4	✓				✓		2
Light cleaning	Hours per week	3	✓				✓		2
Household (cooking, cleaning...)	Hours per week	3			✓	✓		✓	3
Stairs Climbing	Number of floors climbed per day	0.067	✓	✓					2
Walking 1	Meters walked per day	0.00075	✓						1
Walking 2	Hours per week	3		✓	✓	✓	✓	✓	5
Vigorous recreational activities	Hours per week	7.5	✓				✓		2
Moderate recreational activities	Hours per week	5	✓				✓		2
Sport	Hours per week	6		✓	✓	✓		✓	4
Cycling	Hours per week	6		✓	✓	✓		✓	4
Gardening and bricolage	Hours per week	4.25		✓	✓	✓		✓	4

MET (metabolic equivalent of task) values were attributed to each activity based on a compendium<sup>1</sup> and expert opinion.<sup>2</sup>

**eTable 2 Cohort studies on the association between physical activity and Parkinson’s disease incidence.**

Study (Year)	Data source (country)	Follow-up; No. (% women)	PD Definition	Type of PA (assessment, unit)	PA level	Cases (No.)	Baseline Analysis HR (95% CI)	Cases (No.)	Lagged Analysis HR (95% CI)	Other PA exposures		
Chen et al. <sup>3</sup> (2005)	Health Professionals Follow-Up Study (HPFS, US)	1986-2000; 48,574 (0)	Self-report confirmed by neurologist/internists, medical records and validation	<b>Total PA<sup>a</sup></b> (self-report, MET-h/wk)	<b>Men</b>						Moderate and vigorous PA. PA at high school, college, ages 30-40, and early in life	
						<b>252</b>			<b>6y-lag</b>			
					<2.8	46	1.00 (Ref.)	-	1.00 (Ref.)			
					2.8-7.7	68	1.3 (0.9-1.9)	-	1.1 (0.6-2.1)			
					7.8-16.9	58	1.1 (0.7-1.6)	-	0.6 (0.3-1.3)			
	17-34	44	0.8 (0.6-1.3)	-	0.5 (0.2-1.1)							
	≥34	36	0.7 (0.5-1.1)	-	0.5 (0.2-1.1)							
	Nurses’ Health Study (NHS, US)	1986-1998; 77,254 (100)	Self-report confirmed by neurologist/internists, medical records and validation	<b>Total PA<sup>b</sup></b> (self-report, MET-h/wk)	<b>Women</b>						Moderate and vigorous PA	
						<b>135</b>			<b>4y-lag</b>			
					<2.1	18	1.00 (Ref.)	-	1.00 (Ref.)			
2.1-4.6					23	1.1 (0.6-2.0)	-	0.8 (0.4-1.7)				
4.7-10.4					43	2.0 (1.1-3.5)	-	1.9 (1.0-3.7)				
10.5-21.7	22	1.0 (0.5-1.8)	-	0.9 (0.5-1.9)								
>21.7	29	1.3 (0.7-2.3)	-	1.1 (0.5-2.2)								
Logroscino et al. <sup>4</sup> (2006)	Harvard Alumni Health Study (US)	1988-1997; 10,714 (0)	Self-report, death certificates and validation	<b>Total energy expenditure<sup>c</sup></b> (self-report, kcal/wk)	<b>Men</b>						Moderate and vigorous sports/recreation, PA in college, and average energy expenditure (1962/1966/1977/1988)	
						<b>101</b>						
					<1000	42	1.00 (Ref.)	-	-			
					1000-1999	28	1.15 (0.71-1.88)	-	-			
					1999-2999	14	0.92 (0.50-1.71)	-	-			
≥3000	17	0.63 (0.36-1.12)	-	-								
Thacker et al. <sup>5</sup> (2008)	Cancer Prevention study II Nutrition Cohort (US)	1992-2001; 141,339 (55.8)	Self-report confirmed by neurologist/internists/family physicians, medical records and validation	<b>Total recreational PA<sup>d</sup></b> (self-report, MET-h/wk)	<b>Men</b>						-	
						<b>264</b>						
					0	28	1.00 (Ref.)	-	-			
					3.5	72	1.0 (0.7-1.6)	-	-			
					4-13.5	45	0.9 (0.6-1.5)	-	-			
	14-22.5	67	0.9 (0.6-1.5)	-	-							
	≥23	52	0.8 (0.5-1.2)	-	-							
						<b>Women</b>						-
							<b>145</b>					
						0	10	1.00 (Ref.)	-	-		
3.5						40	1.2 (0.6-2.5)	-	-			
4.0-8.5						32	1.8 (0.8-3.7)	-	-			
9.0-18.0	37	1.3 (0.6-2.6)	-	-								
18.5	26	1.0 (0.5-2.2)	-	-								

