Supplementary Material

Prospective Study of Lung Function with Prodromal, Clinical Parkinson's Disease, and Mortality

Supplementary Table 1 Ascertainment for prodromal Parkinson's disease (PD) features in the UK Biobank study

Prodromal PD features	UK Biobank Self Report	ICD 10	ICD 9	Read V2	Read CTV3
Depression	1,286	F204, F32, F328, F33, F330, F331, F332, F333, F334, F338	2962, 2963, 3004, 3119	Eu204, Eu32., Eu32A, Eu32B, Eu32y, Eu330, Eu331, Eu332, Eu333, Eu334, Eu33y	2257., 2257., E0043, E0043, E1131, E1132, E1133, E1134, E1136, E1137, E11y2, E130., E2B0., E2B1., Eu32y, Eu330, Eu331, Eu332, Eu333, Eu334, Eu33y, X00Qy, X00S8, X00SO, X00SO, X00SO, X00SR, X00SR, X00SS, X00SS, X00SU, XE1Y1, XE1Za, XE1Zc, XE1Zd, XE1Ze, XM1GC, XM1GC, Xa0wV, XaB9J, XaB9J, XaB9J, XaCHo, XaCIt, XaCIt, XaCIu, XaCIu, XaX54, XaY2C
RBD		G478		Fy05., Fy06., Fyu58	E274A, E274E, Fyu58, X008C, X008D, X008E, X008G, X008H, X7649, X764K, X76AF, X76AG, Xa0Kk, Xa0Kl, XaJEd, XaZKa
Urinary Incontinence	1,202	N394, R32	7883	Kyu5A, R083., R0830, R0831, R0832, R083z	1A22., 1A23., 1A23., 1A26., 3940., Kyu5A, R083., R0830, R0831, R0832, R083z, X008B, X30C5, X30OH, X30OI, X30OJ, X30OK, X30OM, X30ON, X30OO, X77Tb, Xa1uO, Xa1uP, XaYX9, XaYX9, XabdF, XabdN
Erectile Dysfunction	1,518	N484, F522	3027	Eu522, K27y1, K27y7	E2273, E2273, Eu522, K27y1, X400F, X400F, X400G, X400G, X400H, X400I, X401k, X401k, X401l, X401l, X401m, X401m, X401n, X401n, X76M2, X76M3, X76ME, X76ME, X76MF, X76MM, X76MM, X76MO, X76MO, XE1Zs, Xa044, Xa044, Xa24H, XaXgw, XaXgw, Xaa8r
Constipation	1,599	K590	56409, 56402	J520., J5200, J5201, J5202, J5203, J5204, J520y, J520z	19EA., J520., J5200, J5201, J5202, J520y, J520z, X30Bl, X30Bm, XE0rD, Xa7n2, XaE1r
Anxiety	1,287	F412, F413, F418, F419,	3000, 3001, 3002, 3005, 3009	Eu054, Eu412, Eu413, Eu41y, Eu41z, Eu460, Eu46y, Eu46z	1682., E...., E20.., E20.., E200., E200., E2004, E20y1, E20y3, E272., Eu41., Eu413, Eu41y, Eu41z, Eu46., Eu46y, Eu46z, N2472, Ua1qg, Ua1qh, Ua1qi, Ua1qj, Ua1qk, Ua1ql, Ua1qm, Ua1qn, Ua1qo, Ua1qp, X00RP, X00SO,

	F480, F488, F489, F064			X00Sb, X00Sc, X208I, X40Xl, X767J, XC0CP, XE0rb, XE1YD, XE1Zj, XE1Zp, XE1hk, XE1hl, XM010, XM06b, XM0D3, XM0D3, XM0yx, XM0z0, XM1AV, Xa00x, Xa1a6, Xa1a7, Xa1a9, Xa1aA, Xa7k9, Xa7kB, XaB9J, ZV402
Orthostatic Hypotension	I951	4580	G870.	G870., XM02W
Hyposmia	R430	7811	R0110	2BP3., R0110, X008M, X008N, X008O, XE0rs, XM0CW, XM0CX, XM1Po

Supplementary Table 2. Association between lung function and risk of Parkinson's disease only included participants with both reproducible FEV1 and FVC (n = 269,770).

