

## **Supplemental material**

**Plasma urate, lung function, and chronic obstructive pulmonary disease: a Mendelian randomization study in 114 979 individuals from the general population**

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**Supplemental Table 1. The association of baseline characteristics with urate tertiles, COPD and the urate allele score in the Copenhagen City Heart Study.**

	Urate tertiles				COPD			Allele score
	1 <sup>st</sup>	2 <sup>nd</sup>	3 <sup>rd</sup>	<i>P</i>	No	Yes	<i>P</i>	<i>P</i>
No. of participants	3 396	3 233	3 150		8 010	1 194		
Plasma urate, $\mu\text{mol/L}$	226 (194-270)	300 (269-344)	387 (340-430)		300(240-360)	310(254-365)	$2 \times 10^{-4}$	$2 \times 10^{-53}$
Men, n (%)	1 492(44)	1 390(43)	1 419(45)	0.38	3 391(42)	668(56)	$9 \times 10^{-19}$	0.83
Age, years	55(41-67)	59(44-69)	63(52-71)	$6 \times 10^{-53}$	58(43-69)	64(54-71)	$7 \times 10^{-28}$	0.68
Ever smokers, n (%)	2 458 (72)	2 372 (73)	2 325 (74)	0.19	5 603(70)	1 081(91)	$4 \times 10^{-50}$	0.10
Cumulative tobacco consumption, pack-years	18(7-33)	19(8-34)	20(9-38)	$2 \times 10^{-6}$	17(7-31)	31(16-45)	$1 \times 10^{-70}$	0.79
Body mass index, $\text{kg/m}^2$	24(22-26)	25(22-27)	27(24-30)	$8 \times 10^{-179}$	25(22-28)	24(22-27)	$1 \times 10^{-11}$	0.33
Alcohol consumption, g/week	60(12-132)	72(24-144)	84(24-180)	$3 \times 10^{-18}$	72(24-144)	84(24-180)	$6 \times 10^{-4}$	0.52
High income, n (%)	666 (20)	570 (17)	428 (13)	$1 \times 10^{-10}$	1 452(18)	132(11)	$1 \times 10^{-9}$	0.28
High physical activity in leisure time, n (%)	167(5)	129(4)	116(4)	0.01	342(42)	44(4)	0.34	0.50
High education, n (%)	849(25)	694(21)	481(15)	$4 \times 10^{-22}$	1 782(22)	144(12)	$7 \times 10^{-16}$	0.43
Exposure to occupational dust and fumes, n (%)	531(16)	554(18)	586(18)	$6 \times 10^{-4}$	1 189(15)	303(25)	$3 \times 10^{-24}$	0.06
High intake of meat, % *								
Preexisting cardiovascular disease, n (%)	122(3)	112(3)	212(7)	$5 \times 10^{-11}$	334(4)	72(6)	0.003	0.37
Creatinine, $\mu\text{mol/L}$	86(78-95)	89(81-98)	92(84-102)	$4 \times 10^{-73}$	89(80-98)	91(83-101)	$2 \times 10^{-10}$	0.63
C-reactive protein, $\text{mg/L}$	1.7(1.2-2.1)	1.7(1.3-2.5)	1.8(1.5-3.4)	$1 \times 10^{-75}$	1.7(1.3-2.5)	1.7(1.4-3.1)	$5 \times 10^{-9}$	0.03

Continuous variables are shown as median and interquartile range. *P* is from Cuzick's non-parametric trend test. Urate tertiles were assigned by sex. COPD was defined as lower limit of normal. COPD: chronic obstructive pulmonary disease. Allele score: urate *SLC2A9* rs7442295 variant + urate *ABCG2* rs2331142 variant. \* Data not available in the Copenhagen City Heart Study.

**Supplemental Table 2. The association of baseline characteristics with urate allele score genotype in the Copenhagen General Population Study.**

Copenhagen General Population Study						
	Allele score					<i>P</i>
	0	1	2	3	4	
No. of participants	3 412	27 102	56 194	12 954	878	
Plasma urate, μmol/L	250(190-310)	280(230-340)	300(250-360)	320(260-380)	330(270-400)	<1×10 <sup>-300</sup>
Men, n (%)	1 537(45)	12 247(45)	25 225(45)	5 878(45)	405(46)	0.83
Age, years	58(48-67)	57(48-67)	58(48-67)	58(48-67)	58(48-67)	0.41
Ever smokers, n (%)	2 006(59)	15 689(58)	32 867(58)	7 538(58)	524(60)	0.43
Cumulative tobacco consumption, pack-years	16(6-30)	15(6-30)	15(6-30)	16(6-30)	16(7-30)	0.97
Body mass index, kg/m <sup>2</sup>	26(23-29)	26(23-28)	26(23-28)	26(23-28)	26(23-28)	0.14
Alcohol consumption, g/week	96(48-180)	96(48-180)	96(48-180)	96(48-180)	96(48-180)	0.68
High income, %	1 463(43)	11 685(43)	24 429(43)	5 622(43)	377(43)	0.41
High physical activity in leisure time, n (%)	257(8)	1 750(6)	3 779(7)	901(7)	50(6)	0.67
High education, n (%)	1 528(45)	12 275(45)	25 336(45)	5 940(46)	397(45)	0.41
Exposure to occupational dust and fumes, n (%)	369(11)	2 789(10)	5 704(10)	1 249(10)	87(10)	0.02
High intake of meat, n (%) *	401(12)	3 121(12)	6 508(12)	1 501(12)	114(13)	0.92
Preexisting cardiovascular disease, n (%)	208(6)	1 595(6)	3 323(6)	789(6)	51(6)	0.71
Creatinine, μmol/L	80(72-89)	80(72-89)	80(72-89)	80(72-90)	80(72-89)	0.41
C-reactive protein, mg/L	1.4(0.9-2.4)	1.4(0.9-2.3)	1.4(0.9-2.3)	1.4(0.9-2.3)	1.3(0.9-2.2)	0.94

Continuous variables are shown as median and interquartile range. NA: not applicable (data not available in the CCHS). *P* for trend calculated using Cuzick's nonparametric test for trend. Allele score: urate *SLC2A9* rs7442295 variant + urate *ABCG2* rs2331142 variant.

**Supplemental Table 3. The association of baseline characteristics with urate allele score in the Copenhagen City Heart Study.**

Copenhagen City Heart Study						
	Allele score					<i>P</i>
	0	1	2	3	4	
No. of participants	309	2 596	5 351	1 288	68	
Plasma urate, $\mu\text{mol/L}$	247(200-312)	290(230-344)	301(250-362)	320(260-387)	355(301-408)	$2 \times 10^{-53}$
Men, n (%)	132(43)	1 142(44)	2 377(44)	556(43)	34(50)	0.83
Age, years	60(44-69)	59(45-70)	59(44-69)	59(46-69)	56(41-66)	0.68
Ever smokers, n (%)	223(72)	1 873(72)	3 911(73)	962(75)	51(75)	0.10
Cumulative tobacco consumption, pack-years	20(8-32)	20(8-32)	19(8-35)	19(8-34)	20(8-40)	0.79
Body mass index, $\text{kg/m}^2$	25(22-28)	25(22-28)	25(22-28)	25(22-28)	25(23-29)	0.33
Alcohol consumption, g/week	72(24-168)	72(24-156)	72(24-156)	72(24-156)	72(36-204)	0.52
High income, %	51(17)	428(16)	932(17)	233(18)	9(13)	0.28
High physical activity in leisure time, n (%)	16(5)	104(4)	226(4)	50(4)	10(15)	0.50
High education, n (%)	66(21)	525(20)	1 125(21)	263(20)	22(32)	0.43
Exposure to occupational dust and fumes, n (%)	50(16)	418(16)	929(17)	234(18)	13(19)	0.06
High intake of meat, n (%) *	NA	NA	NA	NA	NA	
Preexisting cardiovascular disease, n (%)	16(5)	115(4)	236(4)	72(6)	3(4)	0.37
Creatinine, $\mu\text{mol/L}$	89(80-97)	89(81-98)	89(81-98)	89(80-99)	87(77-95)	0.63
C-reactive protein, mg/L	1.7(1.3-3.0)	1.7(1.4-2.6)	1.7(1.3-2.5)	1.7(1.3-2.5)	1.7(1.5-2.4)	0.03

Continuous variables are shown as median and interquartile range. NA: not applicable (data not available in the CCHS). *P* calculated using Cuzick's nonparametric test for trend. Allele score: urate *SLC2A9* rs7442295 variant + urate *ABCG2* rs2331142 variant.

**Supplemental Table 4. The association of baseline characteristics with urate *SLC2A9* genotype in the Copenhagen General Population Study and the Copenhagen City Heart Study separately.**

	Copenhagen General Population Study				Copenhagen City Heart Study			
	<i>SLC2A9</i>			<i>P</i>	<i>SLC2A9</i>			<i>P</i>
	GG	GA	AA		GG	GA	AA	
No. of participants	4 338	33 408	62 832		401	3 189	6 028	
Plasma urate, µmol/L	250 (190-310)	285 (230-350)	310 (250-370)	1×10 <sup>-300</sup>	250(200-323)	290(237-350)	310(250-365)	9×10 <sup>-40</sup>
Men, n (%)	1 925 (44)	15 198(45)	28 188(45)	0.35	172 (43)	1 428(45)	2 644(44)	0.69
Age, years	58(48-67)	58(48-67)	58(48-67)	0.69	59(44-69)	59(44-69)	59(44-69)	0.39
Ever smokers, n (%)	2 554(59)	19 414(58)	36 677(58)	0.77	282(70)	2 307(72)	4 436(74)	0.08
Cumulative tobacco consumption, pack-years	15(6-30)	15(6-30)	15(6-30)	0.34	20(8-33)	20(8-35)	19(8-35)	0.47
Body mass index, kg/m <sup>2</sup>	26(23-29)	26(23-28)	26(23-28)	0.73	25(22-28)	25(22-28)	25(22-28)	0.42
Alcohol consumption, g/week	96(48-180)	96(48-180)	96(48-180)	0.74	72(24-168)	72(24-156)	72(24-156)	0.51
High income, %	1 859(43)	14 451(43)	27 279(43)	0.45	69(17)	529(17)	1 057(18)	0.35
High physical activity in leisure time, n (%)	320(7)	2 192(7)	4 227(7)	0.80	21(5)	138(4)	247(4)	0.31
High education, n (%)	1 973(45)	15 088(45)	28 429(45)	0.98	86(21)	644(20)	1 273(21)	0.51
Exposure to occupational dust and fumes, n (%)	448(10)	3 451(10)	6 301(10)	0.09	67(17)	517(16)	1 061(18)	0.10
High intake of meat, n (%) *	517(12)	3 866(12)	7 270 (12)	0.30	NA	NA	NA	
Preexisting cardiovascular disease, n (%)	260(6)	1 983(6)	3 728(6)	0.91	20(5)	152(5)	270(4)	0.46
Creatinine, µmol/L	80(72-89)	80(72-89)	80(72-89)	0.17	89(79-97)	89(81-98)	89(80-99)	0.51
C-reactive protein, mg/L	1.4(0.94-2.3)	1.4(0.94-2.3)	1.4(0.94-2.3)	0.27	1.7(1.3-2.7)	1.7(1.3-2.6)	1.7(1.3-2.6)	0.05

Continuous variables are shown as median and interquartile range. NA: not applicable (data not available in the CCHS). *P* for trend calculated using Cuzick's nonparametric test for trend.