Study (Year)	Data source (country)	Follow-up; No. (% women)	PD Definition	Type of PA (assessment, unit)	PA level	Cases (No.)	Baseline Analysis HR (95% CI)	Cases (No.)	Lagged Analysis HR (95% CI)	Other PA exposures
					<b>Men and women combined</b>					Total recreational PA and moderate to vigorous activity at age 40
						<b>409</b>		<b>256</b>	<b>4y-lag</b>	
						38	1.00 (Ref.)	23	1.0 (Ref.)	
						112	1.1 (0.7-1.6)	67	1.0 (0.5-1.9)	
						77	1.2 (0.6-2.2)	46	1.1 (0.7-1.9)	
						104	1.0 (0.7-1.5)	74	1.2 (0.7-1.9)	
						78	0.8 (0.6-1.2)	46	0.8 (0.5-1.3)	
Xu et al. <sup>6</sup> (2010)	NIH-AARP Diet and Health Study Cohort (US)	2000-2006; 213,701 (NA)	Self-report, medical records and validation	Moderate to vigorous activities <sup>e</sup> (self-report, h/wk)	<b>Men</b>					-
								<b>566</b>	<b>4y-lag</b>	
					Never/rarely			81	1.00 (Ref.)	
					<1	-	-	59	0.94 (0.67-1.32)	
					1-3			150	0.92 (0.70-1.21)	
					4-7			156	0.86 (0.65-1.12)	
					>7			120	0.68 (0.51-0.90)	
					<b>Women</b>					
								<b>198</b>	<b>4y-lag</b>	
					Never/rarely			33	1.00 (Ref.)	
					<1	-	-	31	1.21 (0.74-1.97)	
					1-3			45	0.69 (0.44-1.08)	
					4-7			51	0.74 (0.48-1.15)	
					>7			38	0.60 (0.37-0.95)	
<b>Men and women combined</b>										
			<b>764</b>	<b>4y-lag</b>						
Never/rarely			114	1.00 (Ref.)						
<1	-	-	90	1.02 (0.77-1.34)						
1-3			195	0.85 (0.67-1.07)						
4-7			207	0.82 (0.65-1.03)						
>7			158	0.65 (0.51-0.83)						
Sääksjärvi et al. <sup>7</sup> (2014)	Finnish Mobile Clinic Health Examination Survey (Finland)	1973-1994; 6,715 (NA)	Drug reimbursement, hospital records and validation	<b>Leisure-time PA<sup>f</sup></b> (self-report, h/wk)	<b>Men and women combined</b>					Light, moderate to vigorous activities at ages 15-18, 19-29 and 35-39. Daily routines at work. Changes of PA between ages 35-39 and past 10 years
						<b>97</b>		<b>66</b>	<b>10y-lag</b>	
					None	32	1.00 (Ref.)	23	1.00 (Ref.)	
					Light	62	0.73 (0.47-1.13)	41	0.65 (0.38-1.10)	
			3	0.27 (0.08-0.90)	2	0.25 (0.06-1.09)				

