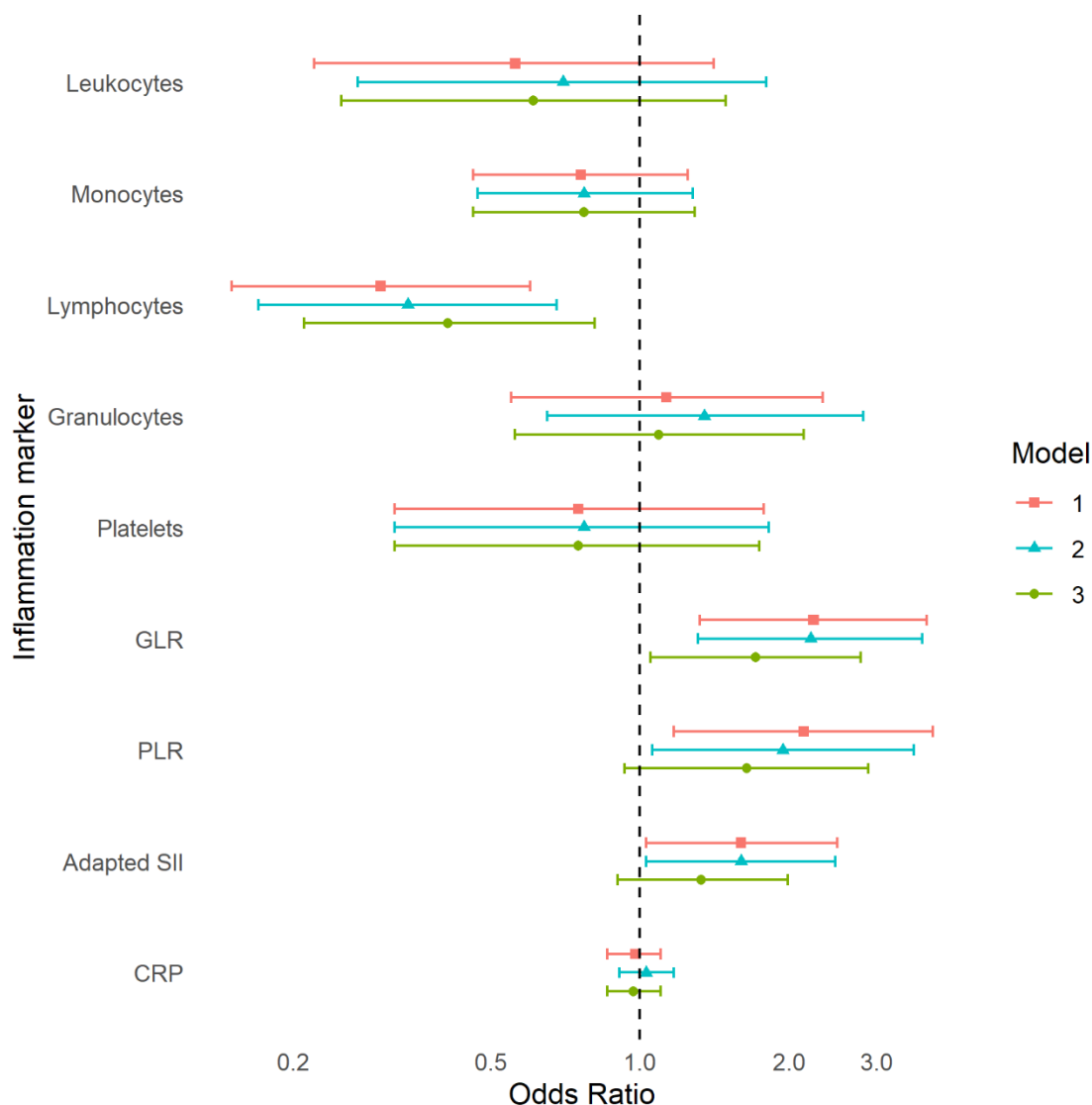


Supplementary Material

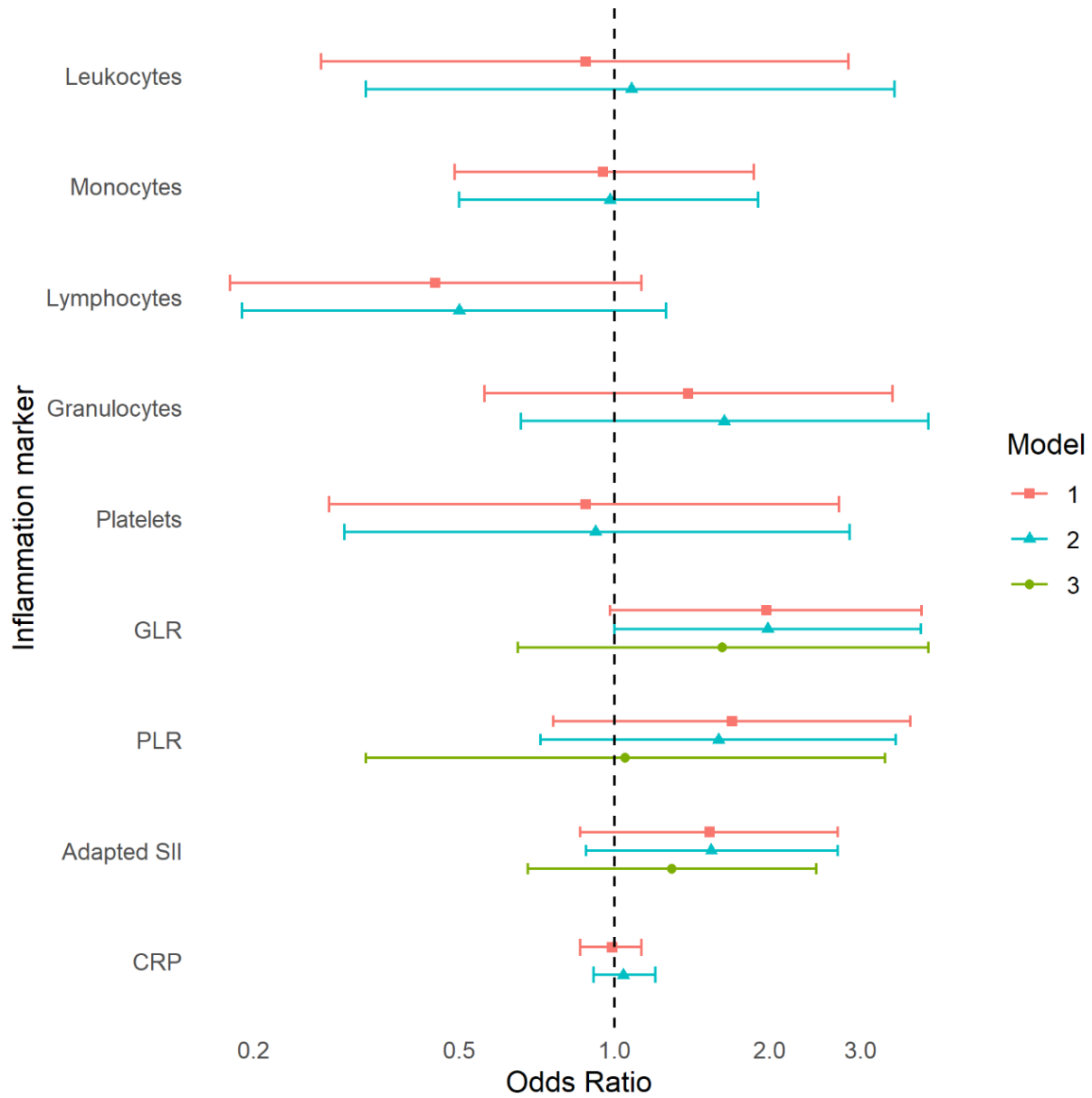
Peripheral Immune Cell Numbers and C-Reactive Protein in Parkinson's Disease: Results from a Population-Based Study

Supplementary Figure 1. Association between peripheral immune cell numbers, CRP, and prevalent Parkinson's disease adjusted for anti-parkinsonian drugs