**Supplemental Table 5. The association of baseline characteristics with urate *ABCG2* rs2331142 genotype in the Copenhagen General Population Study and the Copenhagen City Heart Study separately.**

	Copenhagen General Population Study				Copenhagen City Heart Study			
	<i>ABCG2</i>			<i>P</i>	<i>ABCG2</i>			<i>P</i>
	CC	CA	AA		CC	CA	AA	
No. of participants	79 033	20 162	1 345		7 522	1 980	110	
Plasma urate, $\mu\text{mol/L}$	290 (240-350)	310 (250-370)	320 (260-390)	$5 \times 10^{-100}$	300 (240-355)	310 (250-376)	347 (290-408)	$4 \times 10^{-16}$
Men, n (%)	35 508(45)	9 159(45)	625(46)	0.11	3 306(44)	880(44)	55(50)	0.37
Age, years	58(48-67)	58(48-67)	58(48-67)	0.07	59(45-69)	59(45-69)	56(43-65)	0.70
Ever smokers, n (%)	46 011(58)	11 823(59)	790(59)	0.27	5 487(73)	1 450(73)	83(75)	0.63
Cumulative tobacco consumption, pack-years	15(6-30)	15(6-30)	16(6-31)	0.56	19(8-35)	19(8-35)	22(10-40)	0.62
Body mass index, $\text{kg/m}^2$	26(23-28)	26(23-28)	26(23-28)	0.09	25(22-28)	25(22-28)	25(22-29)	0.57
Alcohol consumption, g/week	96(48-180)	96(48-180)	106(48-185)	0.40	6(2-13)	6(2-13)	6(2-15)	0.83
High income, %	34 232(43)	8 761(43)	583(43)	0.75	1 281(17)	356(18)	16(15)	0.56
High physical activity in leisure time, n (%)	5 238(7)	1 430(7)	69(5)	0.30	304(4)	90(5)	12(11)	0.02
High education, n (%)	35 655(45)	9 211(46)	610(45)	0.18	1 564(21)	408(21)	29(26)	0.65
Exposure to occupational dust and fumes, n (%)	8 089(10)	1 975(10)	134(10)	0.10	1 277(17)	341(17)	26(24)	0.35
High intake of meat, n (%) *	9 117(12)	2 354(12)	174(13)	0.20	NA	NA	NA	
Preexisting cardiovascular disease, n (%)	4 666(6)	1 218(6)	82(6)	0.44	324(4)	113(6)	5(5)	0.02
Creatinine, $\mu\text{mol/L}$	80(72-89)	80(72-90)	80(72-89)	0.75	89(81-98)	89(80-99)	89(80-99)	0.94
C-reactive protein, mg/L	1.4(0.9-2.3)	1.4(0.9-2.3)	1.4(0.9-2.2)	0.12	1.7(1.3-2.6)	1.7(1.3-2.5)	1.7(1.3-2.8)	0.32

Continuous variables are shown as median and interquartile range. NA: not applicable (data not available in the CCHS). *P* for trend calculated using Cuzick's nonparametric test for trend.

**Supplemental Table 6. Symptoms of airway disease and urate allele score in the Copenhagen General Population Study and the Copenhagen City Heart Study**

	Urate allele score					<i>P</i>	Sex and age adjusted OR per 1 allele increase	<i>P</i> for trend
	0	1	2	3	4			
<b>Clinical characteristics in the Copenhagen General Population Study</b>								
No. of participants	3 412	27 102	56 194	12 954	878			
Plasma urate, µmol/L	250(190-310)	280(230-340)	300(250-360)	320(260-380)	330(270-400)			
Any dyspnoea, N (%)	1 076(32)	8 611(32)	17 690(32)	4 083(32)	317(36)	0.81	1.00(0.98-1.02)	0.88
mMRC ≥2, N (%)	276(8)	2 258(8)	4 519(8)	1 066(8)	69(8)	0.52	0.99(0.96-1.02)	0.40
Sputum (>3 months), N (%)	291(9)	2 390(9)	4 956(9)	1 103(9)	87(10)	0.90	1.00(0.97-1.03)	0.85
Any respiratory symptoms, N (%)	1 440(42)	11 591(43)	23 789(42)	5 501(42)	411(47)	0.86	1.00(0.98-1.02)	0.92
Use of asthma/ bronchitis medication, N (%)	209(6)	1 600(6)	3 361(6)	763(6)	45(5)	0.69	0.99(0.96-1.03)	0.65
<b>Clinical characteristics in the Copenhagen City Heart Study</b>								
No. of participants	309	2 596	5 351	1 288	68			
Plasma urate, µmol/L	247(200-312)	290(230-344)	301(250-362)	320(260-387)	355(300-408)			
Any dyspnoea, N (%)	121(39)	1 056(41)	2 192(41)	564(44)	36(53)	0.03	1.07(1.01-1.13)	0.02
mMRC>2, N (%)	43(14)	333(13)	685(13)	200(16)	9(13)	0.14	1.07(0.99-1.17)	0.09
Sputum (>3 months), N (%)	42(14)	318(12)	670(13)	169(13)	8(12)	0.74	1.01(0.93-1.10)	0.73
Any respiratory symptoms, N (%)	168(54)	1 385(53)	2 863(54)	715(56)	45(66)	0.18	1.04(0.98-1.10)	0.16
Use of asthma/ bronchitis medication, N (%)	17(6)	160(6)	270(5)	84(7)	1(1)	0.58	0.97(0.86-1.09)	0.61

Continuous variables are shown as median and interquartile range. *P* is from Cuzick's nonparametric trend test. *P* for trend is from logistic regression with urate allele score (*SLC2A9* rs7442295 + urate *ABCG2* rs2331142) as a continuous variable. OR: odds ratio. CI: confidence interval. mMRC: Modified Medical Research Council Dyspnea Scale.

**Supplemental Table 7. Symptoms of airway disease and plasma urate tertiles in the Copenhagen General Population Study and the Copenhagen City Heart Study within the COPD population.**

	Urate tertiles			<i>P</i>	Multivariable adjusted			<i>P</i> for trend
	1 <sup>st</sup>	2 <sup>nd</sup>	3 <sup>rd</sup>		1 <sup>st</sup> (Ref.)	2 <sup>nd</sup> OR (95%CI)	3 <sup>rd</sup> OR (95%CI)	
<b>Clinical characteristics in the Copenhagen General Population Study</b>								
No. of participants	4 764	4 236	3 957					
Plasma urate, µmol/L	240(200-290)	310(260-350)	400(340-440)					
Any dyspnoea, N (%)	1641(35)	1652(39)	2 040(52)	1×10 <sup>-57</sup>	1	1.08(0.98-1.19)	1.23(1.11-1.36)	1×10 <sup>-4</sup>
mMRC≥2, N (%)	439(9)	475(11)	832(21)	4×10 <sup>-56</sup>	1	1.06(0.91-1.24)	1.35(1.16-1.57)	7×10 <sup>-5</sup>
Sputum (>3 months), N (%)	666(14)	622(15)	720(18)	9×10 <sup>-8</sup>	1	1.03(0.90-1.17)	1.05(0.92-1.20)	0.48
Any respiratory symptoms, N (%)	2 349(49)	2 207(52)	2470(62)	2×10 <sup>-33</sup>	1	1.02(0.92-1.12)	1.10(0.99-1.22)	0.07
Use of asthma/ bronchitis medication, N (%)	227(5)	251(6)	337(9)	1×10 <sup>-12</sup>	1	1.13(0.92-1.38)	1.07(0.87-1.31)	0.56
<b>Clinical characteristics in the Copenhagen City Heart Study</b>								
No. of participants	402	401	391					
Plasma urate, µmol/L	234(194-270)	310(277-344)	398(360-440)					
Any dyspnoea, N (%)	184(46)	202(50)	226(58)	7×10 <sup>-4</sup>	1	0.97(0.70-1.33)	1.13(0.81-1.58)	0.48
mMRC≥2, N (%)	64(16)	78(19)	108(28)	5×10 <sup>-5</sup>	1	0.97(0.63-1.48)	1.32(0.85-2.0)	0.19
Sputum (>3 months), N (%)	84(21)	96(24)	92(24)	0.37	1	1.12(0.76-1.63)	1.11(0.75-1.66)	0.61
Any respiratory symptoms, N (%)	266(66)	266(66)	277(71)	0.16	1	0.89(0.64-1.25)	1.00(0.70-1.43)	0.99
Use of asthma/ bronchitis medication, N (%)	15(4)	18(4)	22(6)	0.20	1	1.03(0.47-2.25)	1.18(0.53-2.62)	0.67

Continuous variables are shown as median and interquartile range. Those without COPD are excluded. Plasma urate tertiles were assigned by sex. *P* is from Cuzick's nonparametric trend test. *P* for trend is from logistic regression with plasma urate tertiles as a continuous variable. Multivariable adjusted was for age, sex, smoking status, cumulative smoking, BMI, physical activity during leisure time, intake of meat (only available in the CGPS), intake of alcohol, income, education, preexisting cardiovascular disease, exposure to occupational dust and fumes, plasma creatinine, plasma C-reactive protein, and lung function in three categories; FEV<sub>1</sub>≥80%,



FEV<sub>1</sub><80% and >50%, and FEV<sub>1</sub>≤50%. OR: odds ratio. CI: confidence interval. mMRC: Modified Medical Research Council Dyspnea Scale. Individuals with self-reported asthma (n=6234 in the CGPS and n=575 in the CCHS) are excluded.