Study (Year)	Data source (country)	Follow-up; No. (% women)	PD Definition	Type of PA (assessment, unit)	PA level	Cases (No.)	Baseline Analysis HR (95% CI)	Cases (No.)	Lagged Analysis HR (95% CI)	Other PA exposures	
Yang et al. <sup>8</sup> (2015)	Swedish National March Cohort (Sweden)	1997-2010; 43,368 (64.3)	Swedish Patient Register	General PA <sup>g</sup> (self-report, MET-h/wk)	<b>Men</b>						Household and community activity, leisure time exercise, total PA in a 24-h day (Energy expenditure questionnaire), physical demanding level of occupational activity
						<b>158</b>		-	<b>8y-lag</b>		
					<3.9	57	1.00 (Ref.)	-	1.00 (Ref.)		
					3.9-6.6	61	1.04 (0.72-1.52)	-	1.11 (0.65-1.90)		
					≥6.6	40	0.53 (0.33-0.85)	-	0.69 (0.36-1.29)		
					<b>Women</b>						
						<b>126</b>		-			
					<4.0	45	1.00 (Ref.)	-	1.00 (Ref.)		
					4.0-6.2	44	0.81 (0.52-1.25)	-	1.03 (0.60-1.77)		
					≥6.2	37	0.85 (0.54-1.34)	-	0.81 (0.44-1.49)		
					<b>Men and women combined</b>						
						<b>286</b>					
					<3.9	104	1.00 (Ref.)	-	1.00 (Ref.)		
3.9-6.4	105	0.88 (0.66-1.18)	-	1.05 (0.71-1.55)							
≥6.4	77	0.72 (0.53-0.99)	-	0.78 (0.51-1.20)							
Llamas-Velasco et al. <sup>9</sup> (2021)	Neurological Disorders in Central Spain study (Spain)	1994-1998; 2,943 (57.1)	Self-report, neurological examination	Daily PA <sup>h</sup> (self-report, hours)	<b>Men and women combined</b>						
						<b>22</b>					
					≤15.6	-	1.00 (Ref.)	-	-		
					>19.4	-	0.42 (0.71-1.04)	-	-		

PA, physical activity; y, years; h/wk, hours per week

<sup>a</sup>Total PA: cumulative sum of average time spent per week on walking/hiking outdoors, jogging, running, bicycling, lap swimming, tennis, squash or racket ball, calisthenics or rowing, and stairs climbed.

<sup>b</sup>Total PA: cumulative sum of average time spent per week on calisthenics/aerobics/aerobic dance/rowing machine, and stairs climbed.

<sup>c</sup>Total energy expenditure: cumulative sum of average time spent per week on walking, stair climbing activities, sports and recreational activities.

<sup>d</sup>Total recreational PA: cumulative sum of average time spent per week on walking, jogging/running/lap swimming, tennis or racquetball, bicycling/stationary bike, aerobics/calisthenics, and dancing.

<sup>e</sup>Moderate to vigorous activities: cumulative sum of time spent on tennis, biking, swimming, and heavy housework.

<sup>f</sup>Leisure-time PA: None; light PA – at least 4h/week doing activities such as walking and cycling; heavy PA –at least 3h/week doing activities such as jogging, skiing, vigorous gardening.

<sup>g</sup>General PA: cumulative sum of average time spent per week on household, community activity and leisure exercise.

<sup>h</sup>Daily PA: Sedentary (≤15.6h doing only minimal house chores or short walks at home), light PA (≤17.6h doing regular house chores, walking independently at home), high PA (>19.4h performing heavy housework, walking more than 1km or practicing any sport regularly).

