

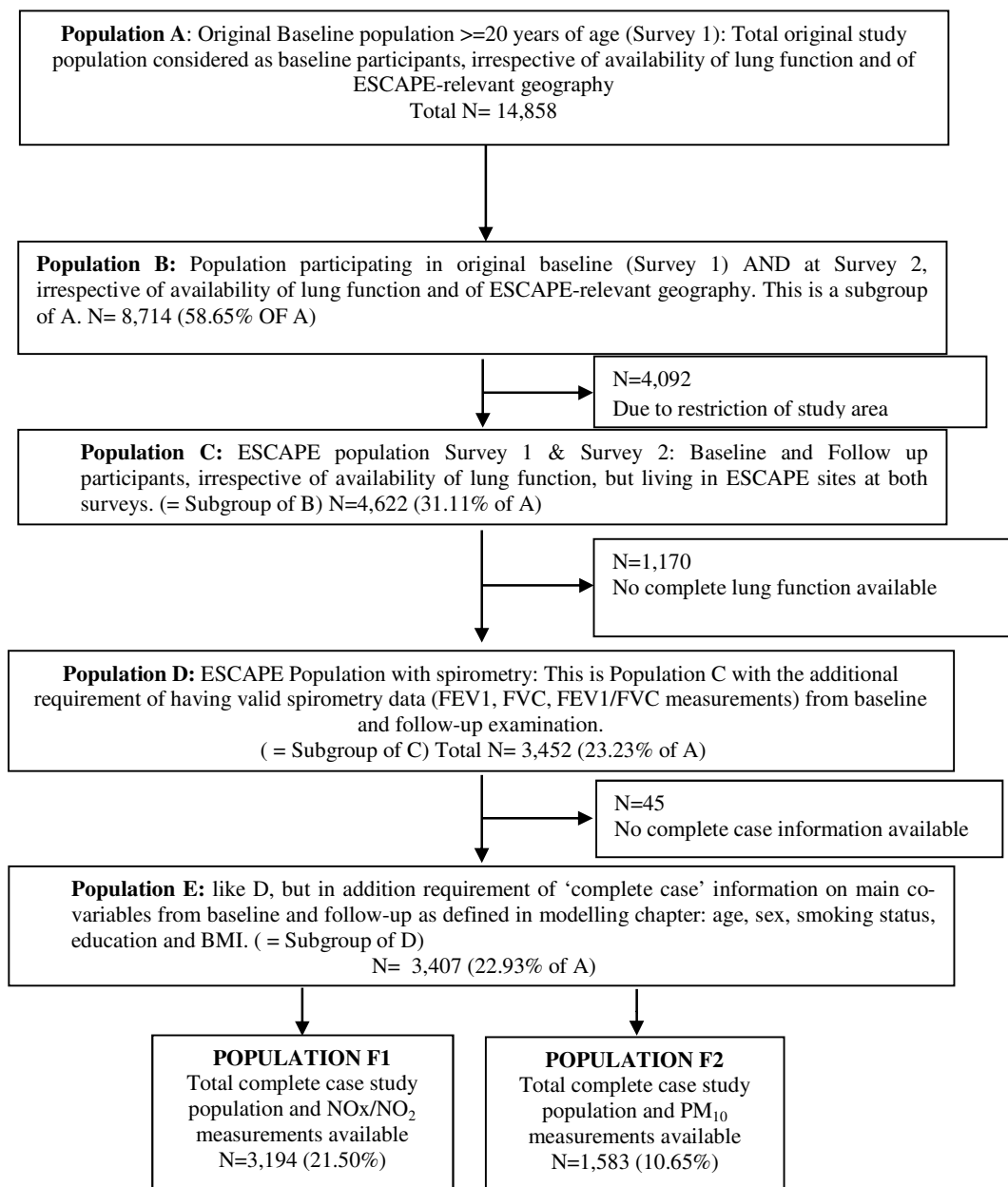
## **Online Supplement material**

### **Effect of ambient air pollution on the prevalence and incidence of COPD**

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## Study population of ECRHS

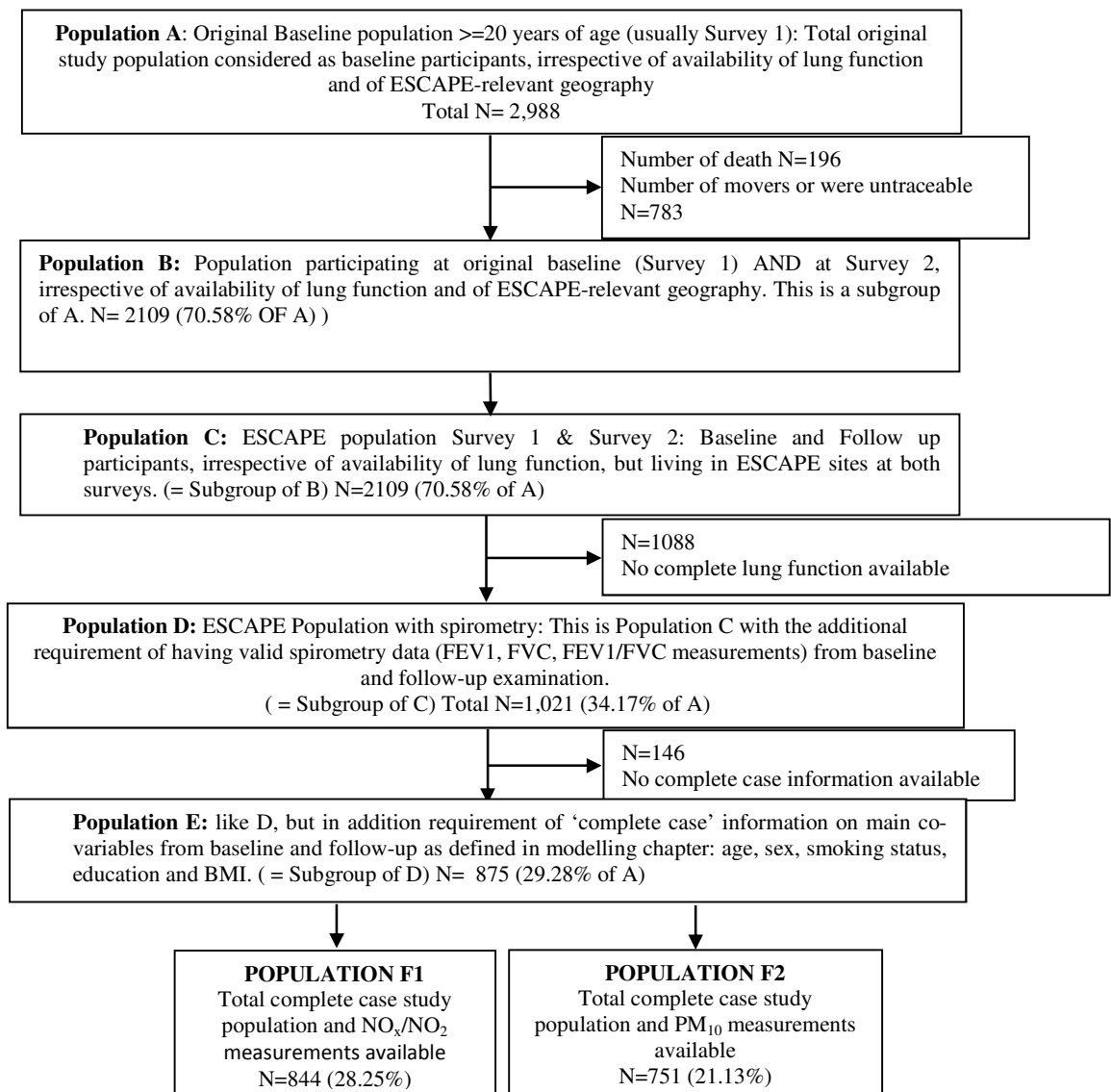
**ECRHS** (European Community Respiratory Health Survey) was initiated in 1991-93 (ECRHS I), followed up in 2001 (ECRHS II). The study included 48 centres from 23 countries. In ECRHS I adults aged between 20 and 44 years were selected at random from available population based registers. The baseline investigation was based on 14,858 subjects. The follow-up had a response rate of 65.3% of the baseline participants. The main objective of ECRHS I was to estimate the variation in the prevalence of asthma, asthma-like symptoms, asthma sensitization and bronchial reactivity. Further, the identification of risk factors and how these explain variation across Europe was determined as well as the estimation of variation in the treatment for asthma in Europe.