**Supplemental Table 8. Symptoms of airway disease and plasma urate tertiles in the Copenhagen General Population Study and the Copenhagen City Heart Study separately on complete cases.**

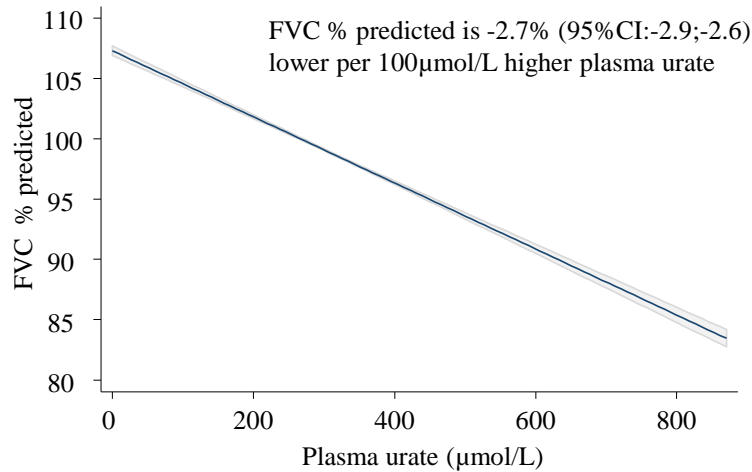
	Urate tertiles			<i>P</i>	Urate tertiles (Multivariable adjusted)			<i>P</i> for trend
	1 <sup>st</sup>	2 <sup>nd</sup>	3 <sup>rd</sup>		1 <sup>st</sup> (Ref.)	2 <sup>nd</sup> OR (95% CI)	3 <sup>rd</sup> OR (95% CI)	
<b>Symptoms of airway disease in the Copenhagen General Population Study</b>								
No. of individuals	33 054	29 822	27 879					
Plasma urate, μmol/L	230(200-280)	290(260-350)	390(330-430)					
Any dyspnoea, n (%)	8 054(25)	8 737(29)	11 328(41)	<1×10 <sup>-300</sup>	1	1.07(1.03-1.12)	1.24(1.19-1.29)	7×10 <sup>-24</sup>
mMRC ≥2, n (%)	1 555(5)	1 823(6)	3 569(13)	4×10 <sup>-297</sup>	1	1.02(0.94-1.10)	1.34(1.25-1.44)	3×10 <sup>-17</sup>
Sputum (>3 months), n (%)	2 422(7)	2 421(8)	2 970(11)	7×10 <sup>-47</sup>	1	1.03(0.97-1.09)	1.09(1.02-1.16)	0.01
Any respiratory symptoms, n (%)	11 672(36)	11 992(41)	14 275(52)	<1×10 <sup>-300</sup>	1	1.07(1.03-1.11)	1.24(1.19-1.29)	6×10 <sup>-27</sup>
Use of asthma/ bronchitis medication, n (%)	1 683(5)	1 674(6)	1 999(7)	8×10 <sup>-27</sup>	1	1.01(0.94-1.08)	1.04(0.97-1.13)	0.26
<b>Symptoms of airway disease in the Copenhagen City Heart Study</b>								
No. of individuals	2 425	2 299	2 271					
Plasma urate, μmol/L	230(200-269)	300(269-347)	390(334-362)					
Any dyspnoea, n (%)	908(37)	903(39)	1 193(53)	<1×10 <sup>-300</sup>	1	0.94(0.82-1.06)	1.23(1.07-1.41)	0.003
mMRC ≥2, n (%)	234(10)	259(11)	462(20)	3×10 <sup>-26</sup>	1	1.02(0.83-1.27)	1.53(1.24-1.89)	2×10 <sup>-5</sup>
Sputum (>3 months), n (%)	295(12)	289(13)	342(15)	0.004	1	1.01(0.83-1.22)	1.16(0.95-1.40)	0.15
Any respiratory symptoms, n (%)	1 228(51)	1 181(51)	1 434(63)	2×10 <sup>-17</sup>	1	0.92(0.81-1.04)	1.22(1.06-1.40)	0.007
Use of asthma/ bronchitis medication, n (%)	117(5)	108(5)	154(7)	0.003	1	0.98(0.73-1.32)	1.31(0.97-1.75)	0.89

Only complete cases are included. Continuous variables are shown as median and interquartile range. Plasma urate tertiles were assigned by sex. *P* is from Cuzick's nonparametric trend test. *P* for trend is from logistic regression with plasma urate tertiles as a continuous variable. Multivariable adjusted was for age, sex, smoking status, cumulative smoking, BMI, physical activity during leisure time, intake of meat (only available in the CGPS), intake of alcohol, income, education, preexisting

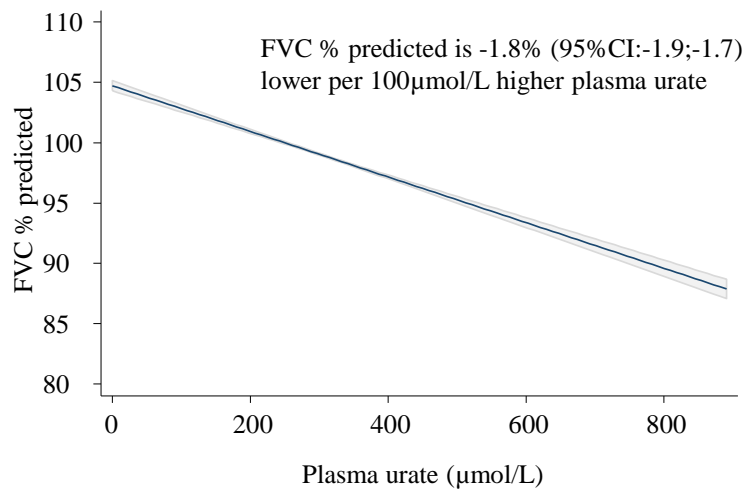
cardiovascular disease, exposure to occupational dust and fumes, plasma creatinine, plasma C-reactive protein, and lung function in three categories;  $FEV_1 \geq 80\%$ ,  $FEV_1 < 80\%$  and  $> 50\%$ , and  $FEV_1 \leq 50\%$ . OR: odds ratio. CI: confidence interval. mMRC: Modified Medical Research Council Dyspnea Scale.