	Lung function						
	Q1	**Q2**	**Q3**	**Q4**	**Q5**	**Per unit decrease**	***p*–trend**
Case/N	**567 / 53,597**	**444 / 54,261**	**327 / 54,652**	**264 / 53,502**	**138 / 53,758**		
FEV1 (L), median	**1.93**	**2.26**	**2.52**	**2.80**	**3.41**		
Model	**1.36 (1.11, 1.67)**	**1.24 (1.01, 1.51)**	1.16 (0.94, 1.43)	1.21 (0.98, 1.49)	Ref	**1.20 (1.06, 1.36)**	0.003
Case/N	**559 / 53,543**	**449 / 53,756**	**300 / 54,019**	**268 /54,131**	**164 / 54,321**		
FVC (L), median	**2.58**	**2.97**	**3.28**	**3.63**	**4.41**		
Model	**1.27 (1.05, 1.54)**	**1.22 (1.01, 1.47)**	1.02 (0.84, 1.24)	1.11 (0.91, 1.35)	Ref	**1.16 (1.05, 1.27)**	0.004
Case/N	**506 / 53,958**	**410 / 53,496**	**357 / 53,956**	**272 /54,153**	**195 / 54,207**		
PEF (L/min), median	266.0	318.0	357.0	399.0	490.0		
Model	1.12 (0.93, 1.32)	1.14 (0.96, 1.34)	1.16 (0.99, 1.37)	1.03 (0.87, 1.23)	Ref	1.04 (0.99, 1.10)	0.12
Case/N	**407 / 53,951**	**402 / 53,949**	**340 / 53,954**	**326 / 53,954**	**265 / 53,962**		
FEV1/FVC, median	0.68	0.74	0.77	0.80	0.83		
Model	0.91 (0.77, 1.08)	0.96 (0.81, 1.13)	0.90 (0.76, 1.06)	0.98 (0.83, 1.17)	Ref	0.98 (0.93, 1.02)	0.31

Models were adjusted for age (years), sex (men or women), PRS (tertiles), education level (high [college or university degree], intermediate [A/AS levels or equivalent, O levels/GCSEs or equivalent], or low [none of the aforementioned]), TDI (quintiles), smoking status (current, past, or never), alcohol use (current, past, or never), have physical activity (yes or no), BMI (< 25.0, 25–29.9, or ≥ 30 kg/m^2), and sleep score (healthy sleep pattern, intermediate sleep pattern, or poor sleep pattern), hypertension (yes or no), diabetes (yes or no), high cholesterol (yes or no), cancer (yes or no), $PM_{2.5}$ (low or high), and NO_2 (low or high).

Data with p–value <0.05 are presented in bold.

FEV1, forced expiratory volume in 1-s; FVC, forced vital capacity; PEF, peak expiratory flow; PRS, standard polygenic risk score; PD, Parkinson's disease; TDI, Townsend deprivation index; BMI, body mass index.

Supplementary Table 3. Association between lung function and risk of Parkinson's disease after excluding participants with cancer at baseline (n = 432,065).