### Study population of NSHD

NSHD (Medical Research Council's National Survey of Health and Development), was originally set in 1946, with the objective to learn about the social and economic costs of child bearing and the distribution and use of obstetric and midwifery services. The cohort of 2'547 women and 2'815 men, a socially stratified sample of all birth that took place in England, Scotland and Wales during the week 3-9 March 1946 [16]. The main objectives since the 1989 follow-up, taken as the baseline follow-up for the ESCAPE study, have therefore been the measurement of physical and mental functioning, the study of pathways to those outcomes, and study of morbidity and mortality for multiple health outcomes.

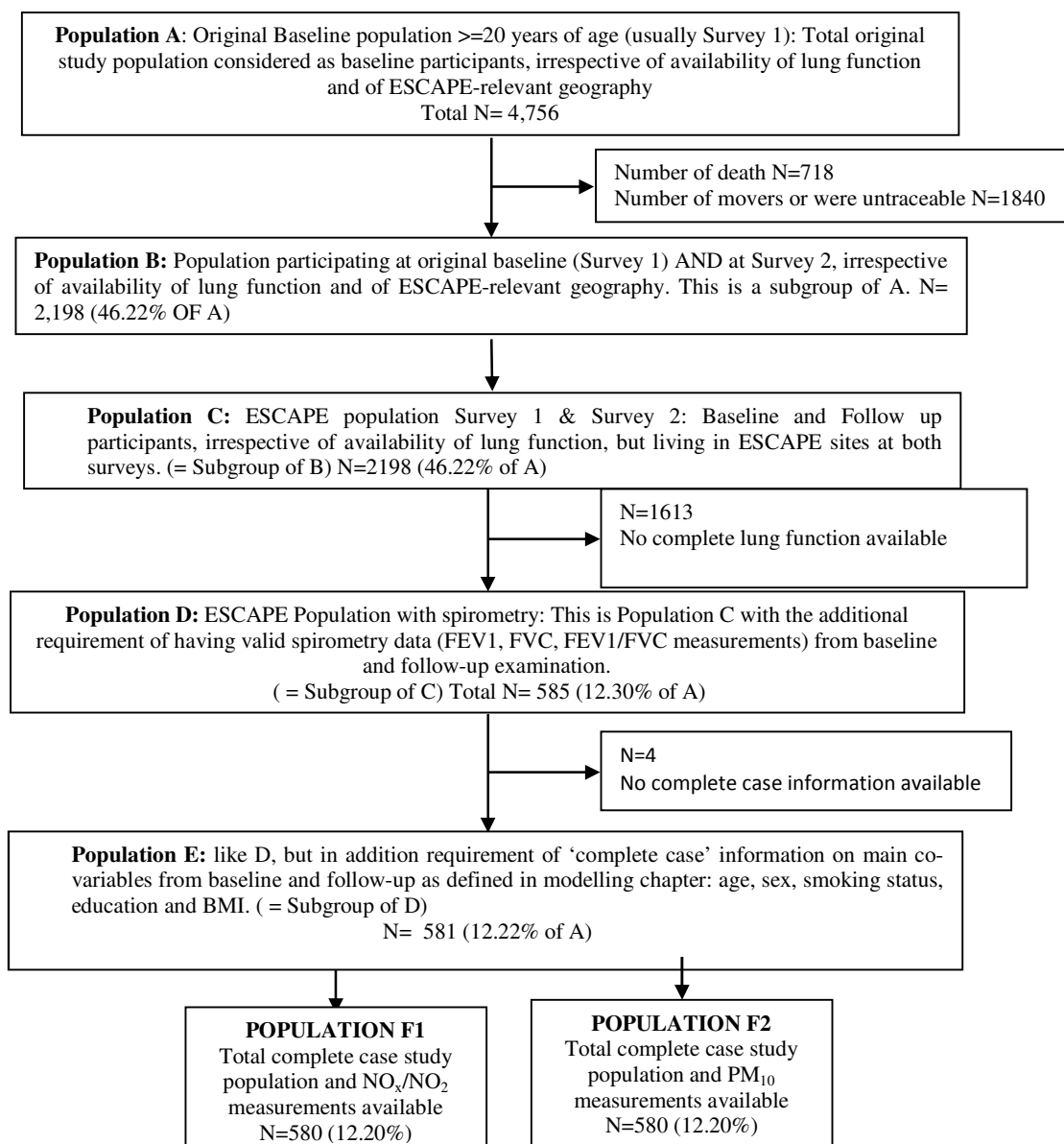
A total of 3'262 individuals were successfully contacted and underwent both questionnaire and clinical assessment including spirometry. This follow-up was repeated when they were 53 years old in 1999, when 3'035 participants were successfully contacted and provided information. In 2006-2011 a range of measurements including spirometry were conducted



### Study population of SALIA

**SALIA** (Study on the influence of Air pollution on Lung function, Inflammation and Aging) study was initiated in 1985 as part of Environmental Health surveys, which were an element of the Clean Air Plan initiated by the Government of North-Rhine Westphalia in Germany. Main objective of the baseline investigations was to monitor health effects of outdoor air pollution in the heavily polluted Ruhr Area. A questionnaire follow-up was conducted in 2006 and in 2007 to 2010 health assessments were performed to investigate the long-term effects of outdoor air pollution and changes in pollution on respiratory health.