## Copenhagen General Population Study

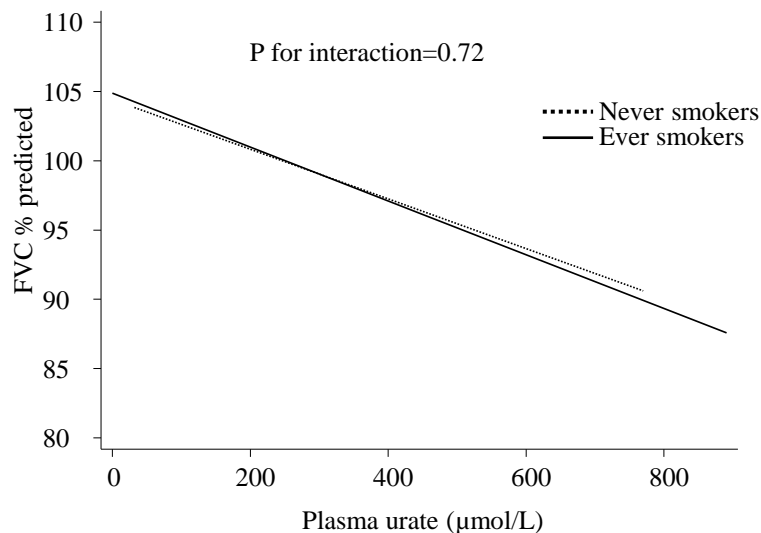
### Sex and age adjusted



### Multivariable adjusted

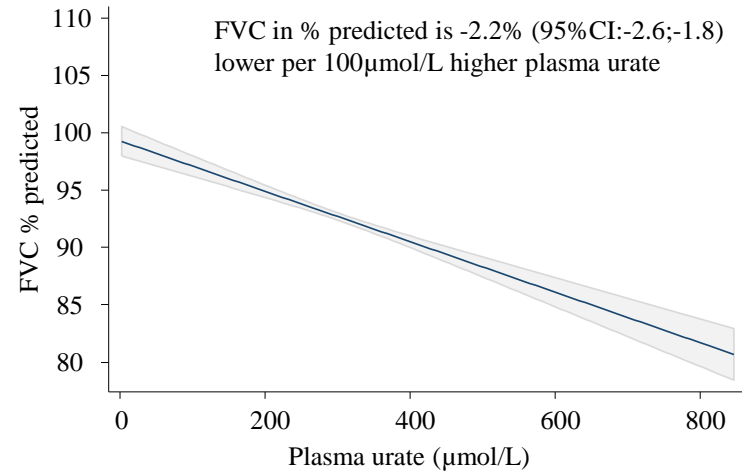


### Stratified on smoking status

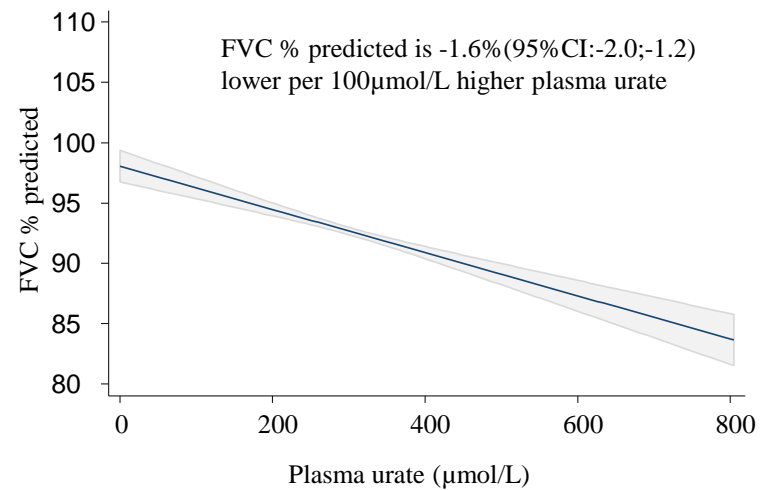


## Copenhagen City Heart Study

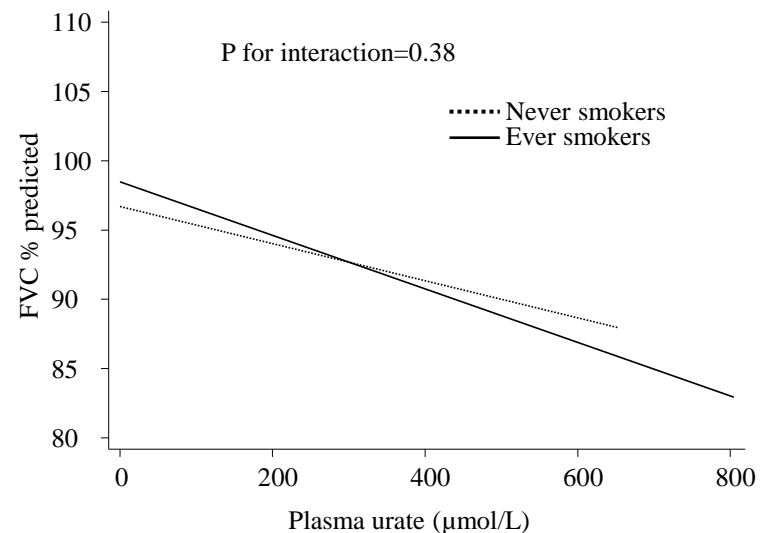
### Sex and age adjusted



### Multivariable adjusted

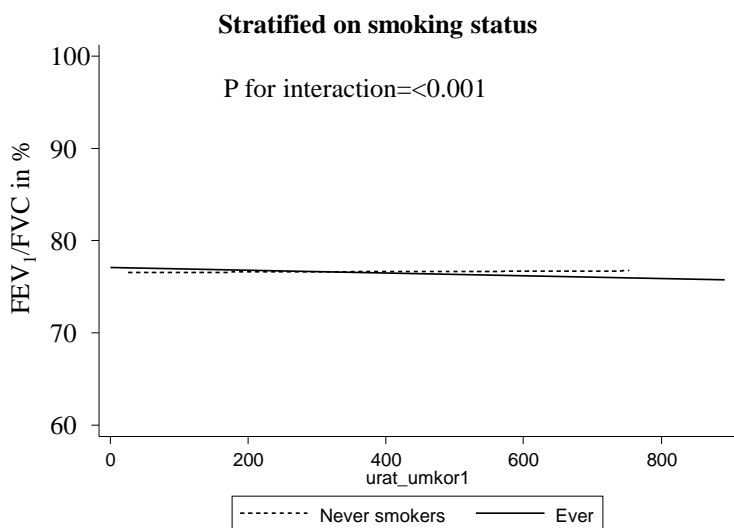
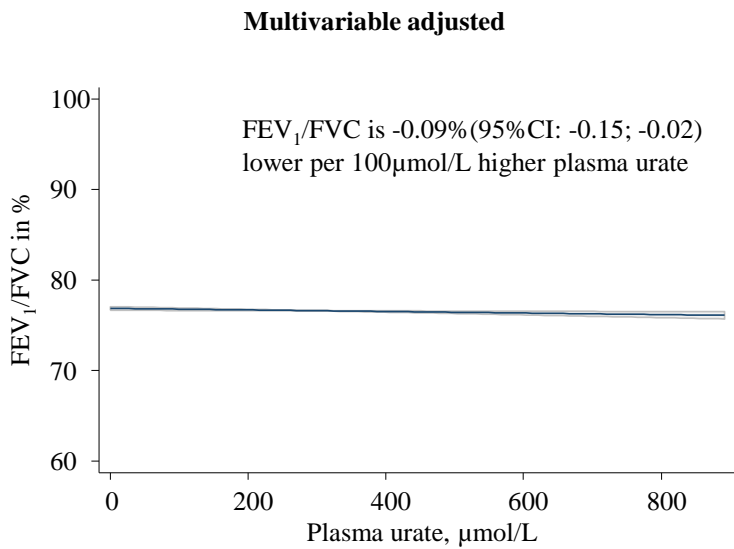
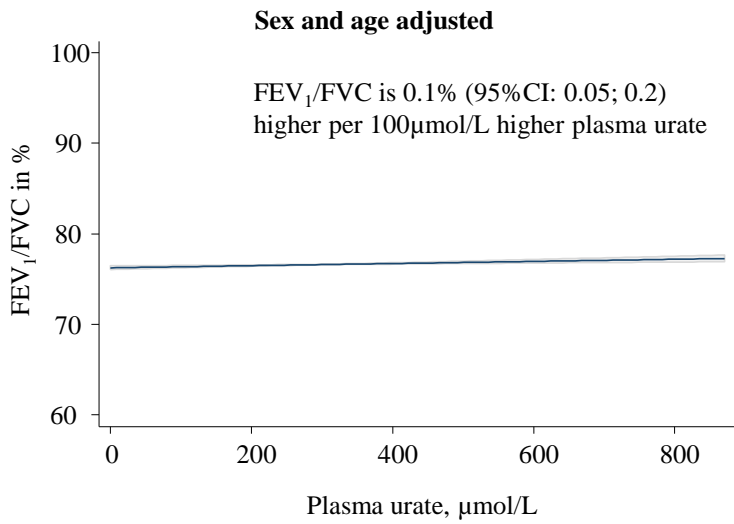


### Stratified on smoking status

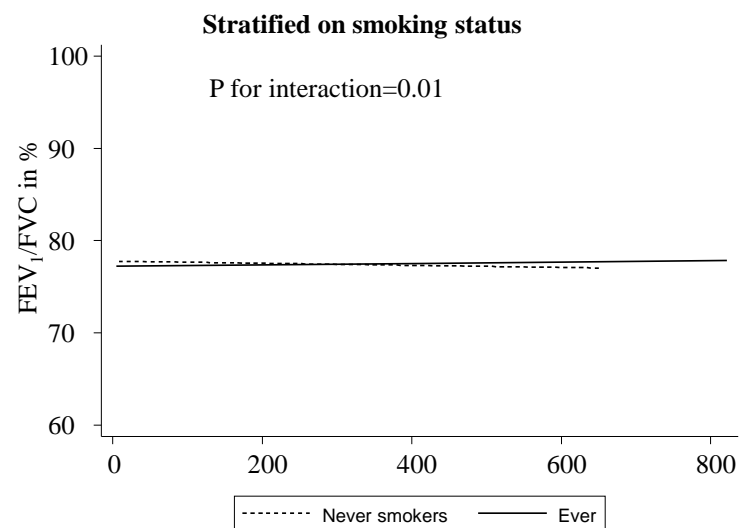
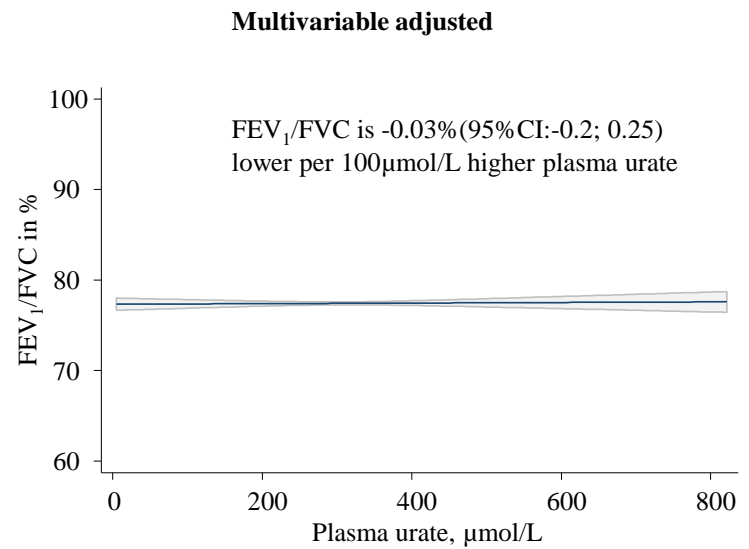
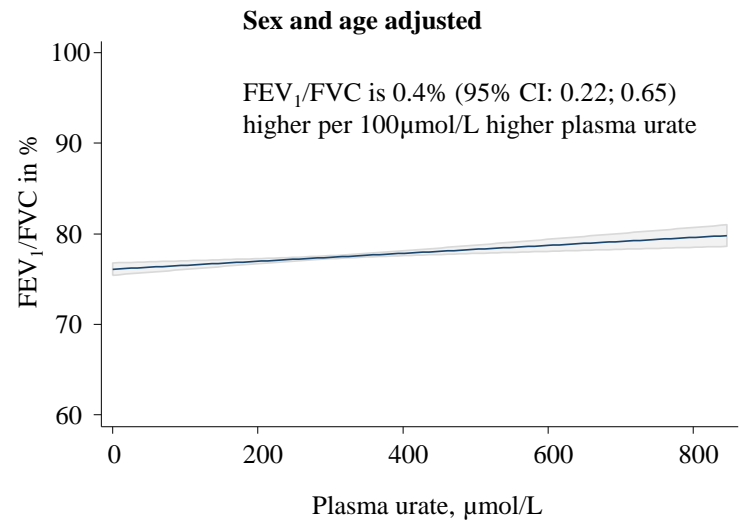


**Supplemental Figure 1. Regression of FVC % predicted on plasma urate in the Copenhagen General Population Study and the Copenhagen City Heart Study separately.** Multivariable adjusted was for age, sex, smoking status, cumulative smoking, body mass index, physical activity during leisure time, intake of meat (only available in the CGPS), intake of alcohol, income, education, preexisting cardiovascular disease, exposure to occupational dust and fumes, plasma creatinine, and plasma C-reactive protein. FVC: forced vital capacity. CGPS: Copenhagen General Population Study. Ever smokers: former and current smokers combined. Regression values in top and middle panel are shown with 95% confidence intervals as shaded area around regression line; bottom panels show regression lines only.

**Copenhagen General Population Study**

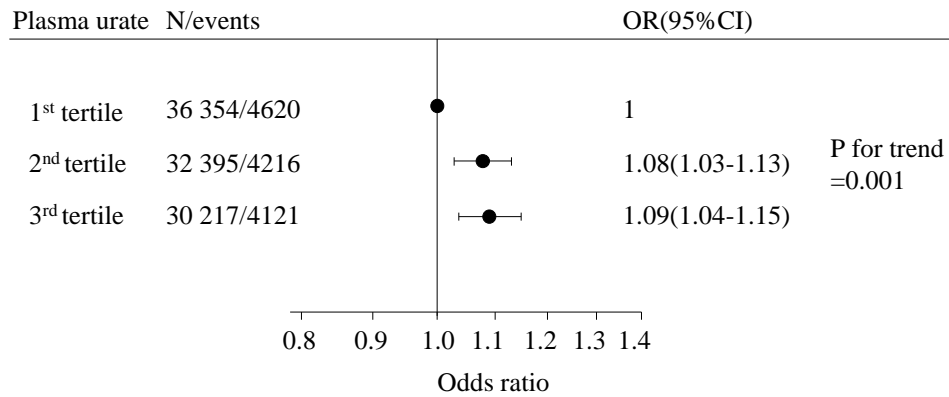


**Copenhagen City Heart Study**

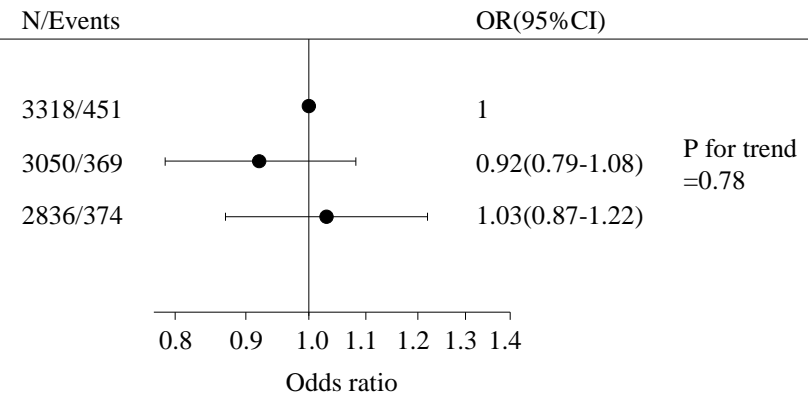


**Supplemental Figure 2. Regression of FEV<sub>1</sub>/FVC on plasma urate in the Copenhagen General Population Study and the Copenhagen City Heart Study separately.** Multivariable adjusted was for age, sex, smoking status, cumulative smoking, body mass index, physical activity during leisure time, intake of meat (only available in the CGPS), intake of alcohol, income, education, preexisting cardiovascular disease, exposure to occupational dust and fumes, plasma creatinine, and plasma C-reactive protein. FEV<sub>1</sub>: forced expiratory volume in 1 s. FVC: forced vital capacity. CGPS: Copenhagen General Population Study. Regression values in top and middle panel are shown with 95% confidence intervals as shaded area around regression line; bottom panels show regression lines only.

