1   **Air pollution, lung function and COPD: results from the population-based**
2   **UK Biobank study**
3

4   Dany Doiron[1,2,3], Kees de Hoogh[2,3], Nicole Probst-Hensch[2,3], Isabel Fortier[1], Yutong
5   Cai[4,5], Sara De Matteis[6], Anna L Hansell[4,7]
6
7   [1]Research Institute of the McGill University Health Centre, Montreal, Quebec, Canada
8   [2]Swiss Tropical and Public Health Institute, Basel, Switzerland
9   [3]University of Basel, Basel, Switzerland
10 [4]Department of Epidemiology and Biostatistics, School of Public Health, Imperial
11 College London, London, UK
12 [5]Department of Analytical, Environmental and Forensic Sciences, School of Population
13 Health and Environmental Sciences, King's College London, London, UK
14 [6]National Heart & Lung Institute, Imperial College London, London, UK
15 [7]Centre for Environmental Health and Sustainability, University of Leicester, Leicester,
16 UK
17
18 **Correspondence**: Dany Doiron, Research Institute of the McGill University Health
19 Centre, 2155 rue Guy, office 458, Montreal, Canada, H3H 2R9. Telephone: 1-514-934-
20 1934 (ex. 71688). Email: dany.doiron@swisstph.ch
21
22

23 **Take home message:** In one of the largest analyses to date, ambient air pollution
24 exposure was associated with lower lung function and increased Chronic Obstructive
25 Pulmonary Disease (COPD) prevalence, with stronger associations seen in those with
26 lower incomes**.**
27

Abstract (250 words)

Ambient air pollution increases the risk of respiratory mortality but evidence for impacts on lung function and chronic obstructive pulmonary disease (COPD) is less well established**.** The aim was to evaluate whether ambient air pollution is associated with lung function and COPD, and explore potential vulnerability factors.

We used UK Biobank data on 303,887 individuals aged 40-69 years, with complete covariate data and valid lung function measures. Cross-sectional analyses examined associations of Land Use Regression-based estimates of particulate matter ($PM_{2.5}$, PM_{10} and PM_{coarse}) and nitrogen dioxide (NO_2) concentrations with forced expiratory volume in 1 second (FEV_1), forced vital capacity (FVC), the FEV_1/FVC ratio, and COPD (FEV_1/FVC < lower limit of normal). Effect modification was investigated for sex, age, obesity, smoking status, household income, asthma status, and occupations previously linked to COPD.

Higher exposures to each pollutant were significantly associated with lower lung function. A 5 $\mu g/m^3$ increase in $PM_{2.5}$ concentration was associated with lower FEV_1 (-83.13 mL [95%CI: -92.50, -73.75]) and FVC (-62.62 mL [95%CI: -73.91, -51.32]). COPD prevalence was associated with higher concentrations of $PM_{2.5}$ (OR 1.52 [95%CI: 1.42, 1.62], per 5 $\mu g/m^3$), PM_{10} (OR 1.08 [95%CI: 1.00, 1.16], per 5 $\mu g/m^3$), and NO_2 (OR 1.12 [95%CI: 1.10, 1.14], per 10 $\mu g/m^3$), but not with PM_{coarse}. Stronger lung function associations were seen for males, individuals from lower income households, and 'at-risk' occupations, and higher COPD associations for obese, lower income, and non-asthmatic participants. Ambient air pollution was associated with lower lung function and increased COPD prevalence in this large study.

Introduction

Ambient air pollution increases the risk of respiratory mortality but evidence for impacts on lung function and obstructive lung disease is less well established. Recent studies and reviews have reported suggestive evidence linking outdoor air pollution and lung function and COPD[1-4]. Recently, the European Study of Cohorts for Air Pollution Effects (ESCAPE) project showed that higher ambient NO_2 and PM_{10} exposure as well as higher traffic load on roads near residences were associated with impaired lung function in adults, using a meta-analysis across five European cohorts[5]. A separate meta-analysis of four of these same cohorts found positive but non-significant associations between chronic exposure to ambient air pollution and COPD[6]. Other large studies have not shown consistent evidence of long-term air pollution exposure on adult-onset COPD[7, 8]. Inconclusive findings have been in part attributable to lack of statistical power to detect small effects. Sample size limitations have also curtailed exploration of associations among population subgroups.

The objectives of this cross-sectional study were to examine whether air pollution was associated with lung function and COPD using a very large UK study. Secondly, potential vulnerability factors of the relationships between air pollution and lung function and COPD were explored.