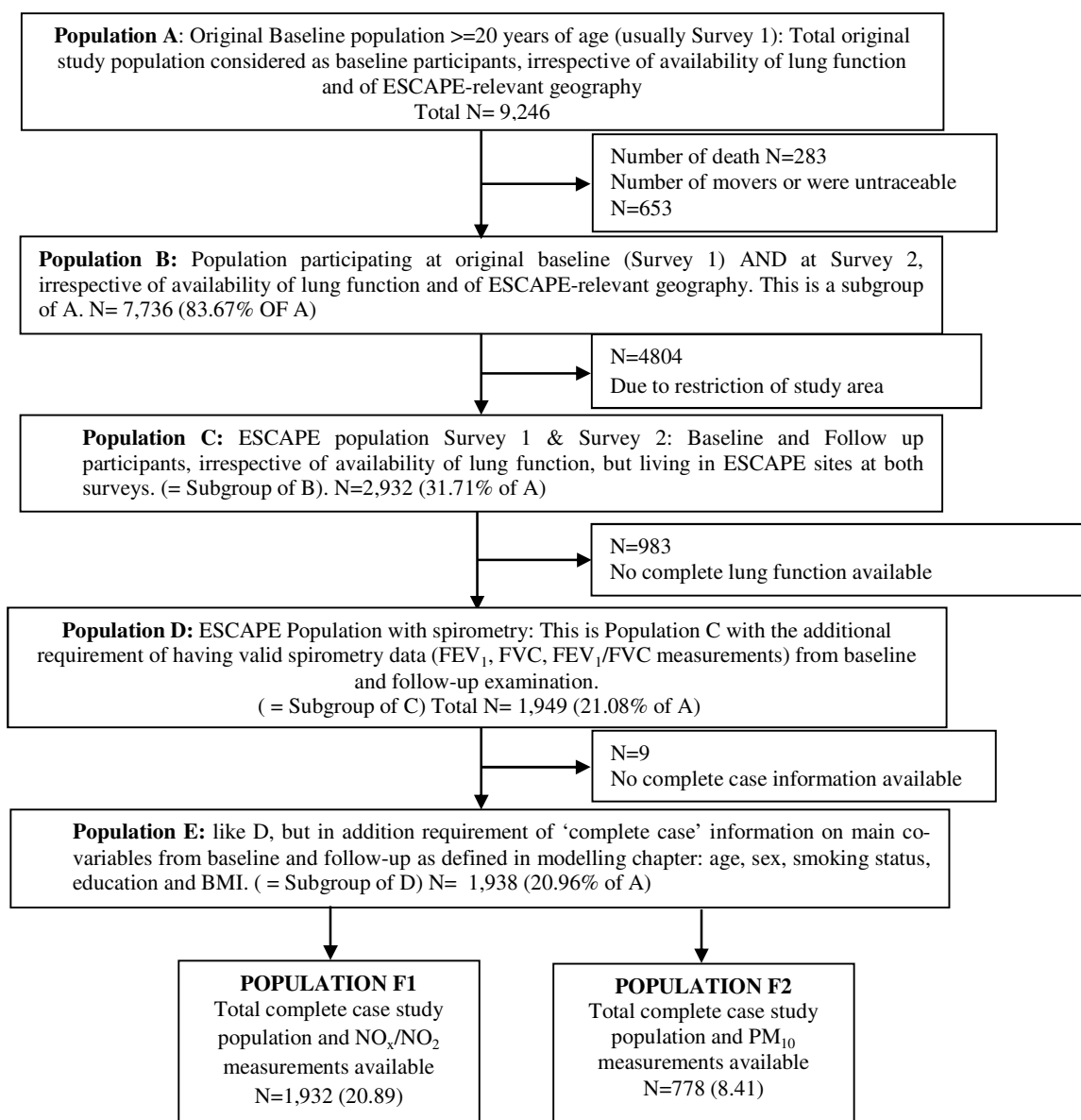
The baseline investigation included 4'757 women. The geographic regions were chosen to represent a range of polluted areas with high traffic load and steel and coal industries. Sampling included all women of German nationality aged 54 to 55 residing in the selected areas.



### Study population of SAPALDIA

**SAPALDIA** (Swiss Cohort Study on Air Pollution and Lung and Heart Diseases in Adults) is a multi-center study that was initiated in 1991 (SAPALDIA 1) in eight geographic areas representing the range of environmental, meteorological and socio-demographic conditions in Switzerland. The main aim of the study was to assess the effect of air pollution (outdoor and indoor) on respiratory and cardiovascular health, with a special focus on how the respiratory and cardiovascular system interact in this regard, and on the role of lifestyle and genetic background.

In 1991, 9'651 subjects, aged 18 to 60 years, were recruited for a detailed interview and more than 90% of them provided valid spirometry results. The follow-up assessment (SAPALDIA 2) was conducted in 2002 and 8'047 (83%) participants provided health information and 6'528 persons underwent physical re-examination.



## Methods

### Definition of COPD

1) *GOLD Definition*: GOLD is widely accepted developed spirometric classifications in order to define and stage COPD based on fixed thresholds [35, 36]. COPD was defined as a forced expiratory volume in one second by forced vital capacity ratio ( $FEV_1/FVC < 0.70$ ).

2) *Lower Limit of Normal (LLN)*: in the sensitivity analyses, COPD was also defined as a  $FEV_1/FVC$  below the statistically derived age and sex-dependent LLN, i.e. the fifth percentile of the  $FEV_1/FVC$  in a large healthy reference group. The LLN was calculated using the NHANES reference equations.

The severity of COPD is defined by the degree of airflow obstruction, measured with  $FEV_1$ . Three cut-offs are generally used to derive four stages of severity, namely  $FEV_1 \geq 80\%$ , 50-80%, 30-50% and for the most severe cases  $< 30\%$  of predicted. The prevalence of COPD stage 3 and 4 was low in our populations. We therefore evaluated prevalence and incidence of COPD for only 2 categories, namely COPD in all stages (stage 1 or higher, i.e. stage 1+) and the combined group of stage 2, 3 and 4 (stage 2+) in all four cohorts.

Prevalent cases of COPD were defined both at baseline, and at follow-up disregarding whether they were disease free at baseline.

An incident case of COPD at follow-up was defined as a study participant without COPD at baseline, but having COPD at follow-up.

### Statistical models

Logistic regression models were used in each study separately to obtain study-specific estimates. Four alternative models were defined. **MODEL 1** was the unadjusted crude analyses, **MODEL 2** was a simple model with adjustment only for age, age squared, height, and sex (both in the prevalence and incidence analyses). **MODEL 3 (Main**

**Model of reference**) was adjusted for a common set of potential confounders, which were available in all studies in a standardised form, based on evidence from previous studies and the assessment and quality of available data within the ESCAPE cohorts. Thus, with respect to Model 2, Model 3 additionally included BMI, education, smoking status and packyears in the prevalence analyses, and BMI, BMI change (BMI at follow-up minus BMI at baseline), education (< 10 years;  $\geq$  10 years of schooling), smoking status (current, former and never smoker), quitting smoking during follow-up, and packyears in the incidence analyses. **Model 3** is used for the assessment of interactions and for the sensitivity analyses and the meta-analyses.