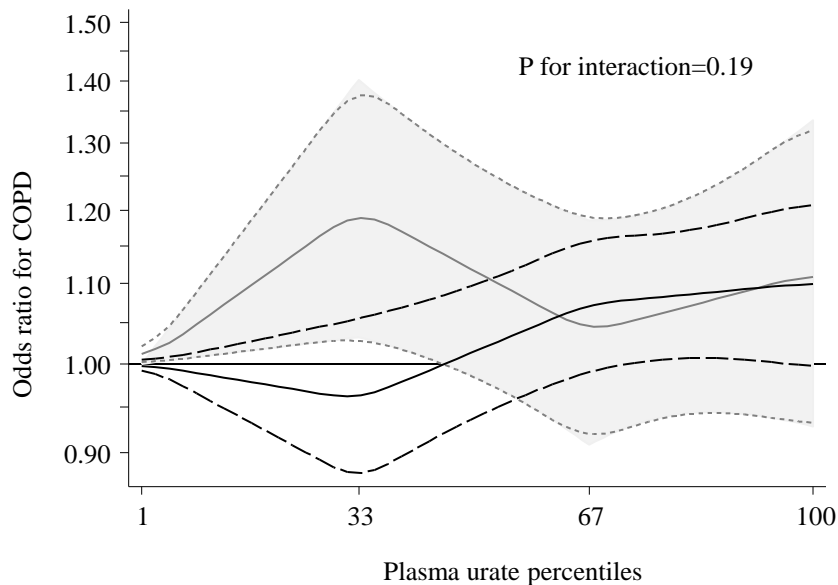
Copenhagen General Population Study



Copenhagen City Heart Study



**Supplemental Figure 3. Tertiles of plasma urate and risk of COPD in the Copenhagen General Population Study and the Copenhagen City Heart Study separately.** Tertiles were assigned by sex. All estimates are multivariable adjusted, which was for age, sex, smoking status, cumulative smoking, body mass index, physical activity during leisure time, intake of meat (only available in the CGPS), intake of alcohol, income, education, preexisting cardiovascular disease, exposure to occupational dust and fumes, plasma creatinine, and plasma C-reactive protein. CGPS: Copenhagen General Population Study. OR: odds ratio. CI: confidence interval. COPD: chronic obstructive pulmonary disease. Individuals with self-reported asthma (n=6234 in the CGPS and n=575 in the CCHS) are excluded.

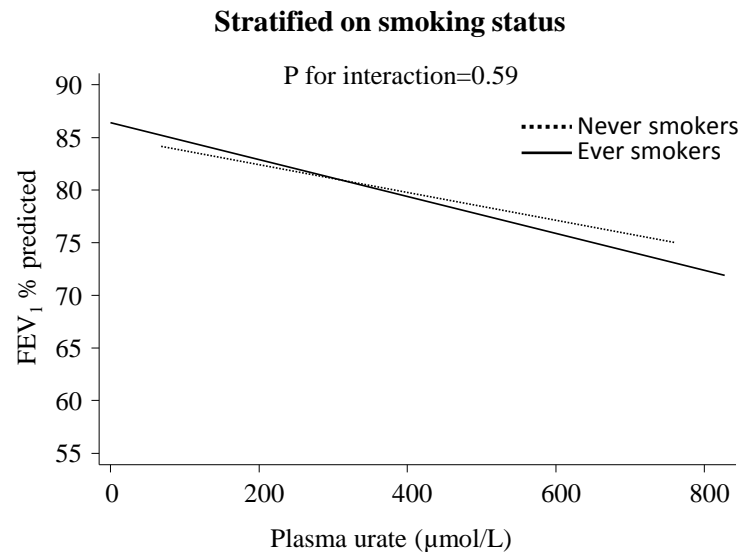
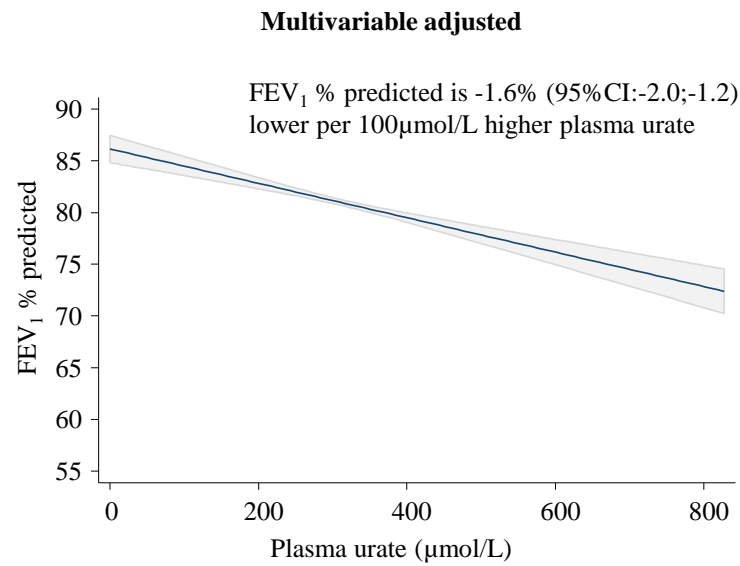
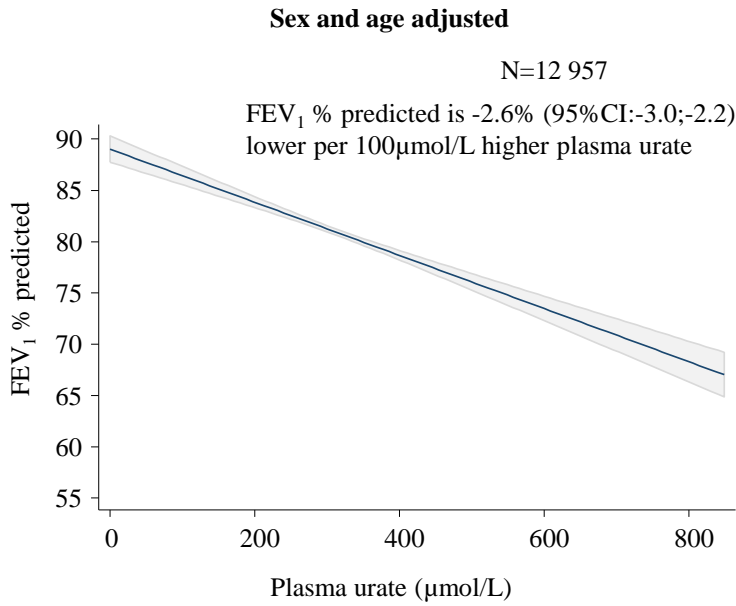


**Supplemental Figure 4. Multivariable adjusted odds ratios for COPD according to plasma urate percentiles in the Copenhagen General Population and the Copenhagen City Heart Study combined, stratified by smoking status.**

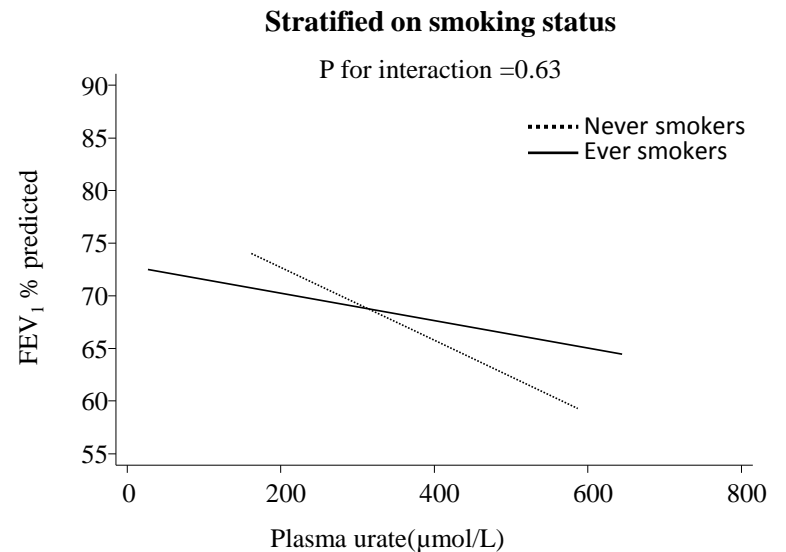
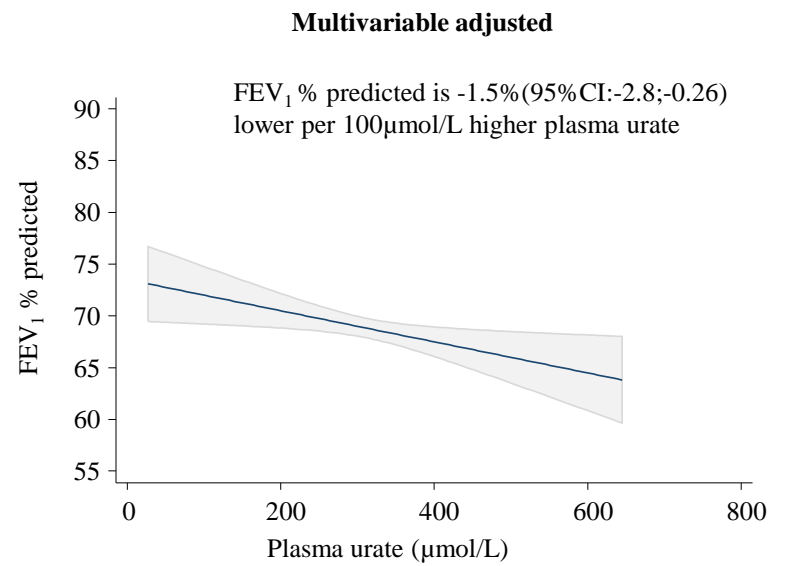
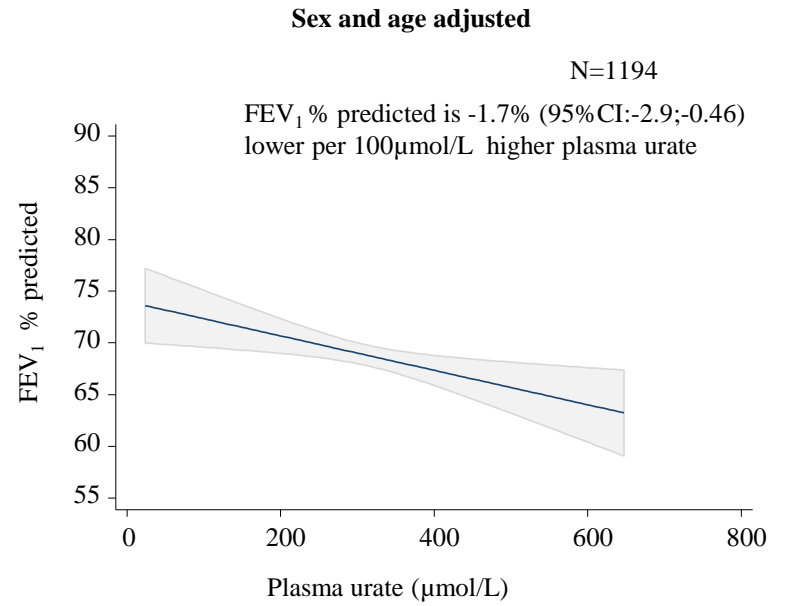
Grey line and shaded area: never smokers (N=43 774). Black line: ever smokers (N=64 396).

Solid lines are multivariable adjusted odds ratios and dashed lines indicate 95% confidence interval derived from restricted cubic spline regression with knots chosen by Akaike information criterion and plotted using a polynomial smoother. Uric acid percentiles were adjusted for sex, study and year of measurement. Multivariable adjustments were for age, sex, smoking status, cumulative smoking, body mass index, physical activity in leisure time, education, income, intake of meat (only available for the Copenhagen General Population Study), intake of alcohol, preexisting cardiovascular disease, exposure to occupational dust and fumes, plasma creatinine, and C-reactive protein. 6809 individuals with self-reported asthma were excluded. COPD: chronic obstructive pulmonary disease.