GRL, granulocyte-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; Adapted SII, adapted systemic immune-inflammation index; CRP, C-reactive protein. Odds ratios are shown per doubling of the marker. Model 1 was adjusted for age and sex. Model 2 was adjusted for age, sex, BMI, smoking, and immune system influencing drugs. Model 3 was adjusted for age, sex, BMI, smoking, immune system influencing drugs, and anti-parkinsonian drugs. A total of 8,553 participants were included in the analyses with leukocytes, 8,550 in analyses with monocytes and lymphocytes, 8,551 in analyses with granulocytes, 8,552 in analyses with platelets, 8,550 in analyses with GLR, 8,548 in analyses with PLR and adapted SII, and 12,426 in analyses with CRP. Prevalent Parkinson's disease was found in 34 participants for all analyses except for analyses with CRP, which included 105 participants with prevalent Parkinson's disease. p-values model 1: Leukocytes: 0.22, Monocytes: 0.28, Lymphocytes: 0.001, Granulocytes: 0.74, Platelets: 0.51, GLR: 0.003, PLR: 0.01, Adapted SII: 0.04, CRP: 0.70. p-values model 2: Leukocytes: 0.46, Monocytes: 0.32, Lymphocytes: 0.002, Granulocytes: 0.42, Platelets: 0.55, GLR: 0.003, PLR: 0.03, Adapted SII: 0.04, CRP: 0.62. p-values model 3: Leukocytes: 0.28, Monocytes: 0.33, Lymphocytes: 0.01, Granulocytes: 0.79, Platelets: 0.50, GLR: 0.03, PLR: 0.09, Adapted SII: 0.15, CRP: 0.66.

Supplementary Figure 2. Association between peripheral immune cell numbers, CRP, and prevalent Parkinson’s disease in subset without comorbidities



GRL, granulocyte-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; Adapted SII, adapted systemic immune-inflammation index; CRP, C-reactive protein. Measurements of participants with cancer, heart failure, COPD, and asthma at the time of the measurement were excluded. Odds ratios are shown per doubling of the marker. Model 1 was adjusted for age and sex. Model 2 was adjusted for age, sex, BMI, smoking, and immune system influencing drugs. Model 3 was adjusted for age, sex, BMI, smoking, immune system influencing drugs, and lymphocytes. A total of 5,550 participants were included in the analyses with leukocytes, 5,548 in analyses with monocytes, granulocytes and platelets, 5,547 in analyses with lymphocytes and GLR, 5,545 in analyses with PLR and adapted SII, and 9,822 in analyses with CRP. Prevalent Parkinson’s disease was found in 22 participants for all analyses except for analyses with CRP, which included 83 participants with prevalent Parkinson’s disease. p-values model 1: Leukocytes: 0.83, Monocytes: 0.89, Lymphocytes: 0.09, Granulocytes: 0.48, Platelets: 0.82, GLR: 0.06, PLR: 0.20, Adapted SII: 0.15, CRP: 0.85. p-values model 2: Leukocytes: 0.90, Monocytes: 0.94, Lymphocytes: 0.14, Granulocytes: 0.29, Platelets: 0.89, GLR: 0.05, PLR: 0.25, Adapted SII: 0.13, CRP: 0.56. p-values model 3: GLR: 0.30, PLR: 0.93, Adapted SII: 0.33.