Methods

Study Participants

We used baseline questionnaire, anthropometric measures and spirometry data from the UK Biobank collected in 2006-2010. UK Biobank is a national cohort study of half a million

74   participants aged 40-69 years, largely in urban areas of England, Wales and Scotland

75   recruited from the United Kingdom's National Health Services register[9]. Full study

76   sampling methods are described elsewhere[9, 10]. A research protocol for our study

77   obtained all necessary approvals from the UK Biobank's review committees.

78

79   ***Lung Function and COPD***

80   Trained healthcare technicians and nurses in UK Biobank assessment centers performed

81   pre-bronchodilation lung function tests using the Vitalograph Pneumotrac 6800

82   spirometer. Contra-indications were: chest infection in the last month, history of detached

83   retina, heart attack or surgery to eyes, chest or abdomen in last 3 months, history of a

84   collapsed lung, pregnancy (1st or 3rd trimester), or currently on medication for

85   tuberculosis. Two blows were recorded for each participant and a third blow was

86   administered if the differences between both forced vital capacity (FVC) and forced

87   expiratory volume in 1 s (FEV_1) of the first two blows were more than 5%. Acceptability of

88   spirometry data was assessed by quality appraisal of a sample of maneuvers, as

89   previously described[11]. The highest values for both FVC and FEV_1 from acceptable

90   blows were used in analyses. Participants reporting having smoked or used an inhaler

91   within an hour prior to spirometry test were excluded.

92   To adjust for normative ageing effects as well as variations according to sex, height and

93   ethnicity, we defined COPD outcomes using the Global Lung Function Initiative (GLI)

94   2012 reference values for lower limit of normal (LLN)[12], which were computed using the

95   GLI R macro[13]. Individuals with a FEV_1/FVC ratio below the LLN were classified as

96   having COPD[14].

97

Air pollution estimates

Land use regression (LUR)-based estimates of nitrogen dioxide (NO_2), particulate matter

with aerodynamic diameter <10 μm (PM_{10}), fine particles with diameter <2.5 μm ($PM_{2.5}$),

and coarse particles with diameter between 2.5 μm and 10 μm (PM_{coarse}) for 2010 were

generated as part of the European Study of Cohorts and Air Pollution Effects

(ESCAPE)[15, 16] and linked to geocoded residential addresses of UK Biobank

participants. Predictor variables used in final pollutant-specific LUR models and model

R^2s are presented in Table S1. Leave-one-out cross-validation, where each site is left out

sequentially whilst the included variables of the models are left unchanged, showed good

model performance for $PM_{2.5}$, PM_{10} and NO_2 (cross-validation R^2=77%, 88%, and 87%,

respectively) and a moderate performance for PM_{coarse} (cross-validation R^2=57%).

Evaluation of ESCAPE LUR estimates was conducted by comparing model predictions

to the UK's Automatic Urban and Rural Network (AURN) monitoring data[17]. The LUR

NO_2 model predicted measured concentrations reasonably well (R^2=0.67), while the LUR

PM_{10} model predicted concentrations moderately well in central and southern areas of

the UK (R^2=0.53), but R^2 values were lower than 0.5 in northern England or Scotland so

these areas were dropped from PM analyses[18].

115

Confounder and Effect Modifier Variables

Socio-demographic and behavioral confounders and potential effect modifiers were

identified *a priori* through literature search. Age was derived from birth date and date of

baseline assessment. Body mass index (BMI) was constructed from measured height and

120   weight. The UK Biobank five-level before-tax household income variable was

121   dichotomized to "less than" or "equal to or above" £ 31,000 category, being closest to the

122   UK median gross household income in 2009/10 (£ 27,789)[19]. Educational attainment

123   was defined as "lower vocational qualification or less" vs "higher vocational qualification

124   or more". The smoking status variable classified participants as never, previous or current

125   tobacco smokers. Passive smoking exposure was defined as exposure >= 1 hour/week

126   to other people's tobacco smoke at home. Asthma status was based on a self-reported

127   doctor diagnosis of asthma. Lastly, participants reporting current employment for one of

128   14 jobs associated with an increased risk (prevalence ratio ≥ 1.30) for COPD identified

129   by De Matteis *et al.*[11] (Table S2) were classified as having an "at-risk" occupation.