**eTable 3 Participant's characteristics at baseline (1990-Q1) according to Parkinson's disease status at the end of the follow-up.**

Baseline characteristics, No. (%)	Parkinson's Disease	
	No	Yes
	95,502 (98.8)	1,163 (1.2)
<b>Age (y), M (SD)</b>	49.3 (6.6)	52.6 (6.5)
≤49	55,862 (58.5)	417 (35.9)
50-59	31,263 (32.7)	562 (48.3)
≥60	8,377 (8.8)	184 (15.8)
<b>Education</b>		
< High school	12,665 (13.8)	150 (13.5)
≥ High school	78,852 (86.2)	962 (86.5)
	<i>Missing</i>	51
<b>Smoking</b>		
Never	51,138 (54.0)	699 (60.6)
Ex	29,363 (31.0)	329 (28.5)
Current	14,260 (15.0)	125 (10.9)
	<i>Missing</i>	741
		10
<b>Age at menarche (y), M (SD)</b>	12.8 (1.4)	12.9 (1.5)
≤ 11	19,512 (20.9)	249 (22.0)
12-13	47,140 (50.5)	516 (45.6)
≥ 14	26,636 (28.6)	366 (32.4)
	<i>Missing</i>	2,214
		32
<b>Menopausal status</b>		
Premenopausal	53,382 (58.0)	424 (37.5)
Natural menopause	31,727 (34.5)	551 (48.7)
Artificial menopause	6,251 (6.8)	137 (12.1)
Unknown type of menopause	664 (0.7)	19 (1.7)
	<i>Missing</i>	3,478
		32
<b>Parity</b>		
Nulliparous	11,451 (12.1)	135 (11.8)
One child	15,420 (16.3)	151 (13.1)
Two children	40,257 (42.5)	467 (40.6)
≥ 3 children	27,614 (29.1)	397 (34.5)
	<i>Missing</i>	760
		13
<b>Place of residence</b>		
Rural	12,959 (14.8)	130 (12.2)
Urban	74,392 (85.2)	935 (87.8)
	<i>Missing</i>	8,151
		98
<b>BMI (kg/m<sup>2</sup>), M (SD)</b>	22.6 (3.2)	22.9 (3.0)
<18.5	3,956 (4.2)	39 (3.4)
18.5-24.9	72,918 (78.3)	883 (77.5)
25.0-29.9	13,466 (14.5)	192 (16.8)
≥30.0	2,834 (3.0)	26 (2.3)
	<i>Missing</i>	2,328
		23
<b>Hypercholesterolemia<sup>a</sup></b>	36,168 (37.9)	406 (34.9)
<b>High blood pressure<sup>a</sup></b>	28,530 (29.9)	313 (26.9)
<b>Diabetes<sup>a</sup></b>	2,621 (2.7)	30 (2.6)
<b>Cardiovascular disease<sup>a</sup></b>	2,717 (2.8)	26 (2.2)

M, mean; SD: Standard deviation; BMI, body mass index.

<sup>a</sup> Assessed at the end of the follow-up.

**eTable 4 Characteristics of cases and controls at the index date (T<sub>0</sub>).**

Characteristics, No. (%)	Controls 23,879 (95.2)	Cases 1,196 (4.8)
<b>Age at time=0 (y), M (SD)</b>	71.9 (7.8)	
<b>Education</b>		
< High school	3,367 (14.1)	157 (13.1)
≥ High school	20,512 (85.9)	1,039 (86.9)
<i>Missing</i>	3,367	157
<b>Smoking</b>		
Never	13,438 (56.3)	722 (60.4)
Ex	8,429 (35.3)	409 (34.3)
Current	1,985 (8.4)	63 (5.3)
<i>Missing</i>	27	2
<b>Age at menarche (y), M (SD)</b>	12.9 (1.4)	12.9 (1.5)
≤ 11	4,682 (20.0)	255 (21.9)
12-13	11,477 (49.2)	531 (45.6)
≥ 14	7,201 (30.8)	378 (32.5)
<i>Missing</i>	519	32
<b>Menopausal status</b>		
Premenopausal	814 (3.5)	50 (4.3)
Natural menopause	19,388 (83.2)	918 (78.9)
Artificial menopause	2,586 (11.1)	162 (13.9)
Unknown type of menopause	516 (2.2)	34 (2.9)
<i>Missing</i>	575	32
<b>Parity</b>		
Nulliparous	2,955 (12.5)	138 (11.7)
One child	3,782 (16.0)	155 (13.1)
Two children	9,352 (39.5)	484 (40.9)
≥ 3 children	7,586 (32.0)	406 (34.3)
<i>Missing</i>	204	13
<b>Place of residence</b>		
Rural	3,060 (14.1)	137 (12.5)
Urban	18,707 (85.9)	959 (87.5)
<i>Missing</i>	2,112	100
<b>BMI (kg/m<sup>2</sup>), M (SD)</b>	24.0 (3.9)	23.8 (3.6)
<18.5	860 (3.6)	43 (3.6)
18.5-24.9	15,218 (63.8)	804 (67.3)
25.0-29.9	6,067 (25.4)	281 (23.5)
≥30.0	1,721 (7.2)	66 (5.6)
<i>Missing</i>	13	2