**MODEL 4** was the “optimal model”, which was an expansion of the main model, including additional variables to take into account passive smoking and occupational exposure to fumes, dust, or gases.

In line with general ESCAPE protocols, the preliminary first analyses were conducted with the air pollution exposure estimates as provided from the ESCAPE LUR model. However, upon availability, models were run with the back-extrapolated estimates as those are more appropriate in our case. All models were run with all nine available markers of air pollution among the respective sub-populations. Models with the traffic proximity markers also included NO<sub>2</sub> background level as a covariate, to ensure the main estimates of interest would only capture effects of local near-road pollutants.

Traffic variables were used both as continuous variables and in categories. We used the following categories:  $\leq 5000$  and  $> 5000$  for traffic intensity on the nearest major road and  $\leq 500.000$  and  $> 500.000$  for the traffic intensity on major roads within a 100m buffer.

Effect modification was tested by stratifying the analyses by gender, smoking status (ever and never smoker) and obesity ( $< 30\text{kg/m}^2$ ,  $\geq 30\text{kg/m}^2$ ).

Sensitivity analyses were conducted using the main Model and for a sub-set of exposures and outcomes. To additionally explore the difference between the ESCAPE exposure modelling approach and the study-specific modelling approach, we ran the analysis using the study-specific exposure models only in SALIA and SAPALDIA and introduced the factors that were different between the two approaches step by step.

## **Meta-analysis**

Meta-analysis of individual study results was performed to provide overall estimates. All meta-analyses were conducted from the main model results only and where appropriate the related subgroup and/or sensitivity analyses results, which are based on the main model as well. The heterogeneity of the effect estimates between the studies was assessed using the  $X^2$  test. In the absence of heterogeneity between studies (i.e., if the p-value of heterogeneity was larger than 0.1), fixed-effect models were used to calculate the summary effect estimates. In presence of heterogeneity, random-effect models were used instead. In addition, the  $I^2$  statistic quantifying heterogeneity was calculated [37].

We assessed the contribution from each cohort to the overall effect estimate by assessing their percent weight.



## References

35. Pauwels RA, Buist AS, Ma P, Jenkins CR, Hurd SS. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: National Heart, Lung, and Blood Institute and World Health Organization Global Initiative for Chronic Obstructive Lung Disease (GOLD): executive summary. *Respir Care* 2001; 46(8): 798-825.
36. Gold PM. The 2007 GOLD Guidelines: a comprehensive care framework. *Respir Care* 2009; 54(8): 1040-1049.
37. DerSimonian R, Laird N. Meta-analysis in clinical trials. *Controlled clinical trials* 1986; 7(3): 177-188.

**Online Supplement Table 1** Prevalence at follow-up and Incidence of COPD in all stages (1+) and in stage 2+ using the GOLD criteria. Presented are all four study populations stratified by sex, and smoking status for population with NO<sub>2</sub> and PM measures, respectively

		All	Females	Males	Ever smoker	Never smoker
<b>ECRHS</b>						
<b>NO<sub>2</sub> population</b>		<b>N=2854</b>	<b>N=1422</b>	<b>N=1432</b>	<b>N=1636</b>	<b>N=1218</b>
		<b>N (%)</b>	<b>N (%)</b>	<b>N (%)</b>	<b>N (%)</b>	<b>N (%)</b>
prevalence	all stages	106 (3.32)	38 (2.36)	68 (4.30)	72 (3.99)	34 (2.45)
	stage 2 plus	34 (1.06)	11 (0.68)	23 (1.45)	28 (1.55)	6 (0.43)
incidence	all stages	61 (1.91)	25 (1.55)	36 (2.28)	44 (2.44)	17 (1.22)
	stage 2 plus	11 (0.34)	4 (0.25)	7 (0.44)	9 (0.50)	2 (0.14)
<b>PM population</b>		<b>N=1390</b>	<b>N=730</b>	<b>N=660</b>	<b>N=747</b>	<b>N=643</b>
		<b>N (%)</b>	<b>N (%)</b>	<b>N (%)</b>	<b>N (%)</b>	<b>N (%)</b>
prevalence	all stages	59 (3.73)	23 (2.77)	36 (4.78)	36 (4.31)	23 (3.08)
	stage 2 plus	15 (0.95)	5 (0.60)	10 (1.33)	12 (1.44)	3 (0.40)
incidence	all stages	36 (2.27)	17 (2.05)	19 (2.52)	23 (2.75)	13 (1.74)
	stage 2 plus	7 (0.44)	3 (0.36)	4 (0.53)	5 (0.60)	2 (0.27)
<b>NSHD</b>						
<b>NO<sub>2</sub> population</b>		<b>N=761</b>	<b>N=416</b>	<b>N=345</b>	<b>N=519</b>	<b>N=242</b>
		<b>N (%)</b>	<b>N (%)</b>	<b>N (%)</b>	<b>N (%)</b>	<b>N (%)</b>
prevalence	all stages	52 (6.20)	29 (6.16)	23 (6.17)	39 (6.79)	13 (4.81)
	stage 2 plus	26 (3.10)	19 (4.03)	7 (1.88)	21 (3.66)	5 (1.85)
incidence	all stages	32 (3.80)	18 (3.82)	14 (3.75)	22 (3.83)	10 (3.70)
	stage 2 plus	15 (1.80)	11 (2.34)	4 (1.07)	11 (1.92)	4 (1.48)
<b>PM population</b>		<b>N=683</b>	<b>N=370</b>	<b>N=313</b>	<b>N=475</b>	<b>N=208</b>
		<b>N (%)</b>	<b>N (%)</b>	<b>N (%)</b>	<b>N (%)</b>	<b>N (%)</b>
prevalence	all stages	47 (6.26)	26 (6.22)	21 (6.31)	35 (6.72)	12 (5.22)
	stage 2 plus	24 (3.20)	17 (4.07)	7 (2.10)	19 (3.65)	5 (2.17)
	all stages	29 (3.86)	17 (4.07)	12 (3.60)	20 (3.84)	9 (3.91)

