Supplemental material

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SUPPLEMENTAL MATERIAL

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Supplemental Table 1. International Classification of Diseases (ICD) and Anatomical Therapeutic Chemical Classification System (ATC) codes definitions used in the study and their positive predictive values (PPVs) in the Danish registries.

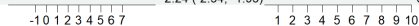| Condition	ICD-10 codes	ATC codes	PPV
Chronic obstructive pulmonary disease	J43-J44		92%[1]
Smoking-related cancers	C00-C06, C09-C22, C25, C32-C34, C39, C50, C65-C67		98%[2]
Non-smoking-related cancers	C00-C99 (excluding codes for smoking-related cancers)		98%[2]
Acute myocardial infarction	I21		97%[3]
Heart failure	I50, I110, I130, I132		76%[3]
Peripheral arterial disease	I70-I74		69%[4]
Stroke	I60-I64, I69		76-94%[2,5,6]
Venous thromboembolism	I801-I803, I26		88%[3]
Diabetes mellitus	E10-E14	A10A, A10B (≥2 prescriptions in last year before index/within one year for incident cases)	96%[2]
Chronic liver disease	K70-K74, K766, I85		100[2]
Ulcer/chronic gastritis	K211, K25-K28, K293-K295		98%[2]
Inflammatory bowel disease	K50-K51		82%[7]
Chronic kidney disease	N18		100%[2]
Prostate disorders	N40	C02CA, G04C (≥2 prescriptions in last year before index/within one year for incident cases)	
Connective tissue disorders	M05-M06, M08-M09, M30-M36, D86		98%[2]
Osteoporosis/hip fractures	M80-M82, S720, S721, S722	M05B, G03XC01, H05AA (≥2 prescriptions in last year before index/within one year for incident cases)	>90%[8]

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Migraine	G43	N02C (≥2 prescriptions in last year before index/within one year for incident cases)	Unknown
Dementia	F00-F03, F051, G30	N06D (≥2 prescriptions in last year before index/within one year for incident cases)	86-98%[2,9]
Mood, stress-related, or anxiety disorders	F32-F34, F40-F48	N06A (≥2 prescriptions in last year before index/within one year for incident cases)	65-83%[10]
Alcohol or substance abuse disorders	F101-F109, F11-F16, F18-F19		Unknown
Bipolar affective disorders	F30-F31		Unknown
Schizophrenia	F20, F25		97%[11]

Supplemental material

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Supplemental Figure 1. Five-year absolute risks among patients with chronic obstructive pulmonary disease (COPD), risk differences (RDs), and subdistribution hazard ratios (SHRs) for a spectrum of comorbidities, ranked according to the largest RD, comparing patients with COPD with matched individuals from the general population, stratified according to sex.