M, mean; SD: Standard deviation; BMI, body mass index.

**eTable 5 Results from the linear mixed model for the trajectories of latent physical activity with a retrospective timescale in the nested case-control study (1,196 PD cases, 23,879 controls).**

Characteristics		Beta (95% CI)	P-value	P-value <sup>a</sup>
Intercept (LPA level in controls at T <sub>0</sub> )		-0.048 (-0.098, 0.001)	0.06	
Parkinson's disease status		-0.164 (-0.230, -0.097)	<0.001	
Time		-0.372 (-0.383, -0.361)	<0.001	
Time <sup>2</sup>		-0.119 (-0.122, -0.115)	<0.001	<0.001
Parkinson's disease status × Time		-0.074 (-0.122, -0.025)	0.003	
Parkinson's disease status × Time <sup>2</sup>		-0.017 (-0.033, -0.000)	0.05	0.003
Age		-0.046 (-0.048, -0.044)	<0.001	
Age × Time		-0.061 (-0.063, -0.060)	<0.001	
Age × Time <sup>2</sup>		-0.016 (-0.017, -0.016)	<0.001	<0.001
Smoking	Never	0.00 (Ref.)	--	
	Ex	-0.049 (-0.067, -0.031)	<0.001	
	Current	-0.050 (-0.068, -0.032)	<0.001	
Menopausal status	Premenopausal	0.00 (Ref.)	--	
	Natural menopause	-0.021 (-0.024, -0.018)	<0.001	
	Artificial menopause	-0.048 (-0.059, -0.036)	<0.001	
	Unknown type of menopause	-0.022 (-0.041, -0.003)	0.02	
Parity	Nulliparous	0.00 (Ref.)	--	
	One child	0.071 (0.026, 0.116)	0.002	
	Two children	0.137 (0.098, 0.176)	<0.001	
	≥ 3 children	0.203 (0.163, 0.243)	<0.001	
Rural residence	Rural	0.00 (Ref.)	.	
	Urban	-0.312 (-0.347, -0.276)	<0.001	
Age at menarche	≤ 11	-0.010 (-0.041, 0.022)	0.55	
	12-13	0.00 (Ref.)	--	
	≥ 14	-0.019 (-0.046, 0.008)	0.17	

Age was centered at 73y; time was in decades.

Please see Figure 2 for a graphical representation.

<sup>a</sup> P-value for the combined effect of the terms including Time and Time<sup>2</sup>.

**eTable 6 Association of time-varying physical activity with Parkinson’s disease incidence: exclusion of physical activity assessed at baseline (Q1).**