130

131   ***Statistical Analyses***

132   We performed descriptive analyses followed by cross-sectional linear regression

133   analyses for lung function and logistic regression analyses for COPD. The associations

134   between baseline FEV_1, FVC and FEV_1/FVC and annual average air pollutant

135   concentrations at place of residence were adjusted for age, age-squared, sex, height,

136   BMI (kg/m^2), household income, education level, smoking status and passive smoking

137   exposure. Associations for COPD (FEV_1/FVC < LLN) at baseline were adjusted for age,

138   sex, BMI, household income, education level, smoking status and passive smoking

139   exposure. In order to allow direct comparison with previous ESCAPE studies on air

140   pollution and lung function impairment and COPD[5, 6, 20], all associations were reported

141   per 5 $\mu g/m^3$ increase of $PM_{2.5}$ and PM_{coarse}, and per 10 $\mu g/m^3$ increase of PM_{10} and NO_2.

142   To allow interquartile range (IQR) comparison of pollutant effects in the UK Biobank

143   population, results were also reported per IQR increase of air pollutant. Sensitivity

144   analyses were conducted by restricting analyses to individuals living at the same address

145   for at least 10 years, to minimize exposure misclassification. We also investigated

146   whether pro-inflammatory characteristics modified the relationship between $PM_{2.5}$ and

147   NO_2 air pollution and lung function and COPD. Stratified analyses were conducted for sex

148   (male vs. female), age (<65 vs. ≥65 years), obesity (non-obese vs. obese), smoking

149   status (never vs. current or past smoker), household income (<£ 31,000 vs. £ 31,000 and

150   above), asthma status (never vs. ever diagnosed), and occupational status ("at-risk" vs.

151   not "at-risk" occupation, see Table S2). Lastly, we calculated attributable fraction of COPD

152   prevalence due to $PM_{2.5}$ exposure above World Health Organization (WHO) air quality

153   guideline levels (>10 µg/m^3), current/past smoking, and passive smoking exposure at

154   home.

155   All statistical analyses were limited to participants with complete exposure and model

156   covariate data and were performed in the R Statistical Software, version 3.4.4[21].

157

158   ***Exclusions and missing data***

159   Study population, exclusions, and missing data are outlined in Figure 1. Of the 502,655

160   UK Biobank participants, 36 had withdrawn from the cohort prior to beginning analyses.

161   48,818 participants had not completed spirometry tests, and an additional 67,823

162   participants were excluded due to invalid spirometry measures (n=59,850) or having

163   smoked or used an inhaler within an hour of lung function test (n=7,973), resulting in

164   385,978 participants with valid FEV_1 and FVC measures. A total of 82,091 participants

165   had missing data for at least one covariate in fully adjusted models, leaving 303,887

166   participants with complete covariate data and valid lung function measures. The COPD

167   outcome variable was available for 303,183 participants, as 704 individuals had no data

168   for the ethnicity variable used to calculate the LLN threshold. After excluding participants

169   with missing air pollution metrics, our final samples for lung function analyses were

170   299,537 (NO_2 population) and 278,228 (PM population). COPD analyses included

171   298,848 and 277,567 participants for NO_2 and PM populations, respectively.

172

173   **Results**

174   Characteristics for participants with complete data in fully adjusted lung function models

175   and for excluded participants due to incomplete data are presented in Table 1. The mean

176   age of participants with complete data was 56 years and about 53% of participants were

177   females. The majority of participants were overweight (43%) or obese (24%), had higher

178   education qualifications (48%), and came from households earning over £ 31,000

179   annually (55%). Three out of five participants were lifetime non-smokers, only 3% were

180   current smokers, and 5% reported exposure to tobacco smoke at home. Approximately

181   11% of study subjects had been diagnosed with asthma and 2% were currently employed

182   in an occupation associated with an increased COPD risk. Lastly, LLN-defined COPD

183   prevalence was 7% in our final sample. Significant differences between individuals with

184   complete data and those with incomplete data (n = 203,082) were found for all variables,

185   except asthma status. Notably, the incomplete data subset had a considerably lower

186   percentage of individuals with higher educational qualifications (38% vs. 48%) and from

187   higher income households (42% vs. 55%), and higher proportions of current smokers

188   (22% vs. 3%) and individuals in occupations "at-risk" for COPD (4% vs. 2%).

189

190   Table 2 shows the distribution of residential ambient air pollution concentrations. Mean

191   annual estimates of $PM_{2.5}$, PM_{10}, PM_{coarse} and NO_2 were 9.94 µg/m^3 (standard deviation

192   [SD]: 1.04), 16.18 µg/m^3 (SD: 1.90), 6.41 µg/m^3 (SD: 0.90), and 26.31 µg/m^3 (SD: 7.49),

193   respectively. NO_2 concentrations were highly correlated with $PM_{2.5}$ (r=0.87), but less so

194   with other PM metrics. PM_{10} and PM_{coarse} were also highly correlated (r=0.81).