	Lung function						
	Q1	**Q2**	**Q3**	**Q4**	**Q5**	**Per unit decrease**	***p*–trend**
Case/N	**886 / 86,146**	**764 / 87,498**	**514 / 86,007**	**410 / 85,628**	**252 / 86,786**		
FEV1 (L), median	**1.92**	**2.28**	**2.54**	**2.82**	**3.57**		
Model	**1.20 (1.04, 1.40)**	**1.21 (1.04, 1.40)**	1.01 (0.86, 1.18)	1.05 (0.90, 1.23)	Ref	**1.15 (1.05, 1.25)**	0.002
Case/N	**869 / 86,215**	**734 / 86,453**	**504 / 85,556**	**414 / 87,846**	**305 / 85,995**		
FVC (L), median	**2.58**	**2.98**	**3.29**	**3.66**	**4.71**		
Model	1.13 (0.98, 1.30)	1.13 (0.98, 1.30)	0.95 (0.82, 1.10)	0.95 (0.82, 1.10)	Ref	**1.09 (1.12, 1.16)**	0.013
Case/N	**819 / 86,893**	**691 / 85,057**	**571 / 87,374**	**438 / 86,430**	**307 / 86,311**		
PEF (L/min), median	261.0	320.0	358.0	402.0	514.0		
Model	**1.26 (1.10, 1.45)**	**1.24 (1.08, 1.42)**	**1.18 (1.02, 1.35)**	1.08 (0.94, 1.25)	Ref	**1.09 (1.04, 1.14)**	<0.001
Case/N	**655 / 86,419**	**644 / 86,421**	**548 / 86,407**	**546 / 86,442**	**433 / 86,376**		
FEV1/FVC, median	0.68	0.74	0.77	0.80	0.83		
Model	0.94 (0.83, 1.07)	1.01 (0.89, 1.14)	0.94 (0.83, 1.07)	1.06 (0.93, 1.20)	Ref	0.98 (0.94, 1.01)	0.19

Models were adjusted for age (years), sex (men or women), PRS (tertiles), education level (high [college or university degree], intermediate [A/AS levels or equivalent, O levels/GCSEs or equivalent], or low [none of the aforementioned]), TDI (quintiles), smoking status (current, past, or never), alcohol use (current, past, or never), have physical activity (yes or no), BMI (< 25.0, 25–29.9, or ≥ 30 kg/m^2), and sleep score (healthy sleep pattern, intermediate sleep pattern, or poor sleep pattern), hypertension (yes or no), diabetes (yes or no), high cholesterol (yes or no), cancer (yes or no), $PM_{2.5}$ (low or high), and NO_2 (low or high).

Data with p–value <0.05 are presented in bold.

FEV1, forced expiratory volume in 1-s; FVC, forced vital capacity; PEF, peak expiratory flow; PRS, standard polygenic risk score; PD, Parkinson's disease; TDI, Townsend deprivation index; BMI, body mass index.

Supplementary Table 4. Association between lung function and risk of Parkinson's disease after excluding incident PD cases within the first two years of follow-up (n = 452,454).

	Lung function						
	Q1	**Q2**	**Q3**	**Q4**	**Q5**	**Per unit decrease**	***p*–trend**
Case/N	**903 / 90,836**	**779 / 89,985**	**543 / 90,229**	**439 / 91,248**	**268 / 90,156**		
FEV1 (L), median	**1.92**	**2.27**	**2.53**	**2.82**	**3.58**		
Model	**1.17 (1.01, 1.35)**	**1.18 (1.02, 1.37)**	1.00 (0.86, 1.16)	1.05 (0.90, 1.22)	Ref	**1.12 (1.03, 1.22)**	0.006
Case/N	**892 / 90,766**	**753 / 90,882**	**538 / 90,599**	**427 / 89,799**	**322 / 90,468**		
FVC (L), median	**2.58**	**2.98**	**3.29**	**3.65**	**4.67**		
Model	1.13 (0.98, 1.29)	1.11 (0.97, 1.27)	0.96 (0.83, 1.10)	0.96 (0.83, 1.11)	Ref	**1.08 (1.02, 1.15)**	0.016
Case/N	**820 / 90,686**	**725 / 90,139**	**605 / 91,459**	**452 / 89,252**	**330 / 90,918**		
PEF (L/min), median	260.0	319.0	358.0	401.0	510.0		
Model	**1.20 (1.05, 1.37)**	**1.22 (1.06, 1.39)**	**1.17 (1.02, 1.34)**	1.06 (0.92, 1.22)	Ref	**1.07 (1.03, 1.12)**	0.001
Case/N	**673 / 90,485**	**661 / 90,498**	**572 / 90,506**	**569 / 90,478**	**457 / 90,487**		
FEV1/FVC, median	0.68	0.74	0.77	0.80	0.83		
Model	0.92 (0.82, 1.04)	0.98 (0.87, 1.11)	0.93 (0.82, 1.05)	1.05 (0.93, 1.18)	Ref	0.97 (0.93, 1.01)	0.09

