

Supplementary material

Supplementary Table 1 ICD codes for identification of inflammatory bowel disease, colorectal cancer and celiac disease.

Diagnosis	ICD-7 up to 1968	ICD-8 1969-1986	ICD-9 1987-1996	ICD-10 1997 onward
Inflammatory bowel disease				
Ulcerative colitis (UC)	572.20, 572.21	563.10, 563.99, 569.02	556	K51
Crohn's disease (CD)	572.00, 572.09	563.00	555	K50
Unclassified (IBD-U)	UC+CD	UC+CD	UC+CD	UC + CD, or K52.3
Colorectal cancer	153,154	153,154	153,154	C18,C19,C20,C21
Celiac disease	286.00	269.00	579A	K900

Supplementary Table 2 ICD codes for identifying comorbidity

	ICD-7 up to 1968	ICD-8 1969-1986	ICD-9 1987-1996	ICD-10 1997 onward
- Myocardial infarction	420.1	410, 411	410.x, 412.x	I21.x, I22.x, I25.2
- Congestive heart failure	434.1, 434.2	427.0, 427.1,428,782.4	428	I09.9, I11.0, I13.0, I13.2, I25.5, I42.0, I42.5-I42.9, I43.x, I50.x, P29.0
- Peripheral vascular disease^a	450.x, 451, 453.3, 455	441, 443.9, 445	441,443.9,785.4, V43.4	I70.x, I71.x, I73.1, I73.8, I73.9, I77.1, I79.0, I79.2, K55.1, K55.8, K55.9, Z95.8, Z95.9
- Cerebrovascular disease	330-334	430-438	430.x-438.x	G45.x, G46.x, H34.0, I60.x-I69.x
- Chronic obstructive pulmonary disease (COPD)	502	491, 492	491,492,496	J41-J44
- Other chronic pulmonary disease^b	523-524	515-517	500-505, 506.4	J60.x-J67.x, J68.4, J70.x, J70.3
- Rheumatologic disease	710.0, 726.3, 727 722.x, 525,	734.0, 734.1, 716.1, 712.1- 712.5, 515.9, 717.9	710.0, 710.1, 710.4, 714.0-714.2, 714.81, 725	M05.x, M06.x, M31.5, M32.x-M34.x, M35.1, M35.3, M36.0
- Osteoarthritis	723	713	715	M15-M19
- Dementia	304, 305, 308	290, 309, 293.4	290	F00.x-F03.x, F05.1, G30.x, G31.1
- Hemiplegia	357, 351, 352	344.1. 344.2	344.1, 342	G04.1, G11.4, G80.1, G80.2, G81.x, G82.x, G83.0-G83.4, G83.9
- Diabetes	260.09 (only in Swedish ICD)	250	250.0, 250.1, 250.2, 250.3,250.7	E10.0, E10.1, E10.6, E10.8, E10.9, E11.0, E11.1, E11.6, E11.8, E11.9, E12.0, E12.1, E12.6, E12.8, E12.9,

				E13.0, E13.1, E13.6, E13.8, E13.9, E14.0, E14.1, E14.6, E14.8, E14.9
- Diabetes with end organ damage	260.20-260.99 (only in Swedish ICD)	250.01-250.05; 250.07-250.09 (only in Swedish ICD)	250.4-250.6	E10.2-E10.5, E10.7, E11.2-E11.5, E11.7, E12.2-E12.5, E12.7, E13.2-E13.5, E13.7, E14.2-E14.5, E14.7
- Moderate or severe renal disease	592, 593, 603, 792	582, 583, 584, 593.2, 792, 593.0	582.x, 583-583.7, 585, 586, 588-588.9	I12.0, I13.1, N03.2-N03.7, N05.2-N05.7, N18.x, N19.x, N25.0, Z49.0-Z49.2, Z94.0, Z99.2
- Mild liver disease	581, 583	571.x, 573	571.2, 571.4, 571.5, 571.6	B18.x, K70.0-K70.3, K70.9, K71.3-K71.5, K71.7, K73.x, K74.x, K76.0, K76.2-K76.4, K76.8, K76.9, Z94.4
- Moderate or severe liver disease	581, 583, 462, 1	571.x, 573, 456.0	572.2, 572.3, 572.4, 572.8, 456.0-456.21	I85.0, I85.9, I86.4, I98.2, K70.4, K71.1, K72.1, K72.9, K76.5, K76.6, K76.7
- Ulcer disease	540, 541, 542	531-534	531-534	K25.x-K28.x
- Any malignancy, including leukemia and lymphoma	140-155, 157-164, 170-204	140-195, 200-209	140-172.9, 174-195.8, 200-208.9	C00.x-C26.x, C30.x-C34.x, C37.x-C41.x, C43.x, C45.x-C58.x, C60.x-C76.x, C81.x-C85.x, C88.x, C90.x-C97.x
- Metastatic cancer	156, 163, 165	196-199	196, 197, 198, 199.0, 199.1	C77.x- C80.x
- HIV/AIDS	not applicable	not applicable	042, 043, 044	B20.x-B22.x, B24.x

