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Supplemental Material

Residential Air Pollution and Associations with Wheeze and Shortness of Breath in Adults: A Combined Analysis of Cross-Sectional Data from Two Large European Cohorts

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Table S1: Netherlands/Belgium area LUR model used for the Lifelines Cohort Study †

Pollutant	Predictor variables in final model[1]	Final LUR model	R^2 of model	R^2 cross validation
PM2.5	• Regional background concentration estimate for each site location, based on inverse distance weighted interpolation of regional background sites (REGIONALESTIMATE) • Road length of major roads in a 50 meter buffer (MAJORROADLENGTH_50) • Total traffic load of major roads in a 1000 meter buffer (sum of (traffic intensity * length of all segments)) (TRAFMAJORLOAD_1000) [2]	9.46 + 0.42 × REGIONALESTIMATE + 0.01 × MAJORROADLENGTH_50 + 2.28 × 10^{-9} × TRAFMAJORLOAD_1000	67%	61%
PM10	• Total traffic load of major roads in a 500 meter buffer (sum of (traffic intensity * length of all segments)) (TRAFMAJORLOAD_500) [2] • Number of inhabitants in a 5000 meter buffer (POP_5000) • Road length of major roads in a 50 meter buffer (MAJORROADLENGTH_50)	23.71 + 2.16E-8*TRAFMAJORLOAD_500 + 6.68E-6*POP_5000 + 0.02*MAJORROADLENGTH_50	68%	60%
PMcoarse	• Total traffic load of all roads in a 1000 meter buffer (sum of (traffic intensity * length of all segments)) (TRAFLOAD_1000) • Surface area of ports in a 5000 meter buffer (PORT_5000) • Traffic intensity on nearest road (TRAFNEAR)	7.59 + 5.02 × 10^{-9} × TRAFLOAD_1000 + 1.38 × 10^{-7}*PORT_5000 + 5.38 × 10^{-5} × TRAFNEAR	51%	38%
NO2	• Regional background concentration estimate for each site location, based on inverse distance weighted interpolation of regional background sites (REGIONALESTIMATE) • Number of inhabitants in a 5000 meter buffer (POP_5000) • Total traffic load of all roads in a 50 meter buffer (sum of (traffic intensity * length of all segments)) (TRAFLOAD_50) • Road length of all roads in a 1000 meter buffer (ROADLENGTH_1000) • Total heavy-duty traffic load of all roads in a 25 meter buffer (sum of (heavy-duty traffic intensity * length of all segments)) (HEAVYTRAFLOAD_25) • Inverse distance to the nearest road in central road network (DISTINVNEARC1) • Total heavy-duty traffic load of all roads in a 25 to 500 meter buffer (sum of (heavy-duty traffic intensity * length of all segments)) (HEAVYTRAFLOAD_25_500)	−7.80 + 1.18*REGIONALESTIMATE + 2.30E-5*POP_5000 + 2.46E-6*TRAFLOAD_50 + 1.06E-4*ROADLENGTH_1000 + 9.84E-5*HEAVYTRAFLOAD_25 + 12.19*DISTINVNEARC1 + 4.47E-7*HEAVYTRAFLOAD_25_500	86%	81%

† Information extracted from Eeftens et al. (2012) and Beelen et al. (2013)

[1] Units used: road length in meters, traffic load and intensity in veh. day^{-1} m, number of inhabitants in numbers, surface area in m^2

[2] Definition of major road for local road network: road with traffic intensity > 5,000 mvh/24h

Table S2: Southeast England area (London/Oxford) LUR model used for UK Biobank study [†]

Pollutant	Predictor variables in final model[1]	Final LUR model	R^2 of model	R^2 cross validation
PM2.5	• Product of inverse distance to the nearest road and nearest major road and traffic intensity on this road (INTMAJORINVDIST)[2] • Road length of all roads in a 500 meter buffer (ROADLENGTH_500)	$7.19 + 1.38 \times 10^{-3} \times$ INTMAJORINVDIST $+ 2.65 \times 10^{-4} \times$ ROADLENGTH_500	82%	77%
PM10	• Inverse distance to the nearest road of the central road network (DISTINVMAJORC1)[3] • Heavy-duty traffic intensity on nearest major road (HEAVYTRAFMAJOR) • Sum of high density and low density residential land in a 300 meter buffer (HLDRES_300)	11.40 + 76.99*DISTINVMAJORC1 + 1.35E-3*HEAVYTRAFMAJOR + 1.30E-5*HLDRES_300	90%	88%
PMcoarse	• Inverse distance and inverse squared distance to the nearest major road in local road network (DISTINVMAJOR1)[2] • Heavy-duty traffic intensity on nearest major road (HEAVYTRAFMAJOR)[2]	5.36 + 33.08*DISTINVMAJOR1 + $7.98 \times 10^{-4} \times$ HEAVYTRAFMAJOR	68%	57%
NO2	• Total traffic load of major roads in a 50 meter buffer (sum of (traffic intensity * length of all segments)) (TRAFMAJORLOAD_50)[2] • Road length of all roads in a 500 meter buffer (ROADLENGTH_500) • Sum of high density and low density residential land in a 5000 meter buffer (HLDRES_5000)	8.51 + 7.30E-6*TRAFMAJORLOAD_50 + 1.10E-3*ROADLENGTH_500 + 2.00E-7*HLDRES_5000	89%	87%