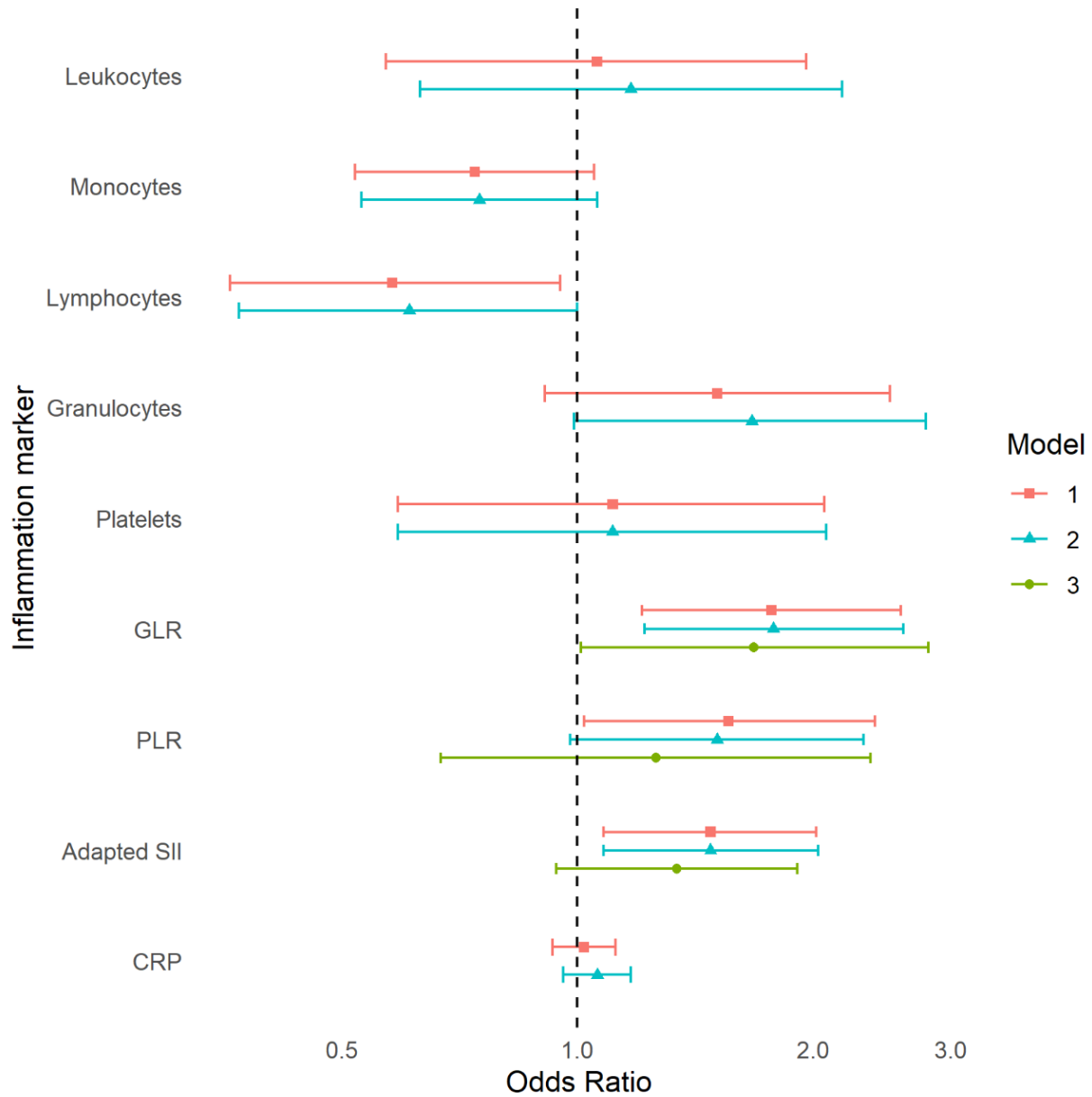
Supplementary Table 1. Association between peripheral immune cell numbers, CRP, and the risk of incident Parkinson's disease in subset without comorbidities

Laboratory assessment	n/N	Incident Parkinson's disease			
		Hazard ratio (95% CI)			
		Model 1	p	Model 2	p
Blood cell types					
Leukocytes	62/6,484	1.00 (0.37-2.67)	1.00	1.24 (0.46-3.36)	0.67
Monocytes	62/6,483	2.21 (0.60-8.13) ^a	0.23	2.46 (0.66-9.24) ^b	0.18
Lymphocytes	62/6,482	1.06 (0.52-2.17)	0.87	1.08 (0.52-2.23) ^b	0.84
Granulocytes	62/6,483	1.18 (0.50-2.79)	0.71	1.30 (0.54-3.14)	0.56
Platelets	62/6,484	0.58 (0.24-1.41)	0.23	0.59 (0.24-1.44) ^b	0.25
Blood cell-based ratios					
GLR	62/6,482	1.09 (0.57-2.09)	0.80	1.11 (0.58-2.13)	0.76
PLR	62/6,481	0.70 (0.40-1.19)	0.19	0.69 (0.40-1.20)	0.19
Adapted SII	62/6,481	0.75 (0.46-1.24)	0.26	0.77 (0.47-1.28) ^b	0.32
CRP	147/10,464	1.06 (0.90-1.26)	0.49	1.10 (0.91-1.33)	0.33