incidence	stage 2 plus	14 (1.86)	10 (2.39)	4 (1.20)	10 (1.92)	4 (1.74)
<b>SALIA</b>						
<b>NO<sub>2</sub> population</b>		<b>N=517</b>	<b>N=517</b>	<b>-</b>	<b>N=106</b>	<b>N=411</b>
		<b>N (%)</b>	<b>N (%)</b>	<b>N (%)</b>	<b>N (%)</b>	<b>N (%)</b>
prevalence	all stages	84 (14.48)	84 (14.48)	-	19 (15.70)	65 (14.16))
	stage 2 plus	26 (4.48)	26 (4.48)	-	10 (8.26)	16 (3.49)
incidence	all stages	61 (10.52)	61 (10.52)	-	16 (13.22)	45 (9.80)
	stage 2 plus	17 (2.93)	17 (2.93)	-	8 (6.61)	9 (1.96)
<b>PM population</b>		<b>N=517</b>	<b>N=517</b>	<b>-</b>	<b>N=106</b>	<b>N=411</b>
		<b>N (%)</b>	<b>N (%)</b>	<b>N (%)</b>	<b>N (%)</b>	<b>N (%)</b>
prevalence	all stages	84 (14.48)	84 (14.48)	-	19 (15.70)	65 (14.16))
	stage 2 plus	26 (4.48)	26 (4.48)	-	10 (8.26)	16 (3.49)
incidence	all stages	61 (10.52)	61 (10.52)	-	16 (13.22)	45 (9.80)
	stage 2 plus	17 (2.93)	17 (2.93)	-	8 (6.61)	9 (1.96)
<b>SAPALDIA</b>						
<b>NO<sub>2</sub> population</b>		<b>N=1587</b>	<b>N=881</b>	<b>N=706</b>	<b>N=899</b>	<b>N=866</b>
		<b>N (%)</b>	<b>N (%)</b>	<b>N (%)</b>	<b>N (%)</b>	<b>N (%)</b>
prevalence	all stages	276 (15.65)	135 (13.78)	141 (17.98)	190 (19.04)	86 (11.23)
	stage 2 plus	82 (4.65)	63 (6.43)	19 (2.42)	61 (6.11))	21 (2.74)
incidence	all stages	188 (10.66)	102 (10.41)	86 (10.97)	118 (11.82)	70 (9.14)
	stage 2 plus	48 (2.72)	40 (4.08)	8 (1.02)	34 (3.41)	14 (1.83)
<b>PM population</b>		<b>N=674</b>	<b>N=386</b>	<b>N=288</b>	<b>N=377</b>	<b>N=297</b>
		<b>N (%)</b>	<b>N (%)</b>	<b>N (%)</b>	<b>N (%)</b>	<b>N (%)</b>
prevalence	all stages	92 (12.62)	49 (11.61)	43 (14.01)	62 (15.27)	30 (9.29)
	stage 2 plus	34 (4.66)	22 (5.21)	12 (3.91)	25 (6.16)	9(2.79)
incidence	all stages	78 (10.70)	44 (10.43)	34 (11.07)	51 (12.56)	27 (8.36)
	stage 2 plus	24(3.29)	17 (4.03)	7 (2.28)	18 (4.43)	6 (1.86)

# Online Supplement Table 2 A-D

Correlation matrix for all individually assigned markers of home outdoor exposures

Online supplement table 2A (ECRHS)

	PM <sub>2.5</sub>	PM <sub>2.5abs</sub>	PM <sub>10</sub>	PM <sub>coarse</sub>	NO <sub>2</sub>	NO <sub>x</sub>	NO <sub>2</sub> background	TRAFNEAR	TRAFMAJORLOAD	Backextrapolated PM <sub>10</sub> to follow-up	Backextrapolated NO <sub>2</sub> to follow-up
PM <sub>2.5</sub> [5 µg/m <sup>3</sup> ]	1 1540										
PM <sub>2.5abs</sub> [1*10 <sup>-5</sup> m <sup>-1</sup> ]	0.80 1540	1 1540									
PM <sub>10</sub> [10µg/m <sup>3</sup> ]	0.89 1540	0.78 1540	1 1540								
PM <sub>coarse</sub> [10 µg/m <sup>3</sup> ]	0.77 1540	0.85 1540	0.90 1540	1							
NO <sub>2</sub> [10 µg/m <sup>3</sup> ]	0.83 1540	0.87 1540	0.85 1540	0.53 1540	1 1540						
NO <sub>x</sub> [20 µg/m <sup>3</sup> ]	0.67 1540	0.77 1540	0.70 1540	0.75 1540	0.91 1540	1 1540					
NO <sub>2</sub> background	0.65 1408	0.51 1540	0.62 1408	0.53 1408	0.64 1408	0.51 1408	1 1408				
TRAFNEAR [5000 cars/day]	0.58 1443	0.57 1443	0.50 1444	0.50 1444	0.52 1443	0.40 1443	0.22 1311	1 1444			
TRAFMAJORLOAD [4'000'00 cars/day*100]	0.53 1311	0.68 1311	0.50 1312	0.62 1312	0.66 1311	0.68 1311	0.30 1311	0.52 1312	1 1312		
Backextrapolated PM <sub>10</sub> to follow-up	0.82 1214	0.57 1214	0.96 1214	0.79 1214	0.74 1214	0.52 1214	0.58 1214	0.49 1214	0.33 1214	1	
Backextrapolated NO <sub>2</sub> to follow-up	0.78 1582	0.90 1320	0.74 1582	0.76 1582	0.96 3194	0.86 3194	0.79 3046	0.52 2175	0.60 2199	0.65 1214	1

Online supplement able 2B (NSHD):

	PM <sub>2.5</sub>	PM <sub>2.5abs</sub>	PM <sub>10</sub>	PM <sub>coarse</sub>	NO <sub>2</sub>	NO <sub>x</sub>	NO <sub>2</sub> background	TRAFNEAR	TRAFMAJORLOAD	Backextrapolated PM <sub>10</sub> to baseline	Backextrapolated NO <sub>2</sub> to baseline
PM <sub>2.5</sub> [5 µg/m <sup>3</sup> ]	1 751										
PM <sub>2.5abs</sub> [1*10 <sup>-5</sup> m <sup>-1</sup> ]	0.64 751	1 751									
PM <sub>10</sub> [10µg/m <sup>3</sup> ]	0.64 751	0.57 751	1 751								
PM <sub>coarse</sub> [10 µg/m <sup>3</sup> ]	0.20 751	0.31 751	0.66 751	1 751							
NO <sub>2</sub> [10 µg/m <sup>3</sup> ]	0.89 751	0.83 751	0.60 751	0.17 751	1 844						
NO <sub>x</sub> [20 µg/m <sup>3</sup> ]	0.89 751	0.74 751	0.60 751	0.19 751	0.92 844	1 844					
NO <sub>2</sub> background	0.58 751	0.83 751	0.43 751	0.12 751	0.86 844	0.70 844	1 844				
TRAFNEAR [5000 cars/day]	0.10 751	0.17 75	0.18 751	0.21 751	0.07 844	0.13 844	-0.06 844	1 844			
TRAFMAJORLOAD [4'000'00 cars/day*100]	0.25 751	0.31 751	0.27 751	0.32 751	0.22 844	0.28 844	0.04 844	0.54 844	1 844		
Backextrapolated PM <sub>10</sub> to baseline	0.48 748	0.42 748	0.74 748	0.52 748	0.45 748	0.44 748	0.33 748	0.09 748	0.19 748	1	
Backextrapolated NO <sub>2</sub> to baseline	0.67 748	0.67 748	0.45 748	0.14 748	0.80 841	0.73 841	0.72 841	0.04 841	0.15 841	0.56 748	1