[†] Information extracted from Eeftens et al. (2012) and Beelen et al. (2013); validation data shown in this table is not specific to the study area included in the present analysis

[1] Units used: road length in meters, traffic load and intensity in veh. day^{-1} m, number of inhabitants in numbers, surface area in m^2

[2] Definition of major road for local road network: road with traffic intensity > 5,000 mvh/24h

[3] Definition of major road for central road network: classes 0, 1, and 2 (+ classes 3 and 4 based on local knowledge and decision)

Table S3: Questionnaire assessment items used by Lifelines and UK Biobank

Variable	Study	Questionnaire assessment items
Outcome variables		
Wheezing	LifeLines	*Have you had wheezing or whistling in your chest at any time?* (Yes, No)[1]
	UK Biobank	*Wheeze or whistling in the chest in last year?* (Yes, No, Don't know, Prefer not to answer)
Shortness of breath	LifeLines	*Have you had an attack of shortness of breath that came on during the day when you were at rest?* (Yes, No) [1]
	UK Biobank	*Shortness of breath walking on level ground?* (Yes, No, Don't know, Prefer not to answer) [1, 2]
Confounding factors and potential modifiers		
Sex	LifeLines	*What is your gender?* (Man, Woman)
	UK Biobank	*Sex* (Female, Male)
Age	LifeLines	*What is your date of birth?* (Day:___ Month:___ Year:___)
	UK Biobank	*Age when attended assessment centre:* ____
Body mass index	LifeLines	*Measured height in cm:* ____ *Measured weight in kg:* ____
	UK Biobank	*Measured height in cm:* ____ *Measured weight in kg:* ____
Education level	LifeLines	*What is your highest level of education?* (Primary education not completed, Primary education, Basic vocational training, Secondary education, Senior secondary vocational education, General senior secondary education, Higher professional education (with applied emphasis), Academic higher education (university))
	UK Biobank	*Which of the following qualifications do you have?* (College or university degree, A levels/AS levels or equivalent, O levels/GCSEs or equivalent, CSEs or equivalent, NVQ or HND or HNC or equivalent, Other professional qualifications eg: nursing, teaching, None of the above, Prefer not to answer)
Income	LifeLines	*How much is your net income (take home pay) per month? If you share the costs with someone, then add the net income of your partner(s) to your income.* (less than € 750, € 750 – € 1000, € 1000 – € 1500, € 1500 – € 2000, € 2000 – € 2500, € 2500 – € 3000, € 3000 – € 3500, more than € 3500, I do not know, I would rather not fill this in)
	UK Biobank	*What is the average total income before tax received by your HOUSEHOLD?* (Less than £18,000, £18,000 to £30,999, £31,000 to £51,999, £52,000 to £100,000, Greater than £100,000, Do not know, Prefer not to answer)
Smoking status	LifeLines	*Do you now smoke, as of one month ago?* (Yes, No) *Have you ever smoked for as long as a year?* (Yes, No)
	UK Biobank	*Smoking status* (Never, Previous, Current, Prefer not to answer)
Passive smoking exposure	LifeLines	*Not counting yourself, how many people in your household smoke regularly?* (___number) *Do people smoke regularly in the room where you work?* (Yes, No, Not applicable, I do not have a job)
	UK Biobank	*At home, about how many hours per WEEK are you exposed to other people's tobacco smoke?* (enter number____, Do not know, Prefer not to answer) *Outside of your home, about how many hours per WEEK are you exposed to other people's tobacco smoke?* (enter number____, Do not know, Prefer not to answer)

