

Online Supplement

Coronary heart disease and heart failure

in asthma, COPD, and asthma-COPD overlap

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Table S1: Details of variables in the Copenhagen General Population Study.

<ul style="list-style-type: none"> • Smoking: never, former or current smoking (self-reported). • Family history of cardiovascular disease: mother diagnosed before 65 years of age, or father diagnosed before 55 years of age (self-reported). • Physical activity in leisure time: low (reports less than 2 hours of light physical activity per week in leisure time), moderate (reports light physical activity in leisure time 2-4 hours per week), high (reports light physical activity more than 4 hour per week or more strenuous physical activity 2-4 hours per week in leisure time), very high (reports more strenuous physical activity more than 4 hours per week in leisure time) (self-reported). 	<ul style="list-style-type: none"> • BMI: Body Mass Index in kg/m² as categorical variable: <18.5, 18.5-24.9, 25.0-29.9, >29.9 (calculated from clinical measurements of weight in kilograms and height in meters (two decimals) at the baseline examination). • Hypertension: blood-pressure above 140 mmHg systolic, or above 90 mmHg diastolic, or reported use of antihypertensive medications (clinically measured). • Diabetes: self-reported diabetes mellitus or a non-fasting blood glucose level ≥ 200 mg/dL (measured on plasma drawn at the day of each individuals baseline examination). • Total cholesterol: in mmol/L, measured on plasma drawn at the day of each individuals baseline examination. • HDL (High-Density Lipoprotein) cholesterol: in mmol/L, measured on plasma drawn at the day of each individuals baseline examination.
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Table S2. Baseline Characteristics* of 42,728 Individuals According to Different Phenotypes of Airway Disease with distribution according to presence/absence of allergy among individuals with asthma and asthma-COPD overlap (ACO).

	No Respiratory Disease (n=30,555)	Asthma no Allergy (n=367)	Asthma with Allergy (n=1,851)	COPD GOLD Stage 1+2 (n=7,447)	COPD GOLD Stage 3+4 (n=521)	ACO with GOLD Stage 1+2 and no Allergy (n=436)	ACO with GOLD Stage 1+2 and Allergy (n=1,230)	ACO with GOLD Stage 3+4 and no Allergy (n=134)	ACO with GOLD Stage 3+4 and Allergy (n=187)
General characteristics									
Men, %	12328/30555 (40)	112/367 (31)	612/1851 (33)	4151/7447 (56)	305/521 (59)	189/436 (43)	553/1230 (45)	67/134 (50)	80/187 (43)
Age, yrs	59 (11)	60 (12)	55 (10)	66 (11)	70 (9)	67 (11)	62 (12)	69 (9)	65 (10)
Respiratory characteristics									
FEV ₁ , liters	3.12 (0.81)	2.68 (0.79)	2.94 (0.80)	2.37 (0.72)	1.10 (0.31)	2.03 (0.69)	2.26 (0.74)	1.02 (0.30)	1.05 (0.32)
FEV ₁ , % of predicted	104 (13)	95 (15)	96 (14)	83 (17)	41 (7)	75 (15)	78 (15)	40 (8)	39 (8)
FEV ₁ /FVC, %	79 (5)	78 (5)	78 (5)	64 (6)	50 (10)	62 (6)	63 (6)	50 (9)	48 (9)
mMRC ≥ 2, %	1352/30389 (4)	72/363 (20)	245/1841 (13)	1152/7393 (16)	298/520 (57)	127/435 (29)	267/1222 (22)	96/133 (72)	121/186 (65)
At least 5 respiratory infections during preceding 10 years, %	151/30155 (1)	26/364 (7)	187/1841 (10)	233/7348 (3)	68/506 (13)	51/429 (12)	148/1219 (12)	39/132 (30)	52/186 (28)
Medication for airway disease, %	135/30178 (0)	263/367 (72)	1162/1836 (63)	449/7346 (6)	194/504 (38)	350/433 (81)	957/1218 (79)	124/134 (93)	171/187 (91)
Asthma, hay fever or eczema as child, %	1425/30499 (5)	85/361 (24)	894/1836 (49)	616/7413 (8)	31/517 (6)	82/431 (19)	587/1219 (48)	15/132 (11)	72/186 (39)
Current allergy	0/30555 (0)	0/367 (0)	1851/1851 (100)	1329/7417 (18)	65/516 (13)	0/436 (0)	1230/1230 (100)	0/134 (0)	187/187 (100)
Cardiovascular risk factors									
Smoking, %									
Never	20074/30366 (66)	238/364 (65)	1213/1844 (66)	0/7326 (0)	0/509 (0)	91/415 (22)	399/1198 (33)	11/129 (9)	28/182 (15)
Former	8954/30366 (29)	114/364 (31)	578/1844 (31)	3915/7326 (53)	261/509 (51)	225/415 (54)	586/1198 (49)	68/129 (53)	79/182 (43)
Current	1338/30366 (4)	12/364 (3)	53/1844 (3)	3411/7326 (47)	248/509 (49)	99/415 (24)	213/1198 (18)	50/129 (39)	75/182 (41)
Packyrs, yrs	2 (3)	2 (3)	2 (3)	36 (23)	46 (26)	25 (27)	16 (22)	41 (27)	29 (24)
Systolic blood pressure, mmHg	138 (21)	140 (23)	136 (20)	142 (21)	146 (24)	143 (20)	140 (21)	144 (21)	147 (22)
Blood pressure medication, %	5709/30306 (19)	80/364 (22)	342/1840 (19)	2166/7385 (29)	174/511 (34)	141/435 (32)	296/1219 (24)	49/133 (37)	57/187 (30)
Diabetes, %	914/30441 (3)	12/363 (3)	54/1845 (3)	412/7416 (6)	37/518 (7)	31/435 (7)	63/1225 (5)	11/133 (8)	18/186 (10)
Body mass index, kg/m ²	26 (4)	27 (5)	27 (5)	26 (4)	26 (5)	26 (4)	26 (4)	26 (5)	27 (5)