Models were adjusted for age (years), sex (men or women), PRS (tertiles), education level (high [college or university degree], intermediate [A/AS levels or equivalent, O levels/GCSEs or equivalent], or low [none of the aforementioned]), TDI (quintiles), smoking status (current, past, or never), alcohol use (current, past, or never), have physical activity (yes or no), BMI (< 25.0, 25–29.9, or ≥ 30 kg/m^2), and sleep score (healthy sleep pattern, intermediate sleep pattern, or poor sleep pattern), hypertension (yes or no), diabetes (yes or no), high cholesterol (yes or no), cancer (yes or no), $PM_{2.5}$ (low or high), and NO_2 (low or high).

Data with *P*–value <0.05 are presented in bold.

FEV1, forced expiratory volume in 1-s; FVC, forced vital capacity; PEF, peak expiratory flow; PRS, standard polygenic risk score; PD, Parkinson's disease; TDI, Townsend deprivation index; BMI, body mass index.

Supplementary Table 5. Association between lung function and risk of Parkinson's disease when PD diagnosis was restricted to ICD codes only (n = 452,518).

	Lung function						
	Q1	**Q2**	**Q3**	**Q4**	**Q5**	**Per unit decrease**	***p*-trend**
FEV1 (L), median	**1.92**	**2.27**	**2.53**	**2.82**	**3.58**		
Case/N	**920 / 90,859**	**791 / 90,005**	**551 / 90,241**	**431 / 91,256**	**264 / 90,157**		
Model	**1.17 (1.01, 1.36)**	**1.19 (1.03, 1.38)**	1.01 (0.87, 1.18)	1.03 (0.88, 1.20)	Ref	**1.13 (1.04, 1.23)**	0.005
FVC (L), median	**2.58**	**2.98**	**3.29**	**3.65**	**4.67**		
Case/N	**909 / 90,789**	**763 / 90,840**	**547 / 90,612**	**421 / 89,807**	**317 / 90,470**		
Model	1.13 (0.99, 1.30)	1.13 (0.98, 1.29)	0.98 (0.85, 1.13)	0.95 (0.82, 1.10)	Ref	**1.09 (1.02, 1.16)**	0.010
PEF (L/min), median	**260.0**	**319.0**	**358.0**	**401.0**	**510.0**		
Case/N	**847 / 90,716**	**728 / 90,154**	**615 / 91,472**	**445 / 89,257**	**322 / 90,919**		
Model	**1.24 (1.09, 1.42)**	**1.23 (1.08, 1.41)**	**1.21 (1.06, 1.39)**	1.06 (0.92, 1.22)	Ref	**1.08 (1.04, 1.13)**	<0.001
FEV1/FVC, median	**0.68**	**0.74**	**0.77**	**0.80**	**0.83**		
Case/N	**668 / 90,514**	**668 / 90,514**	**575 / 90,506**	**569 / 90,500**	**461 / 90,497**		
Model	0.92 (0.82, 1.04)	0.98 (0.87, 1.10)	0.93 (0.82, 1.05)	1.04 (0.92, 1.17)	Ref	0.97 (0.93, 1.01)	0.09

Models were adjusted for age (years), sex (men or women), PRS (tertiles), education level (high [college or university degree], intermediate [A/AS levels or equivalent, O levels/GCSEs or equivalent], or low [none of the aforementioned]), TDI (quintiles), smoking status (current, past, or never), alcohol use (current, past, or never), have physical activity (yes or no), BMI (< 25.0, 25–29.9, or ≥ 30 kg/m^2), and sleep score (healthy sleep pattern, intermediate sleep pattern, or poor sleep pattern), hypertension (yes or no), diabetes (yes or no), high cholesterol (yes or no), cancer (yes or no), $PM_{2.5}$ (low or high), and NO_2 (low or high).

Data with p–value <0.05 are presented in bold.