Comorbidity	5-year risk among COPD patients, % (95% CI)	RD, % (95% CI)	SHR (95% CI)
Mood, stress-related, or anxiety disorders			
Men	12.34 (12.05, 12.63)	5.11 (4.79, 5.44)	1.86 (1.81, 1.91)
Women	15.39 (15.05, 15.73)	6.21 (5.83, 6.59)	1.83 (1.78, 1.88)
Osteoporosis/hip fracture			
Men	8.05 (7.83, 8.29)	4.20 (3.95, 4.45)	2.18 (2.11, 2.26)
Women	15.60 (15.27, 15.93)	6.87 (6.51, 7.25)	1.86 (1.82, 1.91)
Heart failure			
Men	8.53 (8.29, 8.77)	4.54 (4.27, 4.80)	2.33 (2.26, 2.41)
Women	6.23 (6.03, 6.44)	3.83 (3.61, 4.04)	2.83 (2.72, 2.94)
Peripheral artery occlusive disease			
Men	6.14 (5.93, 6.35)	2.74 (2.51, 2.97)	1.89 (1.82, 1.96)
Women	4.61 (4.44, 4.79)	2.68 (2.49, 2.87)	2.50 (2.39, 2.61)
Smoking-related cancers			
Men	6.52 (6.32, 6.73)	2.75 (2.52, 2.98)	1.83 (1.77, 1.89)
Women	7.00 (6.79, 7.22)	2.85 (2.61, 3.09)	1.77 (1.72, 1.83)
Diabetes mellitus			
Men	6.60 (6.39, 6.83)	1.94 (1.69, 2.19)	1.47 (1.42, 1.52)
Women	5.08 (4.89, 5.27)	2.00 (1.80, 2.21)	1.70 (1.63, 1.77)
Chronic kidney disease			
Men	3.88 (3.73, 4.05)	1.54 (1.36, 1.71)	1.74 (1.66, 1.81)
Women	2.53 (2.41, 2.66)	1.36 (1.22, 1.50)	2.23 (2.12, 2.36)
Ulcer/chronic gastritis			
Men	2.93 (2.79, 3.08)	1.40 (1.25, 1.56)	1.99 (1.89, 2.09)
Women	2.67 (2.53, 2.80)	1.28 (1.14, 1.43)	2.00 (1.90, 2.12)
Venous thromboembolism			
Men	3.02 (2.88, 3.16)	1.23 (1.07, 1.38)	1.77 (1.68, 1.86)
Women	3.19 (3.05, 3.34)	1.47 (1.32, 1.63)	1.94 (1.85, 2.04)
Stroke			
Men	5.59 (5.39, 5.79)	0.73 (0.50, 0.96)	1.16 (1.12, 1.21)
Women	4.89 (4.89, 5.26)	1.06 (0.85, 1.27)	1.28 (1.23, 1.33)
Alcohol or substance abuse disorders			
Men	2.34 (2.21, 2.47)	1.49 (1.35, 1.63)	2.85 (2.68, 3.04)
Women	1.29 (1.20, 1.38)	0.86 (0.77, 0.96)	3.13 (2.88, 3.41)
Prostate disorders			
Men	8.81 (8.56, 9.07)	0.52 (0.22, 0.82)	1.07 (1.03, 1.10)
Women	0.39 (0.35, 0.44)	0.15 (0.09, 0.20)	1.65 (1.45, 1.88)
Acute myocardial infarction			
Men	2.96 (2.82, 3.11)	0.48 (0.32, 0.65)	1.23 (1.17, 1.30)
Women	2.37 (2.24, 2.49)	1.06 (0.93, 1.20)	1.87 (1.77, 1.98)
Chronic liver disease			
Men	1.53 (1.43, 1.63)	0.96 (0.86, 1.07)	2.84 (2.63, 3.05)
Women	1.00 (0.92, 1.08)	0.60 (0.52, 0.69)	2.61 (2.39, 2.85)
Connective tissue disorders			
Men	1.33 (1.24, 1.43)	0.19 (0.08, 0.30)	1.19 (1.11, 1.28)
Women	1.76 (1.66, 1.87)	0.17 (0.04, 0.29)	1.14 (1.07, 1.21)
Dementia			
Men	2.81 (2.68, 2.95)	-0.53 (-0.69, -0.36)	0.85 (0.81, 0.89)
Women	3.24 (3.10, 3.38)	-0.35 (-0.52, -0.18)	0.89 (0.85, 0.93)
Non-smoking-related cancers			
Men	5.06 (4.88, 5.25)	-1.57 (-1.80, -1.34)	0.77 (0.74, 0.80)
Women	3.11 (2.97, 3.26)	-0.53 (-0.70, -0.36)	0.87 (0.83, 0.91)

RD axis: -1 0 1 2 3 4 5 6   SHR axis: 0.5 1 2 3 4 5

Supplemental Figure 2. Five-year absolute risks among patients with chronic obstructive pulmonary disease (COPD), risk differences (RDs), and subdistribution hazard ratios (SHRs) for a spectrum of comorbidities, ranked according to the largest RD, comparing patients with COPD with matched individuals from the general population, stratified according to age group.