Asthma status	LifeLines	*Have you ever had asthma?* (Yes, No) If yes, was this confirmed by a doctor (Yes, No)
	UK Biobank	*Has a doctor ever told you that you have had any of the following conditions?* (Blood clot in the leg (DVT), Blood clot in the lung, Emphysema/chronic bronchitis, Asthma, Hayfever, allergic rhinitis or eczema, None of the above, Prefer not to answer)

[1] No time period specified

[2] Only 35% of UK Biobank subjects had data for shortness of breath since it was added to the baseline survey late in recruitment phase (i.e. as of 2009)

Table S4: Harmonized variables used in analyses

Variable	Definition	Categories
Outcome variables		
Wheeze	Self-reported wheeze or whistling in the chest in the past year or more	0: Has not had wheeze symptoms 1: Has had wheeze symptoms
Shortness of breath	Self-reported shortness of breath at rest or walking on level ground	0: Has not had shortness of breath symptoms 1: Has had shortness of breath symptoms
Confounding factors and potential modifiers		
Sex	Sex of the participants	0: Males 1: Female
Age	Age of the participant	
Body mass index	Body mass index of the participant derived using measured height and weight	0: Normal (<25 kg/m^2) 1: Overweight (25 to 29.9 kg/m^2) 2: Obese (≥30 kg/m^2)
Education level	Highest level of education attained derived using the International Standard Classification of Education (ISCED)	0: Secondary education or lower (ISCED levels 0-3) 1: Post-secondary education (ISCED levels 4-8)
Household income	Above or below mean country-specific net disposable household income for 2010 [1]	0: Mean or below mean country-specific net disposable income 1: Higher than mean country-specific net disposable income
Smoking status	Participant's current and past smoking status	0: Never smoker 1: Past smoker 2: Current smoker
Passive smoking exposure	Participant's passive smoking exposure at home or at work	0: Not exposed to second-hand smoke at home or at work 1: Exposed to second-hand smoke at home or at work
Asthma status	Self-reported ever-had asthma	0: Has never had asthma 1: Has had asthma

[1] 2010 mean net disposable income was 25 600 € in the Netherlands (Lifelines) and 20 585 £ in the United Kingdom (UK Biobank) from Organization for Co-operation and Development (OECD) data (OECD, 2016).

Table S5: Prevalence of wheeze and shortness of breath according to smoking status and passive smoking exposure [†]

	Pooled		Lifelines		UK Biobank	
	Wheeze prevalence	**Shortness of breath prevalence**	**Wheeze prevalence**	**Shortness of breath prevalence**	**Wheeze prevalence**	**Shortness of breath prevalence**
Smoking status						
Never smoker	35350 (16.43 %)	8455 (8.85 %)	3944 (16.49 %)	2159 (9.03 %)	31406 (16.42 %)	6296 (8.79 %)
Former smoker	29455 (20.93 %)	6864 (11.07 %)	3147 (19.91 %)	1606 (10.16 %)	26308 (21.06 %)	5258 (11.39 %)
Current smoker	5975 (27.08 %)	1844 (11.52 %)	3505 (28.4 %)	1440 (11.66 %)	2470 (25.41 %)	404 (11.01 %)
Passive smoking exposure						
Not exposed	50219 (17.22 %)	11698 (8.8 %)	7155 (18.7 %)	3574 (9.34 %)	43064 (16.99 %)	8124 (8.58 %)
Exposed	20561 (23.84 %)	5465 (13.45 %)	3441 (24.95 %)	(1631) 11.82 %	17120 (23.63 %)	3834 (14.29 %)

[†] For participants with complete data for PM metrics and age, sex, BMI, income, education, smoking status, passive smoking exposure.

Table S6: Logistic regression model estimates of associations between annual average air pollution exposures at the baseline residence and respiratory symptoms for pooled models 1, 2 and 3 *