Family history of CVD, %	1571/30309 (5)	13/364 (4)	105/1843 (6)	381/7375 (5)	20/510 (4)	29/432 (7)	54/1213 (4)	7/133 (5)	9/184 (5)
Total cholesterol, mmol/l	5.6 (1.0)	5.8 (1.1)	5.7 (1.1)	5.6 (1.1)	5.6 (1.2)	5.7 (1.2)	5.7 (1.1)	5.6 (1.2)	5.8 (1.0)
HDL cholesterol, mmol/l	1.68 (0.51)	1.70 (0.59)	1.64 (0.47)	1.61 (0.54)	1.68 (0.57)	1.70 (0.56)	1.72 (0.57)	1.68 (0.52)	1.85 (0.62)
Physical activity in leisure time, %									
Low	1312/30382 (4)	20/362 (6)	118/1838 (6)	665/7365 (9)	83/516 (16)	34/430 (8)	92/1215 (8)	27/129 (21)	36/182 (20)
Moderate	12240/30382 (40)	146/362 (40)	768/1838 (42)	3421/7365 (46)	292/516 (57)	198/430 (46)	542/1215 (45)	66/129 (51)	98/182 (54)
High	14717/30382 (48)	170/362 (47)	821/1838 (45)	2907/7365 (39)	125/516 (24)	176/430 (41)	503/1215 (41)	31/129 (24)	46/182 (25)
Very high	2113/30382 (7)	26/362 (7)	131/1838 (7)	372/7365 (5)	16/516 (3)	22/430 (5)	78/1215 (6)	5/129 (4)	2/182 (1)
Previous admissions CHD or heart failure, %	1356/30555 (4)	31/367 (8)	87/1851 (5)	891/7447 (12)	103/521 (20)	50/436 (11)	112/1230 (9)	34/134 (25)	33/187 (18)

*Continuous variables are presented as mean (SD). *Continuous variables are presented as mean (SD). CHD=coronary heart disease; CVD=cardiovascular disease; FEV₁=forced expiratory volume in one second; FVC=forced vital capacity; HDL=high-density lipoprotein; mMRC=modified Medical Research Council dyspnea scale.