<b>Latent physical activity</b>	<b>Cases (n)</b>	<b>IR</b>	<b>Age-adjusted HR (95% CI)</b>	<b>P- value</b>	<b>Multivariable HR (95% CI)<sup>a</sup></b>	<b>P- value</b>
<b>5y-lag (FU 1998-2018; N=89,829)</b>	<b>1,015</b>					
Quartile 1	297	0.74	1.00 (Ref.)	-	1.00 (Ref.)	-
Quartile 2	248	0.66	0.90 (0.76-1.06)	0.21	0.89 (0.75-1.05)	0.18
Quartile 3	246	0.63	0.87 (0.73-1.03)	0.11	0.86 (0.73-1.02)	0.08
Quartile 4	224	0.50	0.69 (0.58-0.82)	<0.001	0.68 (0.57-0.81)	<0.001
			<i>P</i> -linear trend	<0.001	<i>P</i> -linear trend	<0.001
<b>10y-lag (FU 2003-2018; N=88,078)</b>	<b>841</b>					
Quartile 1	283	0.80	1.00 (Ref.)	-	1.00 (Ref.)	-
Quartile 2	281	0.79	0.99 (0.82-1.20)	0.92	0.98 (0.81-1.18)	0.83
Quartile 3	260	0.73	0.93 (0.77-1.12)	0.46	0.92 (0.76-1.11)	0.37
Quartile 4	250	0.61	0.77 (0.63-0.93)	0.007	0.76 (0.62-0.92)	0.004
			<i>P</i> -linear trend	0.006	<i>P</i> -linear trend	0.003
<b>15y-lag (FU 2008-2018; N=85,501)</b>	<b>652</b>					
Quartile 1	156	0.81	1.00 (Ref.)	-	1.00 (Ref.)	-
Quartile 2	179	0.94	1.16 (0.93-1.44)	0.18	1.15 (0.92-1.42)	0.21
Quartile 3	165	0.83	1.02 (0.82-1.27)	0.85	1.00 (0.81-1.25)	0.97
Quartile 4	152	0.68	0.83 (0.67-1.04)	0.11	0.82 (0.65-1.02)	0.08
			<i>P</i> -linear trend	0.06	<i>P</i> -linear trend	0.04

FU, follow-up; IR, age-standardized incidence rate of Parkinson’s disease per 1,000 person-years.

Analyses are based on PA assessed starting at Q3 (1993) or later.

Hazard ratios (HR) and 95% confidence intervals (CI) calculated using Cox proportional hazards models for time-varying variables with age as the timescale.

Analyses with lags longer than 15y were not possible due to an insufficient number of cases.

<sup>a</sup> Multivariable models are adjusted for baseline place of residence (rural/urban), age at menarche ( $\leq 11/12-13 \geq 14$  years) and parity (nulliparous/one child/two children/ $\geq$ three children), and time-varying smoking (never/ex/current), and menopausal status (premenopausal/natural menopause/artificial menopause/unknown type of menopause).



**eTable 7 Association of time-varying physical activity with Parkinson’s disease incidence: analyses stratified by median age at diagnosis of PD.**

Latent physical activity	Age ≤ 72.8y			Age > 72.8y		
	Cases (n)	Multivariable HR (95% CI)	P-value	Cases (n)	Multivariable HR (95% CI)	P-value
<b>10y-lag (FU 2000-2018; N=95,354)</b>	<b>497</b>			<b>577</b>		
Quartile 1	125	1.00 (Ref.)	-	161	1.00 (Ref.)	-
Quartile 2	139	1.01 (0.79-1.29)	0.92	135	0.89 (0.70-1.12)	0.31
Quartile 3	132	0.97 (0.76-1.24)	0.80	136	0.87 (0.69-1.10)	0.25
Quartile 4	101	0.78 (0.60-1.01)	0.06	145	0.73 (0.58-0.92)	0.01
		<i>P</i> -linear trend	0.06		<i>P</i> -linear trend	0.01

FU, follow-up.

Analyses were stratified in two age groups based on the median age at diagnosis in PD cases (72.8y).

Hazard ratios (HR) and 95% confidence intervals (CI) calculated using Cox proportional hazards models for time-varying variables with age as the timescale.

Multivariable models are adjusted for baseline place of residence (rural/urban), age at menarche (≤11/12-13/≥14 years), parity (nulliparous/one child/two children/≥three children), and time-varying smoking (never/ex/current) and menopausal status (premenopausal/natural menopause/artificial menopause/unknown type of menopause).