n, number of PD; N, total number; GRL, granulocyte-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; Adapted SII, adapted systemic immune-inflammation index; CRP, C-reactive protein. Measurements of participants with cancer, heart failure, COPD, and asthma at the time of the measurement were excluded. Hazard ratios are shown per doubling of the inflammation marker, confidence intervals are shown in the parentheses. Model 1 was adjusted for age and sex. Model 2 was adjusted for age, sex, BMI, smoking, and immune system influencing drugs.

^aModel with diagonal covariance matrix and only random intercepts was fitted because of convergence issues. ^bModel with diagonal covariance matrix was fitted because of convergence issues.

Supplementary Figure 3. Association between peripheral immune cell numbers, CRP, and prevalent parkinsonism



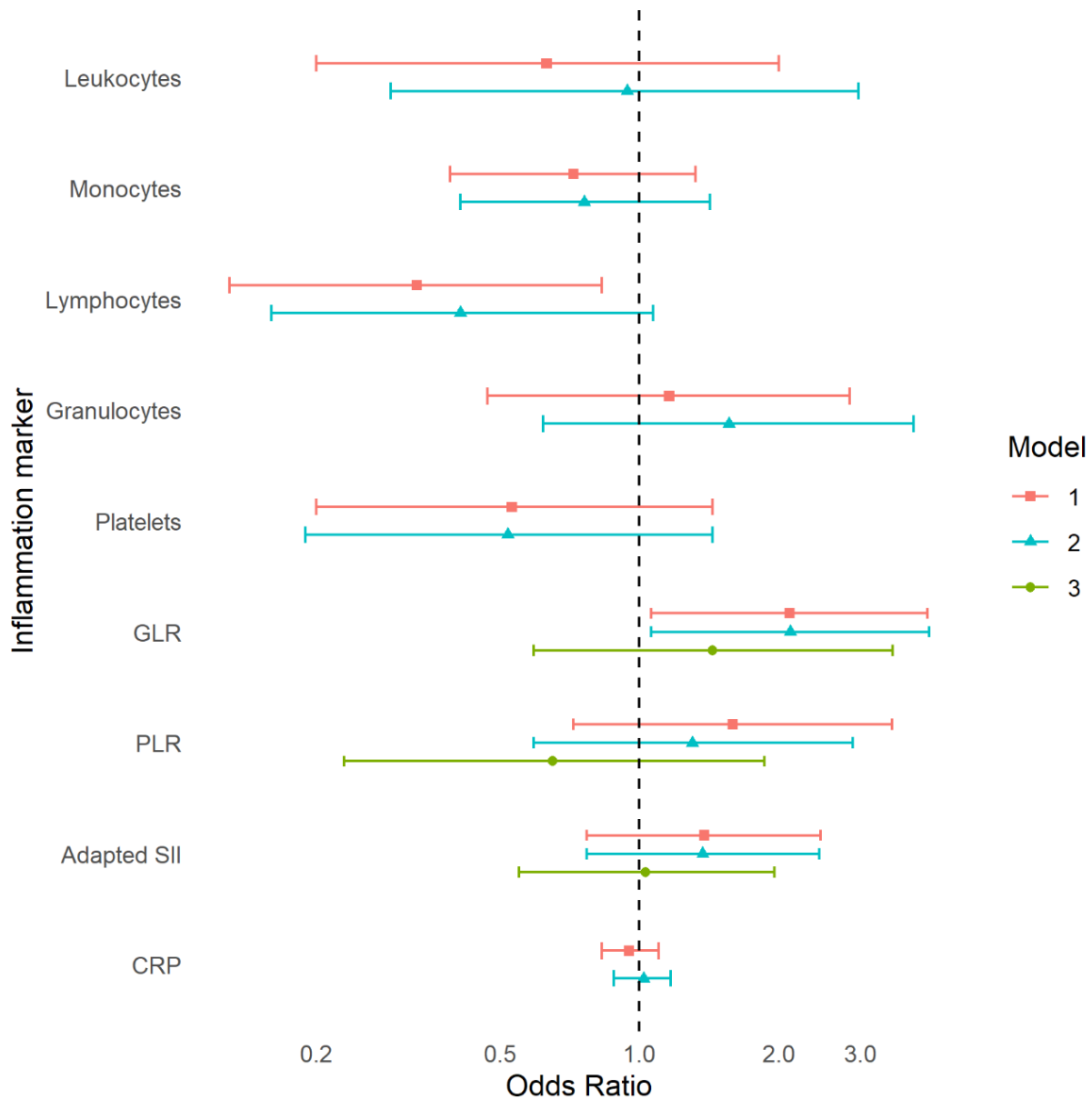
GRL, granulocyte-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; Adapted SII, adapted systemic immune-inflammation index; CRP, C-reactive protein. Odds ratios are shown per doubling of the marker. Model 1 was adjusted for age and sex. Model 2 was adjusted for age, sex, BMI, smoking, and immune system influencing drugs. Model 3 was adjusted for age, sex, BMI, smoking, immune system influencing drugs, and lymphocytes. A total of 8,553 participants were included in the analyses with leukocytes, 8,550 in analyses with monocytes and lymphocytes, 8,551 in analyses with granulocytes, 8,552 in analyses with platelets, 8,550 in analyses