a. Also included surgery codes: 8884, 8885, 8815, 8816, 8817, 8818, 8886, 8887, 8825, 8826, 8827, 8828 from the Swedish Classification of Operations and Major Procedures. b. Other chronic pulmonary diseases including pneumoconiosis, and chronic respiratory conditions due fumes and vapors.

Supplementary Table 3 Irritable bowel syndrome diagnosis and risk of Parkinson's disease in nationwide nested case-control study: sensitivity analyses adjusting for simulated smoking status and constipation

	OR (95% CI) ^a	OR (95% CI) ^b	Approximate RR / E-value ^c (95% CI lower band) ^d
Non IBS	1	1	1
IBS	1.47 (1.30-1.66)	1.24 (1.10-1.40)	1.29 / 1.89 (1.64)

a: model conditional on sex and birth year matching pairs, country of birth, highest achieved education, COPD, comorbidity index, *simulated smoking status*; b. model conditional on sex and birth year matching pairs, country of birth, highest achieved education, COPD, comorbidity index, *simulated constipation status*, c. E-value gauges the robustness of the results to unmeasured confounding. A large E-value indicates more robust results. An E-value of 1.89 indicates that an unmeasured confounder associated with both IBS and PD by the relative risk of 1.89 each would explain away an approximate RR of 1.29 (equivalent to an OR of 1.44, CI: 1.27-1.63). d: The 95% CI lower band of the E-value (i.e. 1.64) was calculated for the 95% CI lower band of 1.27 for the IBS and PD association.

Supplementary Table 4 Irritable bowel syndrome diagnosis and risk of Parkinson’s disease in nationwide nested case-control study: sensitivity analyses restricting to primary PD register diagnosis and adjusting for number of hospital visits

	Restricted to primary PD diagnosis		Adjusting for number of hospital visits	
	PD/control ^a	OR (95% CI) ^a	PD/control ^b	OR (95% CI) ^b
Non IBS	29,106/873,904	1	56311/1,691,716	1
IBS	128/3,116	1.27 (1.07-1.52)	253/5,204	1.23 (1.08-1.40)
Years before index date				
<5	48/1,339	1.09 (0.82-1.46)	93/2,105	1.12 (0.91-1.38)
≥5	80/1,777	1.41 (1.13-1.77)	160/3,099	1.31 (1.11-1.53)
<10	88/2,070	1.30 (1.05-1.61)	166/3,331	1.27 (1.08-1.48)
≥10	40/1,046	1.21 (0.88-1.66)	87/1,873	1.17 (0.94-1.45)
Age at IBS diagnosis, years				
<50	20/572	1.09 (0.70-1.71)	28/766	0.93 (0.63-1.35)
≥50	108/2,544	1.31 (1.08-1.59)	225/4,438	1.28 (1.12-1.47)
Stratified by Sex				
Male	44/1,102	1.23 (0.91-1.67)	89/1,789	1.27 (1.02-1.57)
Female	84/2,014	1.29 (1.04-1.61)	164/3,415	1.21 (1.04-1.42)
Stratified by age on the index date, years				
<70	58/1,242	1.45 (1.11-1.88)	80/1,538	1.29 (1.03-1.62)
70-79	51/1,321	1.19 (0.90-1.58)	101/2,184	1.17 (0.95-1.42)
≥80	19/553	1.08 (0.68-1.71)	72/1,482	1.27 (1.00-1.61)

a. restricted to *primary PD cases* and controls, n=906,254, conditional on sex and birth year matching pairs, country of birth, highest achieved education, chronic obstructive pulmonary disease (COPD), comorbidity index. No statistically significant interaction was found between IBS and age at IBS diagnosis (*p for interaction* = 0.46). b. entire nested case-control study n=1,753,484, conditional on sex and birth year matching pairs, country of birth, highest achieved education, COPD, comorbidity index, *number of hospital visits*. No statistically significant interaction was found between IBS and age at IBS diagnosis (*p for interaction* = 0.11).