**Copenhagen General Population Study**



**Copenhagen City Heart Study**



**Supplemental Figure 5. FEV<sub>1</sub> % predicted according to plasma urate within the COPD population**

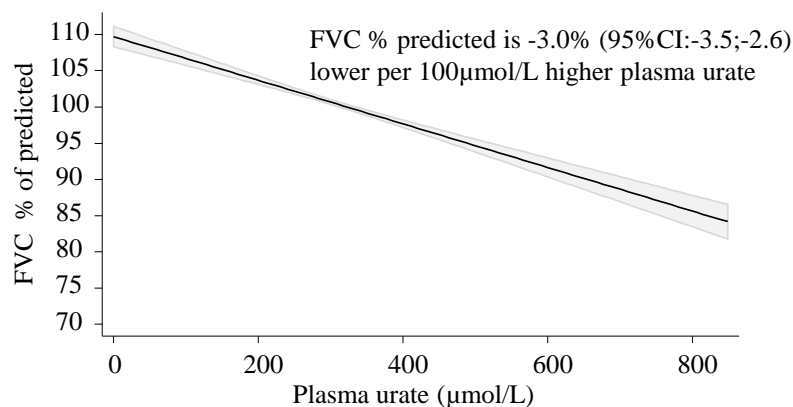
All estimates were multivariable adjusted, which was for age, sex, smoking status, cumulative smoking, body mass index, physical activity during leisure time, intake of meat (only available in the CGPS), intake of alcohol, income, education, preexisting cardiovascular disease, exposure to occupational dust and fumes, plasma creatinine, and plasma C-reactive protein. CGPS: Copenhagen General Population Study. FEV<sub>1</sub>: forced expiratory volume in 1 s. Ever smokers: former and current smokers combined. Individuals with self-reported asthma (n=6234 in the CGPS and n=575 in the CCHS) were excluded. Regression values in top and middle panel are shown with 95% confidence intervals as shaded area around regression line; bottom panels show regression lines only.



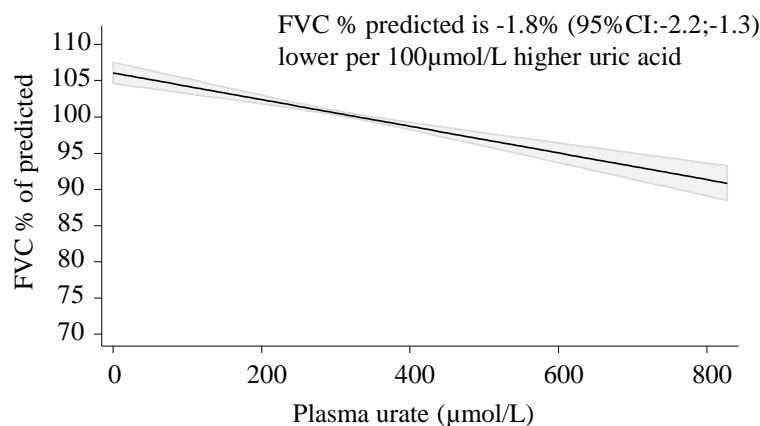
## Copenhagen General Population Study

### Sex and age adjusted

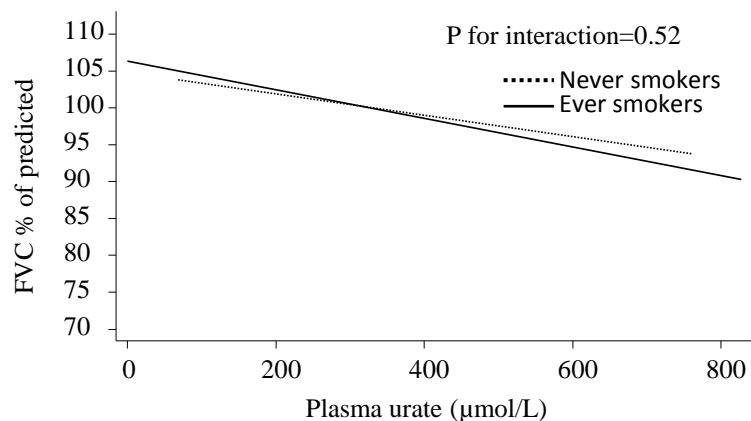
N=12 957



### Multivariable adjusted



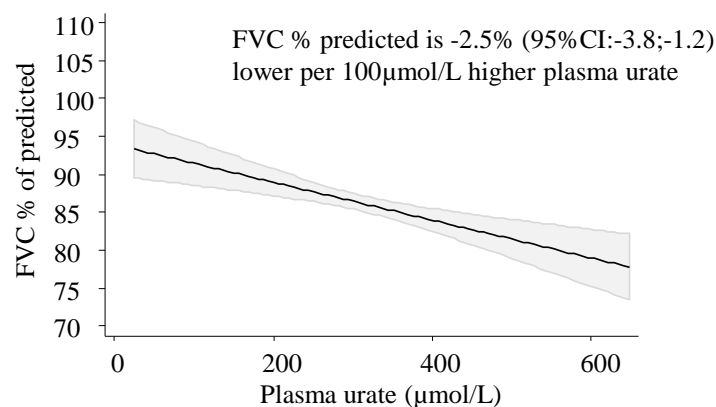
### Stratified on smoking status



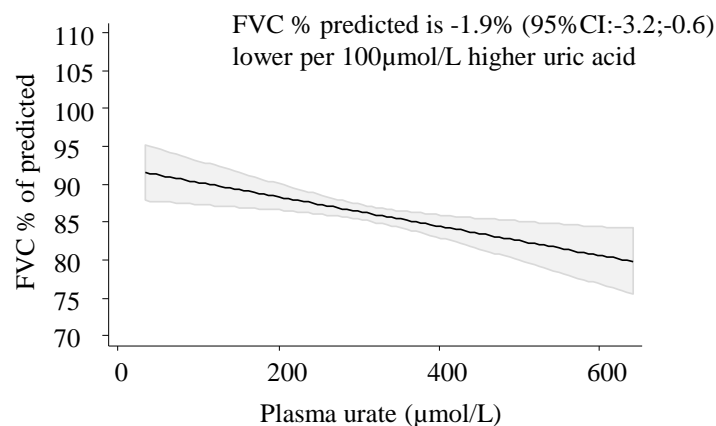
## Copenhagen City Heart Study

### Sex and age adjusted

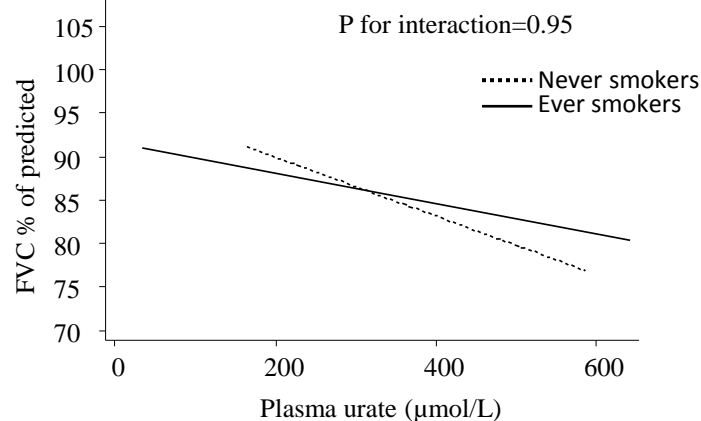
N=1194



### Multivariable adjusted



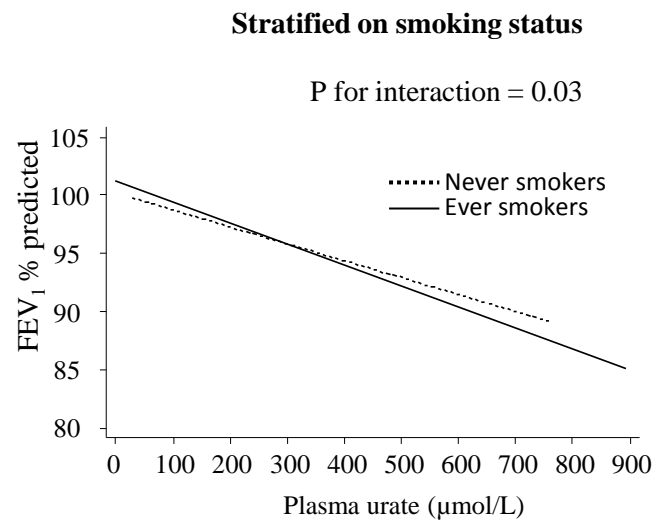
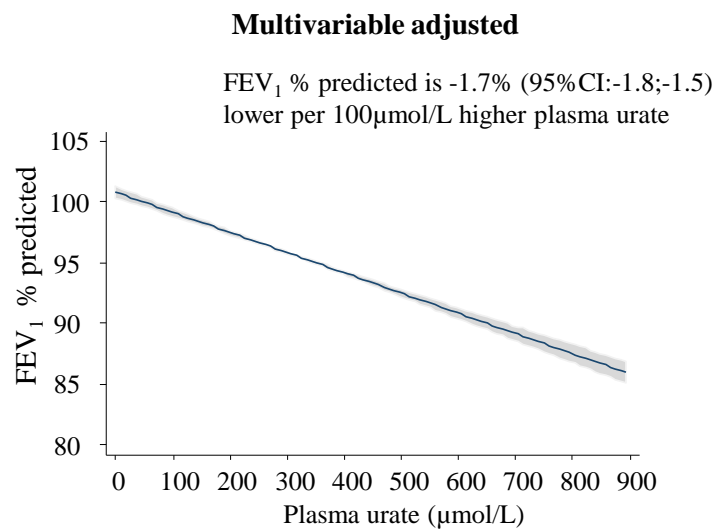
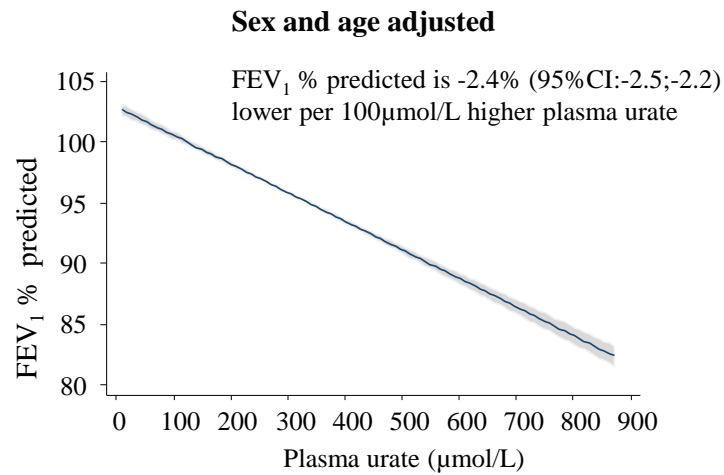
### Stratified on smoking status