Online supplement table 2C (SALIA):

	PM <sub>2.5</sub>	PM <sub>2.5abs</sub>	PM <sub>10</sub>	PM <sub>coarse</sub>	NO <sub>2</sub>	NO <sub>x</sub>	NO <sub>2</sub> background	TRAFNEAR	TRAFMAJORLOAD	Backextrapolated PM <sub>10</sub> to baseline	Backextrapolated NO <sub>2</sub> to baseline
PM <sub>2.5</sub> [5 µg/m <sup>3</sup> ]	1 580										
PM <sub>2.5abs</sub> [1*10 <sup>-5</sup> m <sup>-1</sup> ]	0.90 580	1 580									
PM <sub>10</sub> [10µg/m <sup>3</sup> ]	0.91 580	0.93 580	1 580								
PM <sub>coarse</sub> [10 µg/m <sup>3</sup> ]	0.79 580	0.83 580	0.82 580	1 580							
NO <sub>2</sub> [10 µg/m <sup>3</sup> ]	0.80 580	0.88 580	0.78 580	0.74 580	1 580						
NO <sub>x</sub> [20 µg/m <sup>3</sup> ]	0.80 580	0.83 580	0.77 580	0.73 580	0.98 580	1 580					
NO <sub>2</sub> background	0.74 580	0.79 580	0.70 580	0.71 580	0.80 580	0.81 580	1 580				
TRAFNEAR [5000 cars/day]	0.13 580	0.23 580	0.12 580	0.12 580	0.22 580	0.23 580	0.11 580	1 580			
TRAFMAJORLO AD [4'000'00 cars/day*100]	0.25 580	0.48 580	0.29 580	0.27 580	0.44 580	0.32 580	0.22 580	0.40 580	1 580		
Backextrapolated PM <sub>10</sub> to baseline	0.69 580	0.76 580	0.77 580	0.68 580	0.66 580	0.64 580	0.64 580	0.11 580	0.26 580	1	
Backextrapolated NO <sub>2</sub> to baseline	0.71 580	0.81 580	0.73 580	0.83 580	0.86 580	0.85 580	0.80 580	0.16 580	0.35 580	0.83 580	1

Online supplement table 2D (SAPALDIA):

	PM <sub>2.5</sub>	PM <sub>2.5abs</sub>	PM <sub>10</sub>	PM <sub>coarse</sub>	NO <sub>2</sub>	NO <sub>x</sub>	NO <sub>2</sub> background	TRAFNEAR	TRAFMAJORLOAD	Backextrapolated PM <sub>10</sub> to baseline	Backextrapolated NO <sub>2</sub> to baseline
PM <sub>2.5</sub> [5 µg/m <sup>3</sup> ]	1 729										
PM <sub>2.5abs</sub> [1*10 <sup>-5</sup> m <sup>-1</sup> ]	0.71 729	1 729									
PM <sub>10</sub> [10µg/m <sup>3</sup> ]	0.70 729	0.67 729	1 729								
PM <sub>coarse</sub> [10 µg/m <sup>3</sup> ]	0.62 729	0.79 729	0.80 729	1 729							
NO <sub>2</sub> [10 µg/m <sup>3</sup> ]	0.72 729	0.75 729	0.83 729	0.62 729	1 1764						
NO <sub>x</sub> [20 µg/m <sup>3</sup> ]	0.68 729	0.74 729	0.75 729	0.77 729	0.91 1764	1 1764					
NO <sub>2</sub> background	0.63 729	0.77 729	0.64 729	0.62 729	0.63 1764	0.62 1764	1 1764				
TRAFNEAR [5000 cars/day]	0.15 729	0.09 729	0.28 729	0.25 729	0.20 1764	0.22 1697	0.12 1697	1			
TRAFMAJORLOAD D [4'000'00 cars/day*100]	0.29 729	0.15 729	0.28 729	0.12 729	0.24 1764	0.23 1671	0.03 1671	0.05 1671	1		
Backextrapolated PM <sub>10</sub> to baseline	0.41 726	0.43 726	0.44 726	0.41 726	0.46 726	0.44 726	0.25 726	0.19 726	0.33 726	1	
Backextrapolated NO <sub>2</sub> to baseline	0.40 727	0.46 727	0.40 727	0.47 727	0.53 727	0.53 727	0.23 727	0.24 727	0.32 727	0.88 726	1

### Online supplement table 3

LUR model results for the different pollutants for each study area included in the COPD analysis: model explained variance ( $R^2$ ), leave-one-out cross-validation explained variance (CV  $R^2$ ) and descriptive Statistics of the Measured Concentrations for  $\text{NO}_x$ ,  $\text{NO}_2$ ,  $\text{PM}_{10}$ ,  $\text{PM}_{2.5}$ ,  $\text{PM}_{\text{coarse}}$  and  $\text{PM}_{2.5\text{absorbance}}$