with GRL, 8,548 in analyses with PLR and adapted SII, and 12,426 in analyses with CRP. Prevalent parkinsonism was found in 69 participants for the analyses with leukocytes, monocytes, lymphocytes, granulocytes, and GRL, 68 for analyses with platelets, PLR, and adapted SII, and 174 for analysis with CRP. p-values model 1: Leukocytes: 0.86, Monocytes: 0.10, Lymphocytes: 0.03, Granulocytes: 0.11, Platelets: 0.74, GRL: 0.003, PLR: 0.04, Adapted SII: 0.02, CRP: 0.66. p-values model 2: Leukocytes: 0.61, Monocytes: 0.11, Lymphocytes: 0.05, Granulocytes: 0.05, Platelets: 0.74, GRL: 0.002, PLR: 0.06, Adapted SII: 0.01, CRP: 0.22. p-values model 3: GRL: 0.05, PLR: 0.48, Adapted SII: 0.11.

Supplementary Table 2. Association between peripheral immune cell numbers, CRP, and the risk of incident parkinsonism

Laboratory assessment	n/N	Incident parkinsonism			
		Hazard ratio (95% CI)			
		Model 1	p	Model 2	p
Blood cell types					
Leukocytes	138/8.435	0.75 (0.39-1.45)	0.39	0.90 (0.46-1.75)	0.76
Monocytes	138/8.432	1.63 (0.73-3.68) ^a	0.24	1.74 (0.77-3.92) ^a	0.18
Lymphocytes	138/8.432	0.96 (0.61-1.53)	0.88	0.94 (0.59-1.50)	0.80
Granulocytes	138/8.433	0.87 (0.49-1.55)	0.80	0.95 (0.53-1.71)	0.87
Platelets	138/8.435	0.71 (0.43-1.19)	0.20	0.68 (0.38-1.22) ^b	0.20
Blood cell-based ratios					
GLR	138/8.432	1.01 (0.68-1.52)	0.95	1.03 (0.68-1.55)	0.89
PLR	138/8.431	0.80 (0.57-1.12)	0.19	0.77 (0.55-1.07)	0.12
Adapted SII	138/8.431	0.78 (0.58-1.06)	0.11	0.79 (0.58-1.07)	0.13
CRP	322/12.132	0.92 (0.82-1.04)	0.17	0.94 (0.83-1.07) ^b	0.33