	Pooled Model 1[1]		Pooled Model 2[2]		Pooled Model 3[3]	
Exposure and outcome	**No. cases / non-cases**	**OR [95% CI]**	**No. cases / non-cases**	**OR [95% CI]**	**No. cases / non-cases**	**OR [95% CI]**
Wheeze						
$PM_{2.5}$ (per 5 μg/m^3)	109012 / 410003	**1.41 [1.35, 1.47]**	90105 / 344908	**1.23 [1.18, 1.28]**	70780 / 307174	**1.16 [1.11, 1.21]**
PM_{10} (per 5 μg/m^3)	109012 / 410003	**1.09 [1.07, 1.12]**	90105 / 344908	**1.05 [1.03, 1.07]**	70780 / 307174	**1.03 [1.01, 1.05]**
PM_{coarse} (per 5 μg/m^3)	109012 / 410003	**1.11 [1.05, 1.16]**	90105 / 344908	**1.07 [1.02, 1.12]**	70780 / 307174	1.05 [1.00, 1.10]
NO_2 (per 10 μg/m^3)	115724 / 436593	**1.07 [1.06, 1.08]**	95886 / 368161	**1.05 [1.03, 1.06]**	74959 / 327742	**1.03 [1.02, 1.04]**
Shortness of breath						
$PM_{2.5}$ (per 5 μg/m^3)	26130 / 208841	**2.10 [1.91, 2.32]**	20796 / 176549	**1.69 [1.53, 1.88]**	17163 / 156397	**1.61 [1.45, 1.78]**
PM_{10} (per 5 μg/m^3)	26130 / 208841	**1.28 [1.22, 1.35]**	20796 / 176549	**1.22 [1.16, 1.29]**	17163 / 156397	**1.20 [1.14, 1.27]**
PM_{coarse} (per 5 μg/m^3)	26130 / 208841	**1.34 [1.21, 1.48]**	20796 / 176549	**1.30 [1.17, 1.44]**	17163 / 156397	**1.28 [1.15, 1.42]**
NO_2 (per 10 μg/m^3)	26139 / 208900	**1.19 [1.16, 1.22]**	20804 / 176601	**1.17 [1.14, 1.20]**	17171 / 156443	**1.16 [1.13, 1.19]**

[1] Adjusted for age (continuous), sex, and cohort (Lifelines or UK Biobank)

[2] Adjusted for age (continuous), sex, BMI (normal, overweight, or obese), household income (annual net income ≤ or > the country-specific mean for 2010), education level (≤ secondary or post-secondary), and cohort (Lifelines or UK Biobank)

[3] Adjusted for age (continuous), sex, BMI (normal, overweight, or obese), household income (annual net income ≤ or > the country-specific mean for 2010), education level (≤ secondary or post-secondary), smoking status (never, former, or current), passive smoking exposure (none or any), and cohort (Lifelines or UK Biobank)

* Statistically significant results ($p<0.05$) are given in bold

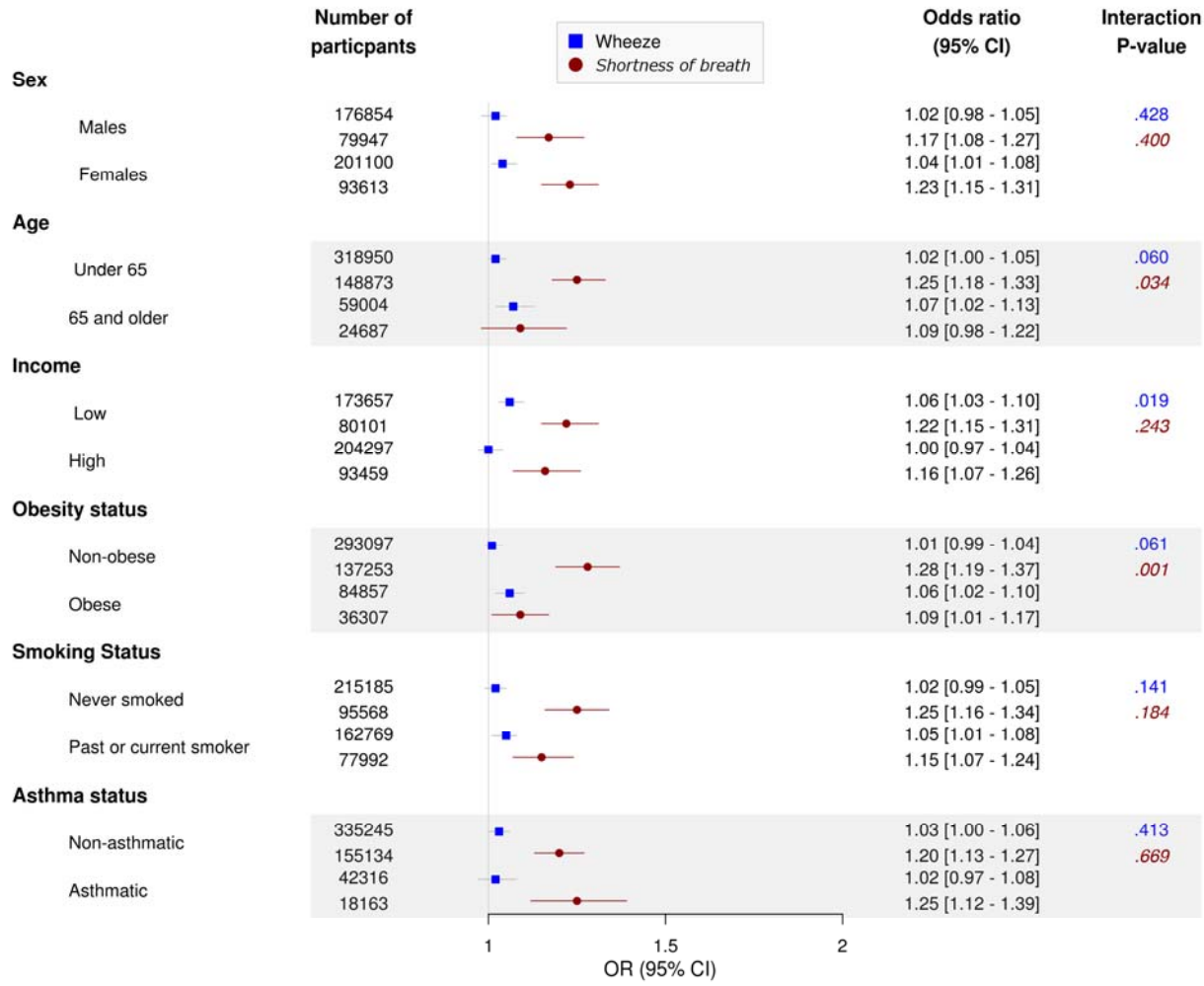
Table S7: Sensitivity analyses: restricting pooled analyses to those living at the same address for more than 5 years and more than 10 years [†, *]