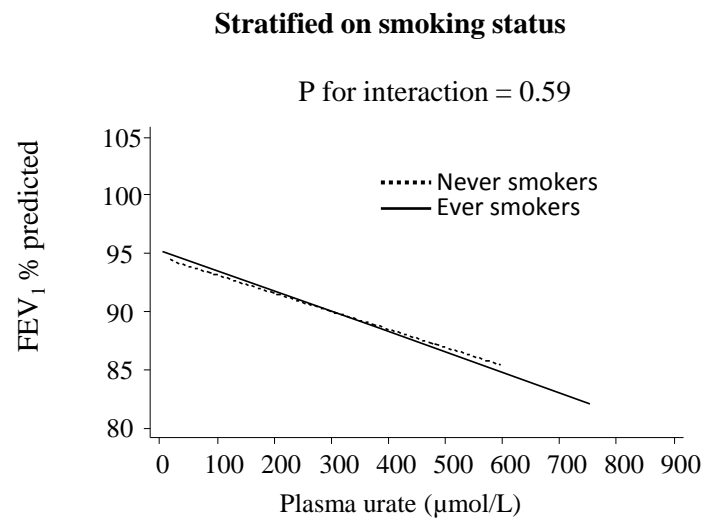
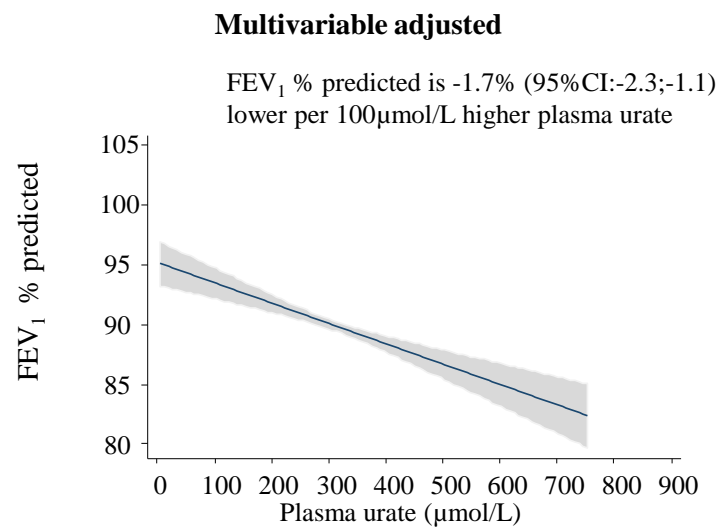
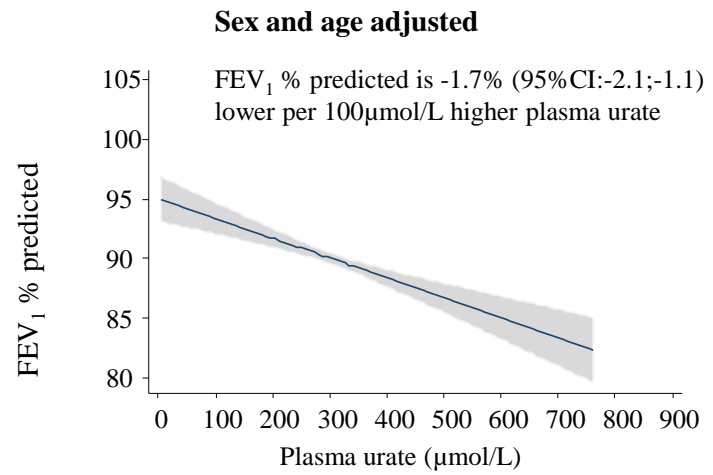
### Supplemental Figure 6. FVC % of predicted according to plasma urate within the COPD population

All estimates were multivariable adjusted, which was for age, sex, smoking status, cumulative smoking, body mass index, physical activity during leisure time, intake of meat (only available in the CGPS), intake of alcohol, income, education, preexisting cardiovascular disease, exposure to occupational dust and fumes, plasma creatinine, and plasma C-reactive protein. CGPS: Copenhagen General Population Study. FVC: forced vital capacity. Ever smokers: former and current smokers combined. Individuals with self-reported asthma (n=6234 in the CGPS and n=575 in the CCHS) were excluded. Regression values in top and middle panel are shown with 95% confidence intervals as shaded area around regression line; bottom panels show regression lines only.

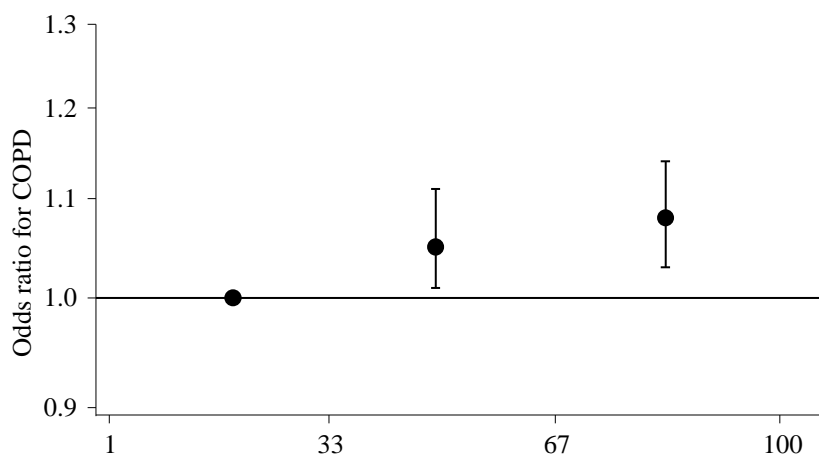
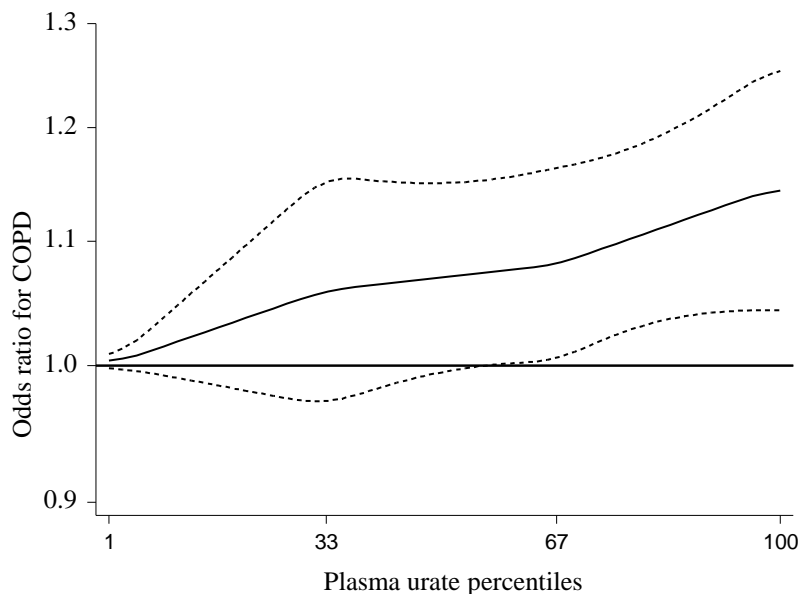
**Copenhagen General Population Study  
Complete cases**



**Copenhagen City Heart Study  
Complete cases**



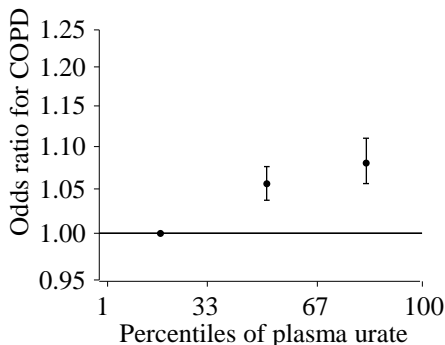
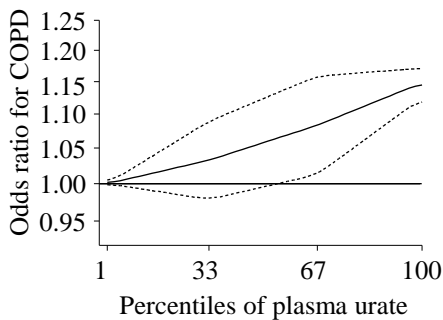
**Supplemental Figure 7. Regression of FEV<sub>1</sub> % predicted on plasma urate in the Copenhagen General Population Study and the Copenhagen City Heart Study separately including only individuals without any missing covariates.**