Comorbidity	5-year risk among COPD patients, % (95% CI)	RD, % (95% CI)	SHR (95% CI)
Mood, stress-related, or anxiety disorders			
Age 40-59 years	14.52 (13.96, 15.08)	8.52 (7.92, 9.13)	2.60 (2.48, 2.73)
Age 60-69 years	12.27 (11.86, 12.69)	7.06 (6.61, 7.51)	2.59 (2.48, 2.70)
Age 70-79 years	14.60 (14.21, 15.01)	5.91 (5.46, 6.36)	1.87 (1.81, 1.93)
Age ≥80 years	13.79 (13.34, 14.25)	1.39 (0.86, 1.93)	1.21 (1.17, 1.25)
Osteoporosis/hip fracture			
Age 40-59 years	7.90 (7.53, 8.27)	5.95 (5.57, 6.34)	4.35 (4.08, 4.63)
Age 60-69 years	11.48 (11.11, 11.86)	7.22 (6.82, 7.63)	2.85 (2.74, 2.97)
Age 70-79 years	13.26 (12.89, 13.65)	6.08 (5.66, 6.50)	1.94 (1.88, 2.01)
Age ≥80 years	12.62 (12.17, 13.08)	1.04 (0.51, 1.58)	1.10 (1.06, 1.15)
Heart failure			
Age 40-59 years	3.49 (3.25, 3.75)	2.79 (2.54, 3.06)	5.33 (4.81, 5.90)
Age 60-69 years	6.10 (5.83, 6.38)	4.37 (4.08, 4.67)	3.79 (3.57, 4.01)
Age 70-79 years	8.79 (8.49, 9.10)	5.07 (4.74, 5.40)	2.63 (2.53, 2.74)
Age ≥80 years	10.45 (10.06, 10.86)	3.64 (3.19, 4.09)	1.68 (1.61, 1.76)
Peripheral artery disease			
Age 40-59 years	2.97 (2.74, 3.21)	2.07 (1.83, 2.32)	3.40 (3.09, 3.74)
Age 60-69 years	5.85 (5.58, 6.13)	3.58 (3.29, 3.88)	2.72 (2.57, 2.87)
Age 70-79 years	7.14 (6.86, 7.42)	3.51 (3.20, 3.82)	2.09 (2.00, 2.18)
Age ≥80 years	4.46 (4.20, 4.73)	1.06 (0.77, 1.36)	1.36 (1.28, 1.44)
Smoking-related cancers			
Age 40-59 years	4.17 (3.90, 4.45)	2.32 (2.03, 2.62)	2.34 (2.17, 2.52)
Age 60-69 years	8.13 (7.82, 8.46)	4.00 (3.66, 4.35)	2.10 (2.01, 2.19)
Age 70-79 years	8.66 (8.36, 8.96)	3.76 (3.43, 4.09)	1.92 (1.84, 1.99)
Age ≥80 years	4.83 (4.57, 5.09)	0.40 (0.10, 0.71)	1.13 (1.07, 1.20)
Diabetes mellitus			
Age 40-59 years	6.96 (6.61, 7.33)	3.58 (3.19, 3.98)	2.13 (2.01, 2.26)
Age 60-69 years	6.92 (6.62, 7.22)	2.72 (2.38, 3.06)	1.71 (1.63, 1.79)
Age 70-79 years	6.02 (5.76, 6.29)	1.66 (1.37, 1.96)	1.42 (1.36, 1.49)
Age ≥80 years	3.34 (3.12, 3.57)	0.27 (0.01, 0.53)	1.12 (1.05, 1.20)
Chronic kidney disease			
Age 40-59 years	1.23 (1.09, 1.39)	0.93 (0.78, 1.09)	4.06 (3.48, 4.74)
Age 60-69 years	2.45 (2.29, 2.63)	1.55 (1.37, 1.73)	2.81 (2.59, 3.05)
Age 70-79 years	4.12 (3.92, 4.32)	1.94 (1.72, 2.16)	2.03 (1.92, 2.14)
Age ≥80 years	4.41 (4.17, 4.66)	1.04 (0.77, 1.32)	1.35 (1.28, 1.44)
Ulcer/chronic gastritis			
Age 40-59 years	2.27 (2.07, 2.48)	1.60 (1.40, 1.82)	3.60 (3.22, 4.02)
Age 60-69 years	2.85 (2.66, 3.04)	1.78 (1.58, 1.98)	2.80 (2.59, 3.02)
Age 70-79 years	3.26 (3.08, 3.45)	1.54 (1.34, 1.74)	1.99 (1.87, 2.12)
Age ≥80 years	2.54 (2.35, 2.73)	0.32 (0.10, 0.54)	1.19 (1.10, 1.28)
Venous thromboembolism			
Age 40-59 years	2.13 (1.94, 2.34)	1.38 (1.17, 1.59)	2.96 (2.66, 3.30)