Centre/Area	$R^2$ in WP4 cohorts	$R^2$ cross validation (LOOCV $R^2$ )	RMSE (cross validation ( $\mu\text{g}/\text{m}^3$ ))	Number of sites†	Moran's I (p-value)	Measured concentration ( $\mu\text{g}/\text{m}^3$ ) mean [min-max]
<b><math>\text{NO}_x</math></b>						
Umea, Region Sweden	87%	82%	7.9	40	-0.13 (0.12)	18.9 [2.3-95.9]
London/Oxford, UK	91%	88%	16.2	40	-0.009 (0.78)	69.3 [18.8-257.4]
Netherlands/Belgium region	87%	82%	11.2	80	-0.16 (0.06)	51.8 [17.5-130.8]
Ruhr area, Germany	88%	81%	13.6	40	-0.03 (0.95)	60.0 [26.9-135.7]
Erfurt, Germany	87%	84%	4.3	39	-0.02 (0.95)	28.8 [15.6-61.8]
Paris, France	75%	67%	31.6	40	-0.06 (0.77)	80.3 [12.7-248.3]
Grenoble, France	82%	74%	11.2	40	-0.07 (0.76)	48.2 [6.5-116.2]
Basel, Switzerland	61%	52%	12.0	40	-0.04 (0.71)	53.1 [21.6-95.7]
Geneva, Switzerland	81%	73%	9.1	40	0.003 (0.23)	55.9 [22.1-108.6]
Lugano, Switzerland	87%	82%	7.4	42	-0.05 (0.28)	47.8 [21.2-116.4]
Turin, Italy	78%	72%	17.0	40	-0.05 (0.36)	101.2 [22.8-101.2]
Pavia, Italy	88%	80%	9.6	20	-0.08 (0.46)	50.9 [29.5-117.9]
Verona, Italy	64%	54%	32.3	40	-0.02 (0.91)	91.8 [33.1-284.4]
Barcelona, Spain	73%	65%	27.7	40	0.02 (0.26)	101.3 [21.0-236.4]
Mid-East Spain: Albacete-Valencia, Spain	88%	84%	11.0	38	0.02 (0.46)	42.7 [0.6-148.6]
Huelva, Spain	56%	31%	11.5	24	-0.15 (0.08)	33.8 [13.3-71.3]
<b><math>\text{NO}_2</math></b>						
Umea, Region Sweden	87%	83%	2.8	40	-0.08 (0.43)	9.3 [1.5-35.8]
London/Oxford, UK	89%	87%	6.6	40	-0.009 (0.71)	37.9 [7.3-102.7]
Netherlands/Belgium region	86%	81%	5.1	80	-0.143 (0.09)	30.9 [12.8-61.5]
Ruhr area, Germany	89%	84%	4.3	40	-0.18 (0.08)	33.2 [20.2-58.4]
Erfurt, Germany	89%	87%	2.1	39	0.01 (0.16)	18.6 [11.0-33.4]
Paris, France	77%	67%	11.6	40	-0.05 (0.71)	39.8 [6.9-96.8]
Grenoble, France	83%	78%	4.8	40	-0.08 (0.82)	27.2 [5.5-53.2]
Basel, Switzerland	67%	58%	4.8	40	-0.05 (0.45)	31.0 [16.0-47.8]
Geneva, Switzerland	87%	81%	3.7	40	0.002 (0.25)	29.3 [16.1-51.3]
Lugano, Switzerland	87%	82%	3.5	42	-0.04 (0.51)	28.6 [12.2-59.1]
Turin, Italy	78%	70%	7.7	40	-0.08 (0.10)	53.3 [15.6-83.7]
Pavia, Italy	92%	87%	3.3	20	-0.05 (0.99)	25.9 [15.7-53.4]
Verona, Italy	64%	55%	10.8	40	-0.05 (0.33)	41.6 [16.3-100.1]
Barcelona, Spain	75%	68%	11.6	40	-0.03 (0.98)	57.7 [13.8-109.0]



Mid-East Spain: Albacete- Valencia, Spain	90%	87%	5.2	38	0.03 (0.37)	26.1 [1.9-75.5]
Huelva, Spain	55%	31%	7.0	24	-0.14 (0.10)	21.9 [8.4-43.4]
<b>PM<sub>10</sub></b>						
London/Oxford, UK	90%	88%	1.5	20	-0.13(0.42)	18.6[12.1-31.2]
Netherlands/Belgium region	68%	60%	2.3	40	0.16 (0.28)	27.1 [21.9-37.0]
Ruhr area, Germany	69%	63%	2.0	20	-0.05 (0.99)	27.9 [22.5-33.6]
Paris, France	87%	77%	3.5	20	-0.13 (0.91)	25.6 [16.6-52.4]
Lugano, Switzerland	87%	80%	1.6	18	-0.13 (0.10)	23.9 [18.5-32.4]
Turin, Italy	78%	69%	3.9	20	-0.07 (0.70)	43.1 [31.5-57.8]
Barcelona, Spain	87%	82%	3.1	20	-0.07 (0.88)	37.4 [17.8-48.5]
<b>PM<sub>2.5</sub></b>						
London/Oxford, UK	82%	77%	1.4	20	-0.19 (0.20)	11.2 [7.0-21.1]
Netherlands/Belgium region	67%	61%	1.2	40	0.02 (0.77)	17.1 [12.7-21.5]
Ruhr area, Germany	88%	79%	0.9	20	-0.02 (0.64)	18.5 [15.5-21.6]
Paris, France	89%	73%	1.8	20	-0.11 (0.83)	16.0 [11.9-30.6]
Lugano, Switzerland	83%	77%	1.1	19	-0.12 (0.10)	17.2 [13.7-22.5]
Turin, Italy	71%	59%	2.0	20	-0.09 (0.45)	29.3 [22.7-36.3]
Barcelona, Spain	83%	71%	2.1	20	0.01 (0.46)	16.3 [8.4-24.4]
<b>PM<sub>2.5abs</sub></b>						
London/Oxford, UK	96%	92%	0.2	20	-0.21(0.16)	1.6 [0.9-4.7]
Netherlands/Belgium region	92%	89%	0.2	40	-0.16 (0.42)	1.7 [0.9-3.0]
Ruhr area, Germany	97%	95%	0.1	20	-0.02 (0.65)	1.6 [1.0-2.6]
Paris, France	91%	81%	0.4	20	-0.16 (0.97)	2.0 [0.8-5.1]
Lugano, Switzerland	79%	71%	0.3	19	-0.13 (0.09)	2.0 [1.2-3.0]
Turin, Italy	88%	81%	0.3	20	-0.06 (0.82)	3.0 [1.6-4.2]
Barcelona, Spain	86%	80%	0.4	20	-0.01 (0.64)	2.7 [0.9-4.9]
<b>PM<sub>coarse</sub></b>						
London/Oxford, UK	68%	57%	1.3	20	-0.17 (0.29)	7.4 [4.4-10.3]
Netherlands/Belgium region	51%	38%	1.7	40	-0.08 (0.75)	9.3 [6.4-15.0]
Ruhr area, Germany	66%	57%	1.2	20	-0.02 (0.73)	9.4 [7.1-12.8]
Paris, France	81%	73%	4.6	20	-0.08 (0.82)	9.6 [3.9-21.8]
Lugano, Switzerland	77%	65%	1.1	18	-0.12 (0.18)	6.8 [3.8-9.9]
Turin, Italy	65%	58%	2.4	20	-0.10 (0.30)	13.8 [7.5-21.5]
Barcelona, Spain	75%	70%	2.3	20	-0.09 (0.61)	21.0 [9.4-26.0]

LOOCV = Leave one out cross validation; RMSE=Root-mean squared error

†Number of sites that were used for the model development.

#### Online supplement Table 4

Adjusted cross-sectional and longitudinal associations between COPD all stages and stage 2 plus according to GOLD criteria and exposure to air pollution and traffic indicators: Results from the random effect meta-analyses of study-specific single pollutant model estimates (OR and 95% CIs) and measures of heterogeneity of effect estimates between cohorts ( $I^2$ -statistic and p-value)