n, number of PD; N, total number; GRL, granulocyte-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; Adapted SII, adapted systemic immune-inflammation index; CRP, C-reactive protein. Hazard ratios are shown per doubling of the inflammation marker, confidence intervals are shown in the parentheses. Model 1 was adjusted for age and sex. Model 2 was adjusted for age, sex, BMI, smoking, and immune system influencing drugs. ^aModel with diagonal covariance matrix and only random intercepts was fitted because of convergence issues. ^bModel with diagonal covariance matrix was fitted because of convergence issues.

Supplementary Figure 4. Association between the first measurement of peripheral immune cell numbers and CRP and prevalent Parkinson's disease



GRL, granulocyte-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; Adapted SII, adapted systemic immune-inflammation index; CRP, C-reactive protein. Odds ratios are shown per doubling of the marker. Model 1 was adjusted for age and sex. Model 2 was adjusted for age, sex, BMI, smoking, and immune system influencing drugs. Model 3 was adjusted for age, sex, BMI, smoking, immune system influencing drugs, and lymphocytes. A total of 8,553 participants were included in the analyses with leukocytes, 8,550 in analyses with monocytes and lymphocytes, 8,551 in analyses with granulocytes, 8,552 in analyses with platelets, 8,550 in analyses with GLR, 8,548 in analyses with PLR and adapted SII, and 12,426 in analyses with CRP. Prevalent Parkinson's disease was found in 22 participants for all analyses except for analyses with CRP, which included 84 participants with prevalent Parkinson's disease. p-values model 1: Leukocytes: 0.43, Monocytes: 0.29, Lymphocytes: 0.02, Granulocytes: 0.75, Platelets: 0.22, GLR: 0.03, PLR: 0.25, Adapted SII: 0.28, CRP: 0.50. p-values model 2: Leukocytes: 0.91, Monocytes: 0.39, Lymphocytes: 0.07, Granulocytes: 0.35, Platelets: 0.21, GLR: 0.03, PLR: 0.52, Adapted SII: 0.28, CRP: 0.82. p-values model 3: GLR: 0.43, PLR: 0.43, Adapted SII: 0.92.

Supplementary Table 3. Association between first measurement of peripheral immune cell numbers and CRP and the risk of incident Parkinson’s disease

Incident Parkinson’s disease					
Laboratory assessment	n/N	Hazard ratio (95% CI)			
		Model 1	p	Model 2	p
Blood cell types					
Leukocytes	73/8.435	0.93 (0.69-1.26)	0.64	0.97 (0.73-1.29)	0.91
Monocytes	73/8.432	1.06 (0.93-1.22)	0.39	1.06 (0.93-1.21)	0.36
Lymphocytes	73/8.432	0.90 (0.61-1.34)	0.61	0.93 (0.64-1.34)	0.74
Granulocytes	73/8.433	0.94 (0.72-1.23)	0.66	0.98 (0.75-1.28)	0.99
Platelets	73/8.435	0.86 (0.66-1.12)	0.25	0.87 (0.66-1.14)	0.29
Blood cell-based ratios					
GLR	73/8.432	0.98 (0.77-1.26)	0.89	1.00 (0.78-1.28)	0.97
PLR	73/8.431	0.94 (0.74-1.21)	0.64	0.94 (0.73-1.20)	0.52
SII	73/8.431	0.96 (0.74-1.24)	0.76	0.98 (0.76-1.26)	0.85
CRP	160/12.132	0.95 (0.76-1.19)	0.65	0.97 (0.78-1.20)	0.81

n, number of PD; N, total number; GRL, granulocyte-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; Adapted SII, adapted systemic immune-inflammation index; CRP, C-reactive protein. Hazard ratios are shown per SD increase of the inflammation marker, confidence intervals are shown in the parentheses. Model 1 was adjusted for age and sex. Model 2 was adjusted for age, sex, BMI, smoking, and immune system influencing drugs.