195

196   Higher exposure to all pollutants showed significant associations with lower lung function

197   (Table 3). In adjusted models, a 5 µg/m^3 increase in $PM_{2.5}$ exposure was associated with

198   lower FEV_1 (-83.13 mL [95% confidence interval [CI]: -92.50, -73.75]), FVC (-62.62 mL

199   [95%CI -73.91, -51.32]), and FEV_1/FVC ratio (-9.68 [95%CI: -10.81, -8.56]). For each 10

200   µg/m^3 increase in NO_2, lower FEV_1 (-33.85 mL [95%CI: -36.34, -31.36]), FVC (-33.47 mL

201   [95%CI: -36.47, -30.46]) and FEV_1/FVC ratio (-2.27 [95%CI: -2.57, -1.96]) were also

202   observed. Results also showed negative associations between PM_{10} and PM_{coarse}

203   concentrations and lung function, with stronger effects on FVC than FEV_1. The FEV_1/FVC

204   ratio showed no association with ambient PM_{10} exposure and a small positive association

205   with PM_{coarse} (1.34 [95%CI: 0.04, 2.63], per 10 µg/m^3). In the main analyses for COPD

206   prevalence, a significant association was observed for $PM_{2.5}$ (OR 1.52 [95%CI: 1.42,

207   1.62], per 5 µg/m^3), PM_{10} (1.08 [95%CI: 1.00, 1.16], per 10 µg/m^3), and NO_2 (1.12 [95%CI:

208   1.10, 1.14], per 10 µg/m^3), but not for PM_{coarse} (Table 4). Associations per IQR increase

209   in exposure are presented in Tables S3 (for lung function) and S4 (for COPD). When

210   compared to associations with smoking status, lower levels of FEV_1 observed per 5 µg/m^3

211   increase in $PM_{2.5}$ represented 65% and 29% of FEV_1 loss associated with being a former

212 and current smoker, respectively (Table S5). Further, the odds of COPD per 5 μg/m3

213 increment of $PM_{2.5}$ was equivalent to over half the odds of COPD associated with passive

214 smoking exposure at home (Table S5). Sensitivity analyses restricted to those who had

215 lived in the same place for the last 10 years did not substantially change lung function or

216 COPD associations (Tables S6 and S7). Finally, attributable fraction of COPD prevalence

217 for residential ambient $PM_{2.5}$ exposure above WHO guidelines was almost half (5.6%)

218 that of current/past tobacco smoking (12.1%) in the cohort and over four times that of

219 passive smoking exposure at home (1.2%).

220

221 Results of $PM_{2.5}$ and NO_2 subgroup analyses for lung function and COPD are shown in

222 Tables 5 and 6, respectively. FEV_1 stratified analyses showed stronger $PM_{2.5}$ and NO_2

223 associations among males, participants from lower income households, and individuals

224 with "at-risk" occupations. The same effect modification patterns were observed for FVC

225 stratified analyses, with never smokers also showing significantly lower FVC per $PM_{2.5}$

226 and NO_2 increase. Individuals from lower income households had approximately twice as

227 low FEV_1 and FVC levels compared to higher income participants and individuals with

228 "at-risk for COPD" occupations showed 3-fold lower FEV_1 and FVC levels compared to

229 individuals not in these occupations, per unit increase in $PM_{2.5}$ or NO_2 (Table 5). Age,

230 obesity, smoking status, and household income but not "at-risk" occupations modified the

231 relationship between the FEV_1/FVC ratio and $PM_{2.5}$ and NO_2, with stronger adverse

232 associations for older, obese, current/past smokers, and lower income individuals. In

233 COPD subgroup analyses (Table 6), $PM_{2.5}$ and NO_2 associations were stronger among

234 obese, lower income and non-asthmatic participants. Again, household income especially

235 influenced the exposure-outcome relationship, with over three times stronger

236 associations between COPD and each pollutant among lower- compared to higher-

237 income individuals.

238

239 **Discussion**

240 Ambient concentrations of particulate matter and NO_2 air pollution were associated with

241 lower lung function and increased COPD prevalence in this very large UK cohort. Given

242 the size of the study, we were able to investigate interactions, finding evidence for effect

243 modification, with larger impacts of air pollution on (i) lung function in males, individuals

244 from lower income households, and individuals with 'at-risk' occupations, and (ii) COPD

245 in obese, lower income and non-asthmatic participants.