Exposure	all stages			stage 2 plus		
	aOR	95% CI	$I^2$ p-value <sub>het</sub>	aOR	95% CI	$I^2$ p-value <sub>het</sub>
<b>Prevalence of COPD at follow-up<sup>†</sup></b>						
NO <sub>2</sub>	1.07	0.95 - 1.20	6.9 p = 0.358	1.08	0.87 - 1.34	24.2 p = 0.266
NO <sub>x</sub>	1.05	0.94 - 1.16	0.0 p = 0.846	1.05	0.89 - 1.23	0.0 p = 0.502
PM <sub>10</sub>	1.03	0.74 - 1.43	0.0 p = 0.588	1.12	0.68 - 1.83	0.0 p = 0.432
PM <sub>2.5</sub>	0.85	0.58 - 1.24	15.3 p = 0.316	0.87	0.46 - 1.66	24.7 p = 0.263
PM <sub>2.5</sub> absorbance	0.97	0.63 - 1.49	37.4 p = 0.187	0.94	0.60 - 1.50	0.0 p = 0.626
PM <sub>coarse</sub>	0.55	0.16 - 1.89	51.4 p = 0.104	0.44	0.10 - 1.94	4.3 p = 0.371
Traffic intensity on nearest road	1.21	0.91 - 1.62	0.0 p = 0.986	1.34	0.87 - 2.06	0.0 p = 0.798
Traffic intensity on major road in a 100m buffer	1.25	0.96 - 1.62	11.5 p = 0.335	1.45	0.75 - 2.80	56.8 p = 0.074
<b>Incidence of COPD at follow-up<sup>††</sup></b>						
NO <sub>2</sub>	0.99	(0.87, 1.14)	0.0 p=0.635	1.04	(0.75, 1.46)	36.5 p=0.193
NO <sub>x</sub>	0.97	(0.86, 1.11)	0.0 p = 0.894	0.99	(0.76, 1.30)	18.0 p = 0.301
PM <sub>10</sub>	0.85	(0.55, 1.30)	0.0 p= 0.476	0.89	(0.26, 3.06)	38.7 p = 0.180
PM <sub>2.5</sub>	0.73	(0.51, 1.03)	0.0 p= 0.500	0.57	(0.13, 2.40)	89.9 p = 0.000
PM <sub>2.5</sub> absorbance	0.71	(0.49, 1.02)	0.0 p = 0.418	0.93	(0.46, 1.91)	4.6 p = 0.370
PM <sub>coarse</sub>	0.47	(0.14, 1.57)	34.2 p = 0.207	0.24	(0.01, 5.08)	63.2 p = 0.043
Traffic intensity on nearest road	1.29	(0.92, 1.81)	0.0 p = 0.774	1.60	(0.92, 2.79)	0.0 p = 0.947
Traffic intensity on major road in a 100m buffer	1.26	(0.96, 1.67)	0.0 p = 0.688	1.68	(0.73, 3.87)	66.0 p = 0.032

\*Associations are presented for the following increments in exposure: 10 µg/m<sup>3</sup> for NO<sub>2</sub>, 20 µg/m<sup>3</sup> for NO<sub>x</sub>, 1 10<sup>-5</sup>m<sup>-1</sup> for PM<sub>2.5</sub> absorbance, 5 µg/m<sup>3</sup> for PM<sub>2.5</sub>, 10 µg/m<sup>3</sup> for PM<sub>10</sub>, 5 µg/m<sup>3</sup> for PM<sub>coarse</sub>, 5,000 veh/day for traffic intensity on the nearest street; and 4,000,000 veh·day<sup>-1</sup>·m for traffic load on major roads within a 100 m buffer and the unit millions·day<sup>-1</sup>.

<sup>†</sup> MAIN MODEL, i.e. adjusted for sex, age, height, , education, smoking status, and BMI at follow-up; associations with traffic intensity and traffic load were additionally adjusted for background NO<sub>2</sub> concentrations

<sup>††</sup>MAIN MODEL, i.e. adjusted for sex, age, height, education, BMI and smoking at baseline; smoking cessation and change in BMI during the follow-up, ; associations with traffic intensity and traffic load were additionally adjusted for background NO<sub>2</sub> concentrations



NO <sub>2</sub>	1.09	(0.96, 1.23)	0.0	0.875	1.08	(0.85, 1.37)	38.7	0.180
NO <sub>x</sub>	1.06	(0.94, 1.20)	0.0	0.928	1.12	(0.92, 1.35)	0.0	0.435
PM <sub>10</sub>	1.02	(0.91, 1.14)	0.0	0.928	0.71	(0.24, 2.11)	95.8	0.000
PM <sub>2.5</sub>	0.87	(0.63, 1.22)	0.0	0.901	1.03	(0.89, 1.20)	0.0	0.683
PM <sub>2.5</sub> absorbance	1.07	(0.75, 1.53)	0.0	0.937	1.11	(0.88, 1.40)	0.0	0.580
PM <sub>coarse</sub>	0.42	(0.10, 1.73)	94.0	0.000	0.29	(0.03, 2.89)	35.3	0.200
Traffic intensity on nearest road	0.98	(0.72, 1.34)	0.0	0.959	1.21	(0.77, 1.90)	0.0	0.861
Traffic intensity on major road in a 100m buffer	1.22	(0.85, 1.75)	0.0	0.959	1.26	(0.47, 3.37)	78.3	0.003
<b>Never smoker</b>								
NO <sub>2</sub>	1.05	(0.79, 1.38)	48.4	0.121	1.02	(0.66, 1.59)	21.1	0.284
NO <sub>x</sub>	1.03	(0.85, 1.25)	17.9	0.302	1.04	(0.63, 1.72)	42.7	0.155
PM <sub>10</sub>	0.78	(0.29, 2.06)	43.9	0.148	1.24	(0.13, 11.97)	74.1	0.021
PM <sub>2.5</sub>	0.77	(0.32, 1.83)	48.3	0.122	0.89	(0.13, 6.11)	28.4	0.248
PM <sub>2.5</sub> absorbance	0.70	(0.31, 1.57)	60.1	0.057	1.07	(0.40, 2.87)	0.0	0.780
PM <sub>coarse</sub>	0.57	(0.17, 1.89)	9.3	0.347	0.25	(0.01, 6.09)	0.0	0.999
Traffic intensity on nearest road	1.55	(0.77, 3.11)	45.6	0.138	2.83	(0.67, 11.99)	37.8	0.201
Traffic intensity on major road in a 100m buffer	1.31	(0.90, 1.92)	0.0	0.982	<b>2.97</b>	<b>(1.47, 6.01)</b>	0.0	0.810

\*Associations are presented for the following increments in exposure: 10 µg/m<sup>3</sup> for NO<sub>2</sub>, 20 µg/m<sup>3</sup> for NO<sub>x</sub>, 1 10<sup>-5</sup>m<sup>-1</sup> for PM<sub>2.5</sub> absorbance, 5 µg/m<sup>3</sup> for PM<sub>2.5</sub>, 10 µg/m<sup>3</sup> for PM<sub>10</sub>, 5 µg/m<sup>3</sup> for PM<sub>coarse</sub>, 5,000 veh·day<sup>-1</sup>·m for traffic intensity on the nearest street; and 4,000,000 veh·day<sup>-1</sup>·m for traffic load on major roads within a 100 m buffer.

† Adjusted for sex at baseline, smoking at follow-up, maximum educational level, age at follow-up, height at baseline, BMI at follow-up of all participants; associations with traffic intensity and traffic load were additionally adjusted for background NO<sub>2</sub> concentrations

#without SALIA