Age 60-69 years	3.15 (2.95, 3.35)	1.80 (1.59, 2.01)	2.48 (2.31, 2.66)
Age 70-79 years	3.58 (3.39, 3.77)	1.50 (1.29, 1.72)	1.81 (1.71, 1.92)
Age ≥80 years	3.19 (2.99, 3.41)	0.57 (0.34, 0.82)	1.29 (1.20, 1.38)
Stroke			
Age 40-59 years	3.00 (2.78, 3.24)	1.70 (1.46, 1.96)	2.41 (2.21, 2.63)
Age 60-69 years	4.88 (4.64, 5.14)	2.03 (1.76, 2.31)	1.76 (1.67, 1.84)
Age 70-79 years	6.28 (6.02, 6.55)	1.01 (0.71, 1.31)	1.24 (1.19, 1.30)
Age ≥80 years	6.63 (6.32, 6.95)	-1.90 (-2.29, -1.50)	0.80 (0.76, 0.84)
Alcohol or substance abuse disorders			
Age 40-59 years	3.39 (3.13, 3.67)	2.77 (2.50, 3.05)	5.72 (5.09, 6.43)
Age 60-69 years	2.60 (2.42, 2.79)	1.79 (1.60, 1.99)	3.29 (3.02, 3.59)
Age 70-79 years	1.36 (1.24, 1.48)	0.66 (0.53, 0.79)	2.05 (1.87, 2.26)
Age ≥80 years	0.53 (0.45, 0.62)	0.17 (0.08, 0.27)	1.53 (1.30, 1.81)
Prostate disorders			
Age 40-59 years	2.00 (1.82, 2.19)	0.53 (0.32, 0.74)	1.38 (1.25, 1.52)
Age 60-69 years	4.58 (4.35, 4.83)	0.73 (0.46, 1.00)	1.20 (1.13, 1.26)
Age 70-79 years	5.48 (5.24, 5.72)	0.71 (0.44, 1.00)	1.08 (1.03, 1.13)
Age ≥80 years	3.53 (3.31, 3.77)	0.25 (-0.02, 0.53)	0.88 (0.82, 0.94)
Acute myocardial infarction			
Age 40-59 years	1.80 (1.63, 1.99)	0.86 (0.67, 1.07)	1.96 (1.76, 2.18)
Age 60-69 years	2.56 (2.39, 2.75)	1.12 (0.93, 1.32)	1.85 (1.71, 1.99)
Age 70-79 years	3.06 (2.88, 3.25)	0.92 (0.72, 1.13)	1.51 (1.42, 1.61)
Age ≥80 years	2.91 (2.71, 3.12)	0.09 (-0.15, 0.34)	1.06 (0.99, 1.14)
Chronic liver disease			
Age 40-59 years	2.28 (2.09, 2.49)	1.81 (1.61, 2.02)	5.10 (4.51, 5.77)
Age 60-69 years	1.76 (1.62, 1.91)	1.13 (0.97, 1.29)	2.93 (2.66, 3.23)
Age 70-79 years	0.94 (0.85, 1.04)	0.45 (0.35, 0.56)	2.03 (1.82, 2.26)
Age ≥80 years	0.37 (0.31, 0.45)	0.07 (-0.01, 0.15)	1.21 (1.00, 1.47)
Connective tissue disorders			
Age 40-59 years	1.45 (1.29, 1.62)	0.68 (0.51, 0.86)	1.98 (1.75, 2.23)
Age 60-69 years	1.63 (1.50, 1.78)	0.29 (0.13, 0.46)	1.27 (1.16, 1.39)
Age 70-79 years	1.93 (1.79, 2.07)	0.14 (-0.02, 0.31)	1.10 (1.02, 1.18)
Age ≥80 years	1.00 (0.89, 1.13)	-0.31 (-0.45, -0.16)	0.77 (0.69, 0.87)
Dementia			
Age 40-59 years	0.37 (0.29, 0.46)	0.19 (0.11, 0.29)	2.18 (1.72, 2.77)
Age 60-69 years	1.26 (1.14, 1.39)	0.40 (0.27, 0.54)	1.51 (1.36, 1.68)
Age 70-79 years	3.97 (3.77, 4.18)	-0.17 (-0.40, 0.07)	1.00 (0.95, 1.05)
Age ≥80 years	6.13 (5.84, 6.42)	-2.90 (-3.26, -2.54)	0.69 (0.66, 0.73)
Non-smoking-related cancers			
Age 40-59 years	2.27 (2.07, 2.48)	0.25 (0.03, 0.49)	1.15 (1.05, 1.26)
Age 60-69 years	4.30 (4.07, 4.53)	-0.43 (-0.70, -0.15)	0.95 (0.90, 1.00)
Age 70-79 years	4.99 (4.76, 5.22)	-1.60 (-1.88, -1.32)	0.77 (0.73, 0.80)
Age ≥80 years	3.99 (3.76, 4.24)	-2.24 (-2.54, -1.93)	0.66 (0.62, 0.70)