246

247 Lung function is a good indicator of respiratory morbidity and mortality, especially among

248 COPD patients[22]. Given an average FEV_1 loss of 32 to 46 mL/year after age 30

249 years[12], the associations per 5 µg/m^3 exposure of $PM_{2.5}$ found in our study are

250 approximately equivalent to an additional two years of normal loss of lung function in

251 healthy individuals if results in this cross-sectional study are confirmed in future

252 longitudinal follow-up. We found significant reductions on lung function, even at a

253 relatively low levels of ambient $PM_{2.5}$, thereby echoing the need for more actions to be

254 taken to control air pollution[23].

255

256 ***Comparison with Studies Using the Same Air Pollution Estimates***

257   The current study replicated cross-sectional analyses in the European Study of Cohorts

258   and Air Pollution Effects (ESCAPE), the previous largest European study to date, using

259   a single cohort with >10-fold higher numbers and the same models to estimate air

260   pollutant exposures[15, 16] and similar covariate adjustment. Findings from two ESCAPE

261   meta-analyses[5, 6] and from a Dutch study using ESCAPE air pollution estimates[20]

262   are presented in Figure 2. Our large sample size resulted in much smaller confidence

263   intervals, with more statistically significant results and stronger evidence of an adverse

264   effect of air pollution (Figure 2). We found stronger (more negative) effects on lung

265   function than in the studies by Adam *et al.*[5] or de Jong *et al.*[20] for each of the four air

266   pollutants studied ($PM_{2.5}$, PM_{10}, PM_{coarse}, NO_2). For COPD, our confidence intervals were

267   much tighter than but overlapped with those in the study conducted by Schikowski *et*

268   *al.*[6], but unlike that study, we found significant associations with both $PM_{2.5}$ and NO_2.

269

270   The mean and range of estimated annual NO_2 concentrations in our study were similar

271   to those of studies included in the original ESCAPE meta-analyses[5, 6], whereas mean

272   PM concentrations were generally lower in our study, with the exception of the British

273   National Survey of Health and Development, which were comparable (Tables S8 and S9).

274   The range of air pollutant concentrations used in de Jong *et al.* (2016) was smaller than

275   in our own study (Table S10). Using similar air pollution models to those used in past

276   ESCAPE studies means that differences in lung function and COPD associations are less

277   likely to be due to differences in exposure estimates[24]. However, given that the original

278   ESCAPE meta-analyses by Adam *et al.*[5] and Schikowski *et al.*[6] back-extrapolated air

279   pollution estimates to date of lung function measurement by up to two decades for some

280   participating cohorts, the larger effect size seen in our study may in part relate to reduced

281   air pollution exposure misclassification. Finally, the same spirometers and spirometry

282   protocols were applied in UK Biobank, whereas this was not the case across original

283   ESCAPE studies. This may have also contributed to more precise estimates in our study.

284

285

286   ***Comparison with Studies Using Other Air Pollution Estimates***

287   Our results are consistent with the small number of studies investigating PM_{10}, $PM_{2.5}$, and

288   NO_2 in relation to lung function, but few studies have investigated PM_{coarse}. In a study of

289   UK residents, Forbes *et al.* reported comparable results for FEV_1, showing a 92 ml and

290   22 ml decrease per 10 µg/m^3 increase in PM_{10} and NO_2, respectively[25]. A study of 9,651

291   healthy never-smokers in the Swiss Study of Air Pollution and Lung Disease in Adults

292   (SAPALDIA) also found negative effects of both NO_2 and PM_{10} exposure on FEV_1 and

293   FVC[26]. An analysis of Framingham Heart Study participants by Rice *et al.* found

294   significant negative associations of residential $PM_{2.5}$ exposure with both FEV_1 and FVC

295   levels, and a faster decline in lung function levels[3].