Figure S1

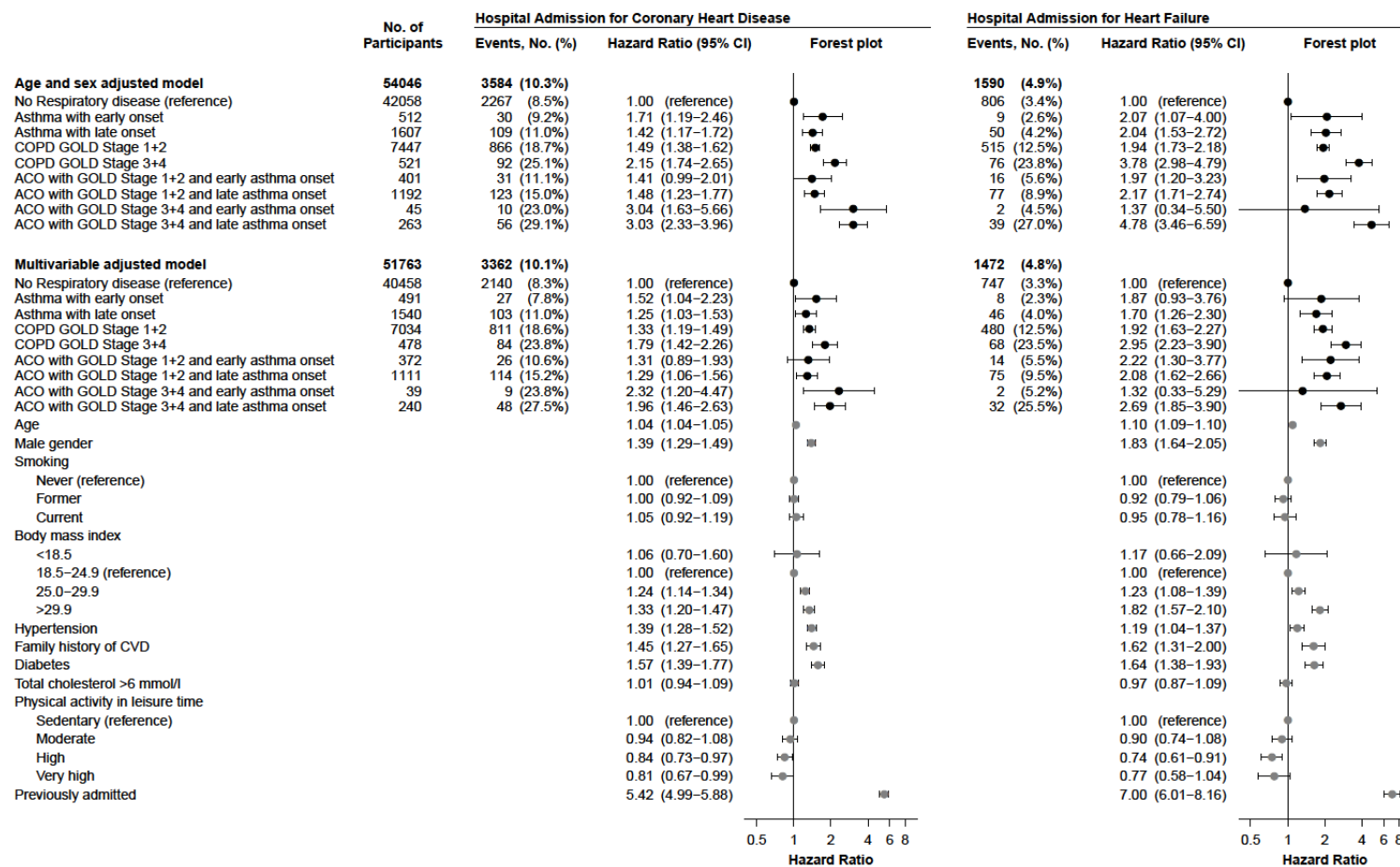


Figure S1: Risk of hospitalizations for coronary heart disease or heart failure in the Copenhagen General Population Study, by eight phenotypes of airway disease with no respiratory disease as reference. Asthma individuals are divided by early versus late onset using twenty years of age as cut-point. Percentages are Kaplan-Meier estimates. Left part shows coronary heart disease and right part shows heart failure. Top-down: base model or multivariable model ("Age and sex adjusted model" or "Multivariable adjusted model"), the number of

participants included ("No. of Participants"), number of events recorded during follow-up ("Events No."), hazard ratio from Cox-regression analyses with 95% confidence intervals ("Hazard Ratio (95% CI)"). ACO=asthma-COPD overlap; COPD=Chronic Obstructive Pulmonary Disease; FEV₁=forced expiratory volume in one second. Table S1 in the Online Data Supplement shows details of variables included in multivariable modeling.