-1 0 1 2 3 4 5 6 7 | 1 2 3 4 5 6 7 8 9 10

Supplemental Figure 3. Five-year absolute risks among patients with chronic obstructive pulmonary disease (COPD), risk differences (RDs), and subdistribution hazard ratios (SHRs) for a spectrum of comorbidities, ranked according to the largest RD, comparing patients with COPD with matched individuals from the general population, after restricting the study population to those with ≥2 visits to a general practitioner within one year before the index date.

Comorbidity	5-year risk among COPD patients, % (95% CI)	RD, % (95% CI)	SHR (95% CI)
Mood, stress-related, or anxiety disorders	13.88 (13.66, 14.11)	4.90 (4.64, 5.16)	1.69 (1.65, 1.72)
Osteoporosis/hip fracture	11.66 (11.45, 11.86)	5.10 (4.87, 5.33)	1.86 (1.83, 1.90)
Heart failure	7.43 (7.27, 7.59)	3.99 (3.81, 4.17)	2.41 (2.35, 2.48)
Peripheral artery occlusive disease	5.40 (5.26, 5.54)	2.56 (2.41, 2.72)	1.99 (1.94, 2.05)
Smoking-related cancers	6.74 (6.59, 6.90)	2.65 (2.48, 2.82)	1.74 (1.70, 1.79)
Diabetes mellitus	5.82 (5.67, 5.96)	1.81 (1.65, 1.98)	1.45 (1.42, 1.50)
Chronic kidney disease	3.25 (3.15, 3.36)	1.30 (1.18, 1.41)	1.79 (1.73, 1.85)
Ulcer/chronic gastritis	2.80 (2.70, 2.90)	1.20 (1.09, 1.31)	1.84 (1.77, 1.91)
Venous thromboembolism	3.12 (3.02, 3.22)	1.27 (1.15, 1.38)	1.78 (1.72, 1.84)
Stroke	5.37 (5.24, 5.52)	0.68 (0.51, 0.84)	1.19 (1.15, 1.22)
Alcohol or substance abuse disorders	1.75 (1.67, 1.83)	1.13 (1.04, 1.21)	2.78 (2.64, 2.94)
Prostate disorders	4.16 (4.04, 4.29)	0.46 (0.32, 0.61)	1.03 (1.00, 1.06)
Acute myocardial infarction	2.67 (2.57, 2.77)	0.72 (0.61, 0.84)	1.42 (1.37, 1.48)
Chronic liver disease	1.25 (1.18, 1.31)	0.74 (0.68, 0.82)	2.51 (2.36, 2.66)
Connective tissue disorders	1.57 (1.50, 1.65)	0.10 (0.02, 0.19)	1.10 (1.05, 1.15)
Dementia	3.11 (3.01, 3.21)	-0.74 (-0.86, -0.61)	0.85 (0.82, 0.88)
Non-smoking-related cancers	4.09 (3.97, 4.21)	-1.20 (-1.35, -1.05)	0.79 (0.77, 0.81)

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