No. of participants	33 001	31 035	28 027
No. of COPD	4 231	3 981	3 826

**Supplemental Figure 8. Risk of COPD among complete cases.**

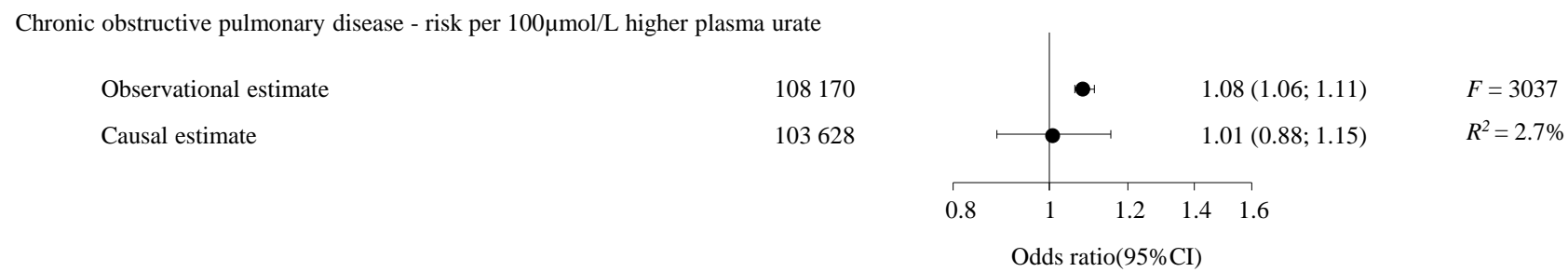
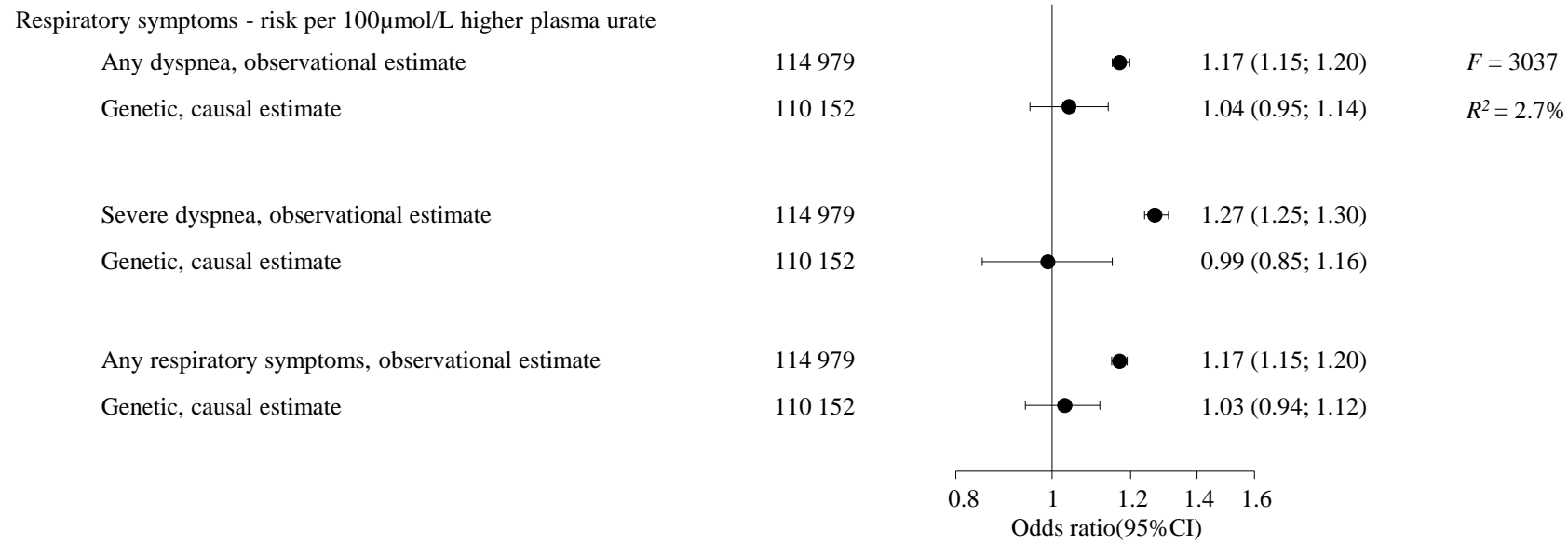
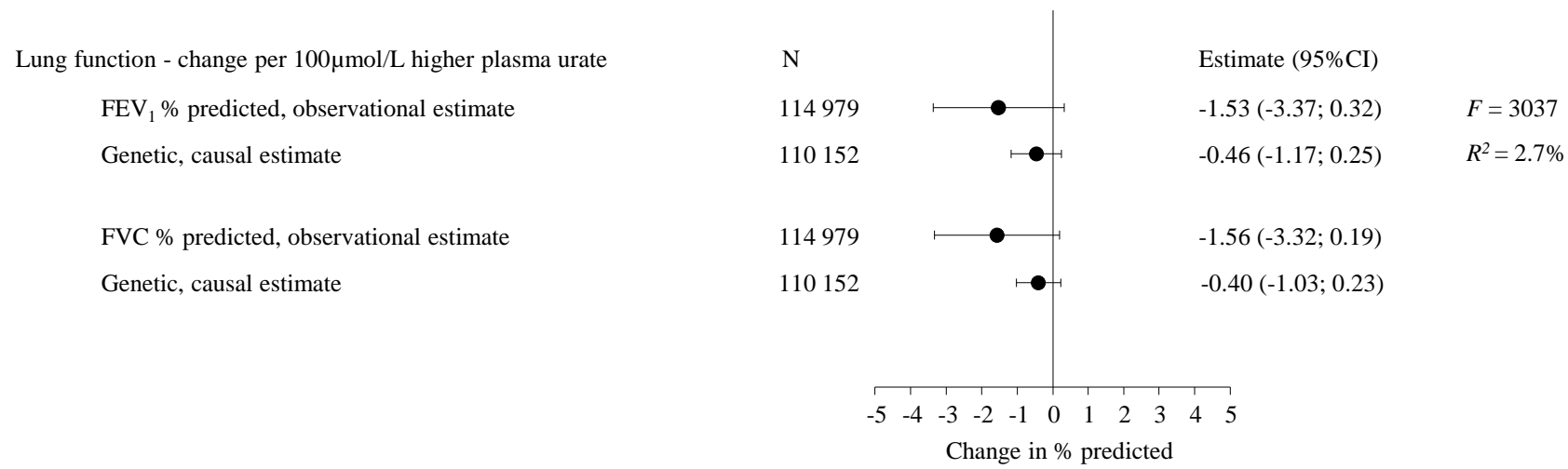
All individuals with missing information in one or several covariates have been removed from analyses. Solid lines are multivariable adjusted odds ratios using a polynomial smoother and dashed lines indicate 95% confidence interval derived from restricted cubic spline regression. Plasma urate percentiles are assigned by sex, study, and year of measurement. The analyses were multivariable adjusted for age, sex, smoking status, cumulative smoking, body mass index, physical activity during leisure time, intake of meat (only available for CGPS), intake of alcohol, income, education, preexisting cardiovascular disease, exposure to occupational dust and fumes, plasma creatinine, plasma C-reactive protein, and study. Individuals with self-reported asthma were excluded. COPD: chronic obstructive pulmonary disease.



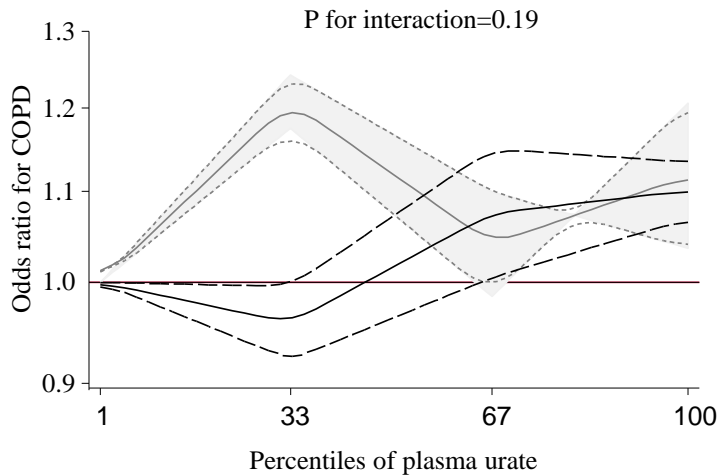
Percentiles	1-33	34-67	68-100
No. of participants	39 611	35 622	32 937
No. of COPD	5 048	4 590	4 513

**Supplemental Figure 9. Multivariable adjusted odds ratios for COPD according to plasma urate percentiles in the Copenhagen General Population and the Copenhagen City Heart Study combined, adjusted for study using the *cluster* command.** Solid lines are multivariable adjusted odds ratios using a polynomial smoother and dashed lines indicate 95% confidence interval derived from restricted cubic spline regression. Plasma urate percentiles are assigned by sex, study, and year of measurement. The analyses were multivariable adjusted for age, sex, smoking status, cumulative smoking, body mass index, physical activity during leisure time, intake of meat (only available for CGPS), intake of alcohol, income, education, preexisting cardiovascular disease, exposure to occupational dust and fumes, plasma creatinine, plasma C-reactive protein, and study. 6809 individuals with self-reported asthma were excluded. COPD: chronic obstructive pulmonary disease.

Copenhagen General Population Study and Copenhagen City Heart Study combined



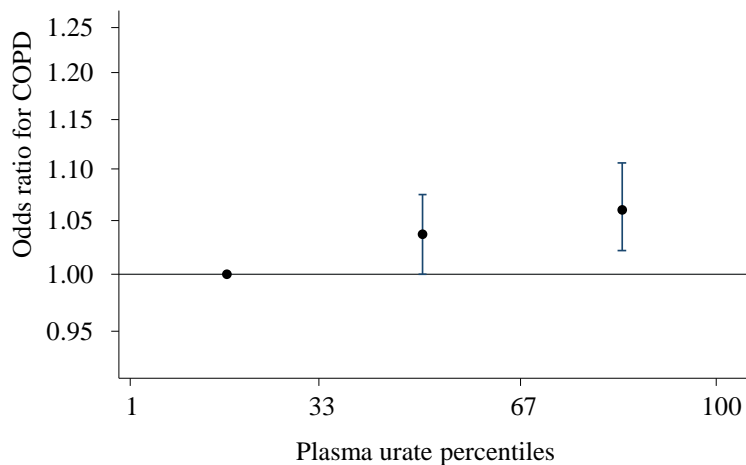
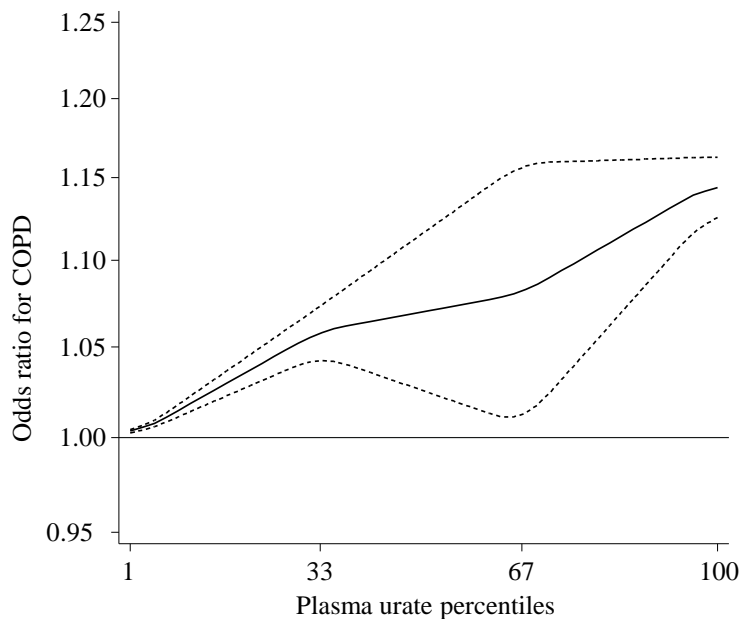
**Supplemental Figure 10. Observational and causal, genetic estimates for lung function, risk of respiratory symptoms, and risk of COPD for a 100μmol/L higher plasma urate in the Copenhagen General Population Study and Copenhagen City Heart Study combined, adjusted for study using the *cluster* command.** Observational estimates are multivariable adjusted and adjusted for clustering by study. Severe dyspnea was defined as mMRC≥2. Genetic, causal estimate is an odds ratio obtained by using the control function estimator which yields odds ratios for genetically determined increases in plasma urate, and confidence intervals are estimated using bootstrap with bias correction. CI: confidence interval. *F*-statistics evaluates the strength of the instrument. *R*<sup>2</sup>: measure of variation explained by the allele score.



**Supplemental Figure 11. Multivariable adjusted odds ratios for COPD according to plasma urate percentiles in the Copenhagen General Population and the Copenhagen City Heart Study combined, stratified by smoking status and adjusted for study by using the *cluster* command.**

Grey line and shaded area: never smokers (N=43 774). Black line: ever smokers (N=64 396).

Solid lines are multivariable adjusted odds ratios and dashed lines indicate 95% confidence interval derived from restricted cubic spline regression with knots chosen by Akaike information criterion and plotted using a polynomial smoother. Uric acid percentiles were adjusted for sex, study and year of measurement. Multivariable adjustments were for age, sex, smoking status, cumulative smoking, body mass index, physical activity in leisure time, education, income, intake of meat (only available for the Copenhagen General Population Study), intake of alcohol, preexisting cardiovascular disease, exposure to occupational dust and fumes, plasma creatinine, and C-reactive protein. 6809 individuals with self-reported asthma were excluded. COPD: chronic obstructive pulmonary disease.



No. of participants	33 001	31 035	28 027
No. of COPD	4 231	3 981	3 826

**Supplemental Figure 12. Risk of COPD among complete cases in the Copenhagen General Population and the Copenhagen City Heart Study combined, adjusted using the *cluster* command.**

All individuals with missing information in one or several covariates have been removed from analyses. Solid lines are multivariable adjusted odds ratios using a polynomial smoother and dashed lines indicate 95% confidence interval derived from restricted cubic spline regression. Plasma urate percentiles are assigned by sex, study, and year of measurement. The analyses were multivariable adjusted for age, sex, smoking status, cumulative smoking, body mass index, physical activity during leisure time, intake of meat (only available for CGPS), intake of alcohol, income, education, preexisting cardiovascular disease, exposure to occupational dust and fumes, plasma creatinine, plasma C-reactive protein, and study. Individuals with self-reported asthma were excluded. COPD: chronic obstructive pulmonary disease.