Exposure and outcome	5 years at baseline residence		10 years at baseline residence	
	No. cases / non-cases	OR [95% CI]	No. cases / non-cases	OR [95% CI]
Wheeze				
$PM_{2.5}$ (per 5 μg/m^3)	58083 / 256002	**1.16 [1.11, 1.22]**	44963 / 200715	**1.17 [1.11, 1.24]**
PM_{10} (per 5 μg/m^3)	58083 / 256002	**1.03 [1.00, 1.05]**	44963 / 200715	**1.03 [1.01, 1.07]**
PM_{coarse} (per 5 μg/m^3)	58083 / 256002	1.04 [0.99, 1.10]	44963 / 200715	**1.06 [1.00, 1.13]**
NO_2 (per 10 μg/m^3)	61555 / 273579	**1.03 [1.01, 1.04]**	47737 / 215122	**1.03 [1.01, 1.04]**
Shortness of breath				
$PM_{2.5}$ (per 5 μg/m^3)	13548 / 127882	**1.65 [1.47, 1.85]**	10212 / 98098	**1.61 [1.41, 1.83]**
PM_{10} (per 5 μg/m^3)	13548 / 127882	**1.19 [1.12, 1.26]**	10212 / 98098	**1.20 [1.12, 1.28]**
PM_{coarse} (per 5 μg/m^3)	13548 / 127882	**1.22 [1.08, 1.37]**	10212 / 98098	**1.25 [1.10, 1.43]**
NO_2 (per 10 μg/m^3)	13552 / 127919	**1.17 [1.14, 1.20]**	10216 / 98123	**1.17 [1.13, 1.21]**

[†] Adjusted for age (continuous), sex, BMI (normal, overweight, or obese), household income (annual net income ≤ or > the country-specific mean for 2010), education level (≤ secondary or post-secondary), smoking status (never, former, or current), passive smoking exposure (none or any), and cohort (Lifelines or UK Biobank)