**eTable 8 Association of time-varying physical activity with Parkinson's disease incidence: alternative criteria for the definition of Parkinson's disease.**

Latent physical activity (10y-lag; N=95,354)	Main analysis		
	Cases (n)	HR (95% CI)	P-value
<b>All cases</b>	<b>1,074</b>		
Quartiles 1+2+3	828	1.00 (Ref.)	-
Quartile 4	246	0.79 (0.68-0.91)	0.001
<b>Definite and probable PD cases only<sup>b</sup></b>	<b>655</b>		
Quartiles 1+2+3	504	1.00 (Ref.)	-
Quartile 4	151	0.81 (0.67-0.97)	0.02
<b>Definite PD cases only<sup>c</sup></b>	<b>560</b>		
Quartiles 1+2+3	427	1.00 (Ref.)	-
Quartile 4	133	0.85 (0.70-1.03)	0.098
<b>More specific version of the algorithm<sup>d</sup></b>	<b>1,033</b>		
Quartiles 1+2+3	795	1.00 (Ref.)	-
Quartile 4	238	0.80 (0.69-0.92)	0.003

FU, follow-up.

Hazard ratios (HR) and 95% confidence intervals (CI) calculated using Cox proportional hazards models for time-varying variables with age as the timescale.

Models are adjusted for baseline place of residence (rural/urban), age at menarche ( $\leq 11/12-13/\geq 14$  years), parity (nulliparous/one child/two children/ $\geq$ three children), and time-varying smoking (never/ex/current) and menopausal status (premenopausal/natural menopause/artificial menopause/unknown type of menopause).

<sup>a</sup> PD patients validated based on medical records and an algorithm based on drug claims (main analysis available in Table 2).

<sup>b</sup> PD patients (definite, probable) validated based on medical records; other PD cases are excluded from the analysis.

<sup>c</sup> PD patients (definite) validated based on medical records; other PD cases are excluded from the analysis.

<sup>d</sup> PD patients validated based on medical records and a more specific version of the algorithm based on drug claim databases (sensitivity=specificity=90%).

**eTable 9 Association between latent physical activity and Parkinson’s disease (10y-lag; N=95,354, 1,074 PD cases): impact of adjustment for potential mediators.**

<b>Latent physical activity</b>	<b>HR Q4 vs. Q1 (95% CI)</b>	<b>P-value</b>	<b>PR<sup>a</sup></b>
<b>Model A<sup>b</sup></b>	0.75 (0.63-0.89)	0.001	--
<b>Model A + BMI</b>	0.74 (0.62-0.88)	0.001	4.7
<b>Model A + Hypercholesterolemia</b>	0.75 (0.63-0.89)	0.001	0.0
<b>Model A + High blood pressure</b>	0.75 (0.63-0.89)	0.001	0.7
<b>Model A + Diabetes</b>	0.75 (0.63-0.89)	0.001	0.5
<b>Model A + Cardiovascular diseases</b>	0.75 (0.63-0.89)	0.001	0.6
<b>Model A + BMI, hypercholesterolemia, high blood pressure, diabetes and cardiovascular diseases</b>	0.74 (0.62-0.88)	0.001	5.5

Q, quartile; BMI, body mass index.

Hazard ratios (HR) and 95% confidence intervals (CI) calculated using Cox proportional hazards models for time-varying variables with age as the timescale and a 10y-lag (follow-up, 2000-2018).

<sup>a</sup> The percentage reduction (PR) represents the percentage of the association between latent physical activity and Parkinson’s disease in Model A explained by potential mediators, and is computed as  $100 \times (\log\text{HR}_{\text{Model } i} - \log\text{HR}_{\text{Model A}}) / \log\text{HR}_{\text{Model A}}$ .

<sup>b</sup> Model A (Table 2) is adjusted for baseline place of residence (rural/urban), age at menarche ( $\leq 11/12-13/\geq 14$  years), parity (nulliparous/one child/two children/ $\geq$ three children), and time-varying smoking (never/ex/current) and menopausal status (premenopausal/natural menopause/artificial menopause/unknown type of menopause).

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