Figure S2

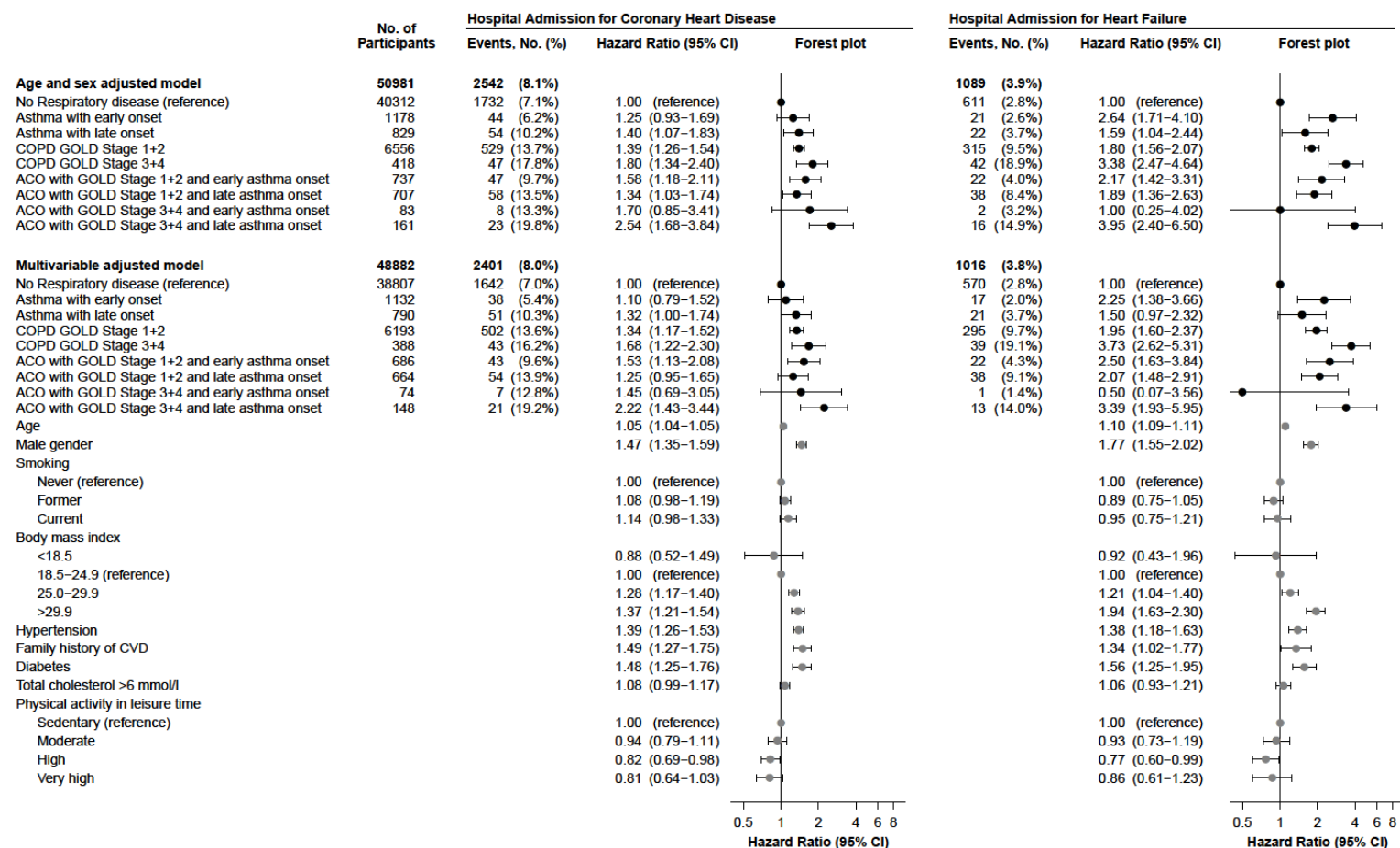


Figure S2: Risk of hospitalizations for coronary heart disease or heart failure in the Copenhagen General Population Study, by eight phenotypes of airway disease with no respiratory disease as reference. Individuals with previous admissions of coronary heart disease or

heart failure have been excluded from the analysis. Percentages are Kaplan-Meier estimates. Left part shows coronary heart disease and right part shows heart failure. Top-down: base model or multivariable model ("Age and sex adjusted model" or "Multivariable adjusted model"), the number of participants included ("No. of Participants"), number of events recorded during follow-up ("Events No."), hazard ratio from Cox-regression analyses with 95% confidence intervals ("Hazard Ratio (95% CI)"). ACO=asthma-COPD overlap; COPD=Chronic Obstructive Pulmonary Disease; FEV₁=forced expiratory volume in one second. Table S1 in the Online Data Supplement shows details of variables included in multivariable modeling.