* Statistically significant results ($p<0.05$) are given in bold

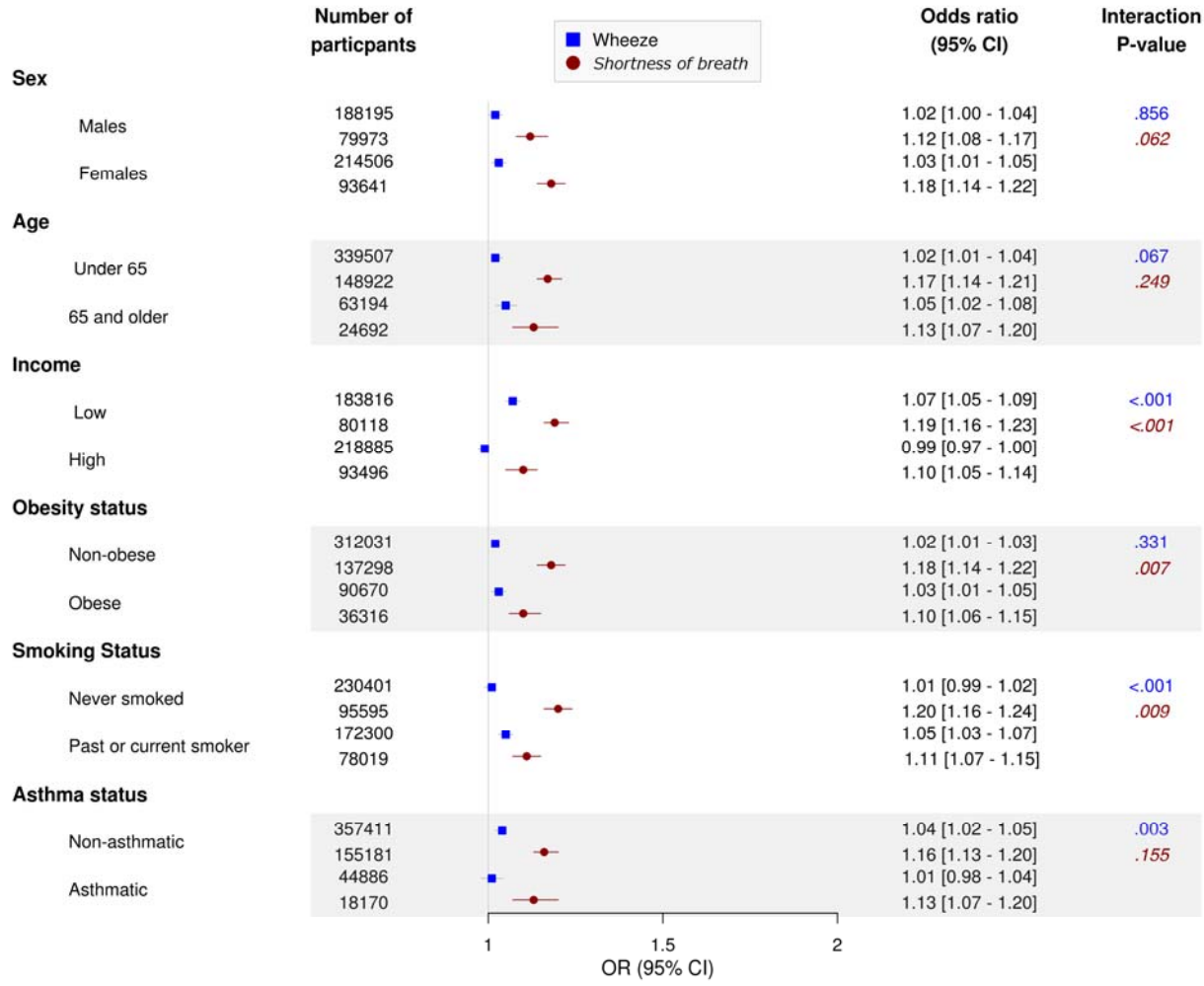
Figure S1: Adjusted odds ratios (and 95% CI) for respiratory symptoms in association with a 5-ug/m3 increase in ambient PM_{10} at participant residences among population subgroups based on pooled data from the Lifelines and UK Biobank cohorts [†, *]



[†] Logistic regression model adjusted for age (continuous), sex, BMI (normal, overweight, or obese), household income (annual net income ≤ or > the country-specific mean for 2010), education level (≤ secondary or post-secondary), smoking status (never, former, or current), passive smoking exposure (none or any), and cohort (Lifelines or UK Biobank)

*Interaction p-values are Wald p-values for product interaction terms between air pollutants and stratification variables, blue font for wheeze symptoms and red *italics* font for shortness of breath symptoms

Figure S2: Adjusted odds ratios (and 95% CI) for respiratory symptoms in association with a 10-ug/m3 increase in ambient NO_2 at participant residences among population subgroups based on pooled data from the Lifelines and UK Biobank cohorts [†, *]



[†] Logistic regression model adjusted for age (continuous), sex, BMI (normal, overweight, or obese), household income (annual net income ≤ or > the country-specific mean for 2010), education level (≤ secondary or post-secondary), smoking status (never, former, or current), passive smoking exposure (none or any), and cohort (Lifelines or UK Biobank)

*Interaction p-values are Wald p-values for product interaction terms between air pollutants and stratification variables, blue font for wheeze symptoms and red *italics* font for shortness of breath symptoms