Figure S3

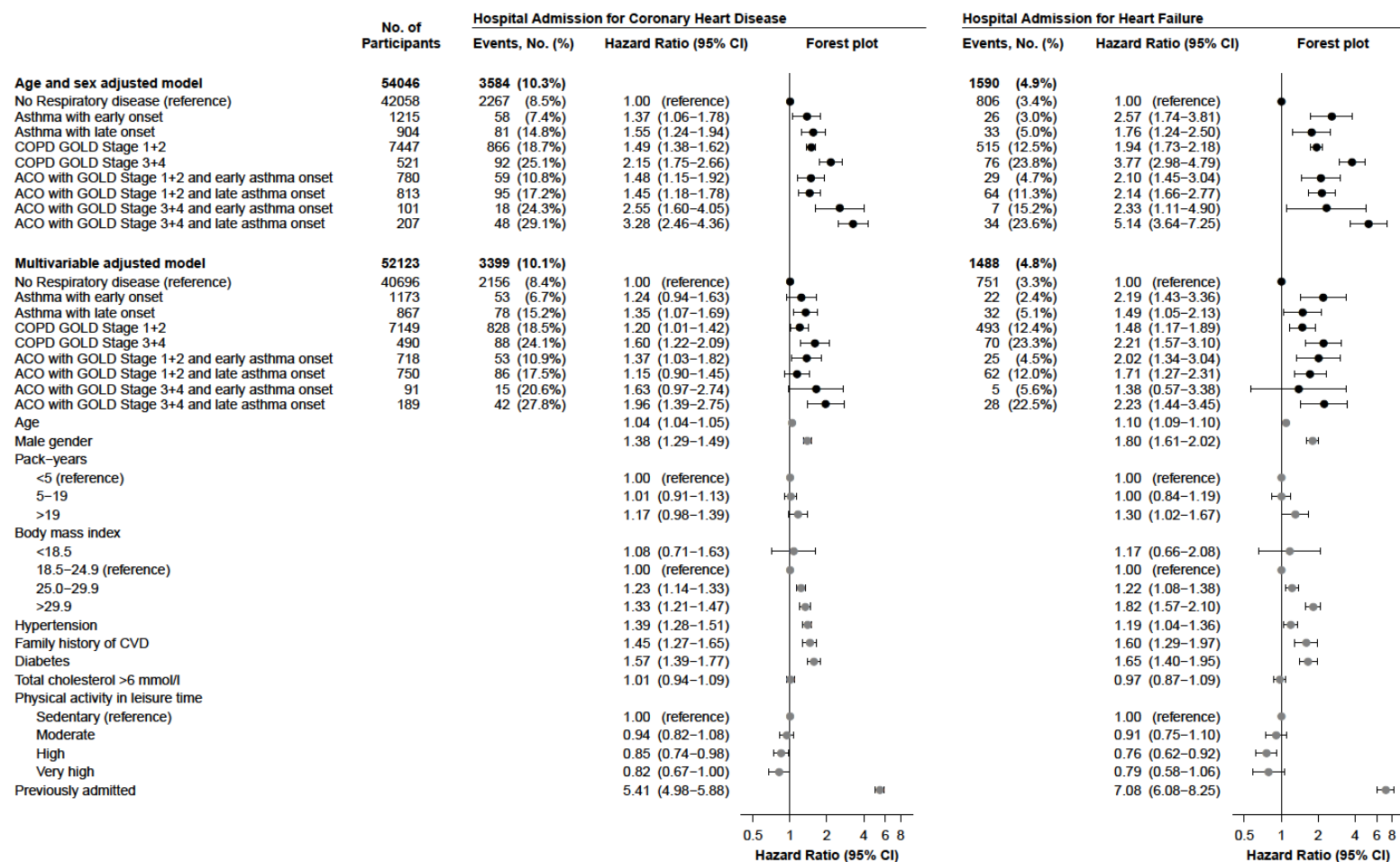


Figure S3: Risk of hospitalizations for coronary heart disease or heart failure in the Copenhagen General Population Study, by eight phenotypes of airway disease with no respiratory disease as reference. The multivariable model includes cumulated smoking exposure in

pack-years as covariate. Percentages are Kaplan-Meier estimates. Left part shows coronary heart disease and right part shows heart failure. Top-down: base model or multivariable model ("Age and sex adjusted model" or "Multivariable adjusted model"), the number of participants included ("No. of Participants"), number of events recorded during follow-up ("Events No."), hazard ratio from Cox-regression analyses with 95% confidence intervals ("Hazard Ratio (95% CI)"). ACO=asthma-COPD overlap; COPD=Chronic Obstructive Pulmonary Disease; FEV₁=forced expiratory volume in one second. Table S1 in the Online Data Supplement shows details of variables included in multivariable modeling.