296

297   Our findings of associations between $PM_{2.5}$ and airflow obstruction and COPD are

298   consistent with a recent study of 285,000 Taiwan residents showing significant

299   associations between ambient $PM_{2.5}$ and reduced FEV_1/FVC ratio, and risk of COPD[4];

300   also with findings from the German Study on the Influence of Air pollution on Lung,

301   Inflammation and Aging (SALIA) cohort in relation to NO_2 and FEV_1/FVC ratio, and

302   spirometrically defined COPD[27]. A separate analysis of SALIA participants also showed

303 a decline in COPD with reduced NO_2 concentrations[28]. However, in contrast to our

304 findings, no associations of NO_2 or $PM_{2.5}$ exposure with FEV_1/FVC were reported by

305 Forbes *et al.*[25] or Rice *et al.*[3].

306

307 ***Effect Modifiers of Air Pollution***

308 We observed considerably stronger associations for lung function and COPD among

309 individuals from lower income households. The greater vulnerability of lower-income

310 individuals to the respiratory health effects of air pollution exposure is in line with previous

311 studies[18, 29, 30], and is likely due to numerous factors, including more childhood

312 respiratory infections, poorer housing conditions and indoor air quality, poor nutrition and

313 occupational exposures[31].

314

315 Our study found occupational status in a job judged at risk of COPD to be an important

316 effect modifier of associations between air pollution exposure and lung function, but not

317 its associations with COPD. The latter may be due to the 'healthy worker' effect whereby

318 those with COPD are less likely to be employed in an 'at risk' job – we did not have

319 information on past occupation. Few studies are available for comparison, but the Harvard

320 Six Cities Study found higher relative risks of death per unit of $PM_{2.5}$ among individuals

321 reporting workplace exposure to dust or fumes[32].

322

323 We observed stronger $PM_{2.5}$ and NO_2 associations with FEV_1 and FVC among males and

324 stronger associations between $PM_{2.5}$ exposure and COPD for females. Equivocal

325 evidence has been found regarding effect modification of sex in associations between air

326   pollution exposure and lung function and COPD in adults[33]. In studies reporting stronger

327   effects in men, work-related exposures leading to greater predisposition to airway

328   disease, and more time spent outdoors potentially resulting in higher exposures for a

329   given concentration have been suggested as potential sources of differential effects[34,

330   35]. Hypotheses for a larger impact of air pollution on lung health among women include

331   more time spent at home leading to better accuracy of residential air pollution exposure

332   assignment, as well as biological factors such as greater airway reactivity[36, 37].

333

334   We also found significant effect modification by obesity, with higher air pollution

335   associations with COPD risk and reduced lung function for obese individuals, which is

336   consistent with other studies using ESCAPE air pollution estimates[5, 20]. Mechanistic

337   studies have shown greater than additive effects of excess body fat and air pollutant

338   exposure on systemic inflammation and oxidative stress[38, 39], suggesting an enhanced

339   response to inflammatory stimuli[39], resulting in airway damage and inflammation in

340   obese individuals.

341

342   Stronger negative effects of air pollution on respiratory disease among never smokers

343   have been previously reported[6, 8, 40], which our analyses also found. As smoking might

344   already reduce pulmonary function through inflammatory pathways, any additional impact

345   of air pollution on respiratory abnormalities could be smaller or harder to detect in this

346   subgroup.

347

348   We also found that asthma status modified the associations between $PM_{2.5}$ and NO_2 and

349   COPD prevalence, with significantly stronger associations in non-asthmatics. This may

350   be related to treatment in asthmatics, modifying adverse impacts of air pollution or

351   alternatively, avoidance in that asthmatics aware of impact of air pollution on symptoms

352   may choose to live in less polluted areas.

353

354   ***Strengths and Limitations***

355   The large sample size of our study provided good statistical power to assess effects of

356   air pollution, even in relatively small subgroups such as individuals in occupations with

357   increased COPD risk. An additional strength of our study was the use of a single well-

358   respected cohort with a rigorously defined protocol.

359

360   A potential major limitation of the study is the large number of participants with missing

361   data for covariates included in our final regression models. This did not appear to be

362   missing at random (therefore difficult to address using imputation) but gave us a wealthier

363   and healthier cohort. This does not invalidate findings, but may affect generalizability.

364   Given our findings of interactions with lower socio-economic status individuals, we might

365   expect this would underestimate associations of air pollution and lung function and COPD

366   in a general population.

367

368   Another limitation is that while COPD should be classified using post-bronchodilator

369   spirometry tests, only pre-bronchodilator measures were available, similar to the

370   ESCAPE five cohort analysis[5]. The extent that air pollution affects FEV_1 and FEV_1/FVC

371   could potentially have been mitigated if assessed post-bronchodilator.

372

373   Common to most other ambient air pollution studies, we used place of residence to

374   estimate air pollution exposure, which will result in exposure misclassification. Further,

375   annual air pollution estimates at recruitment address were modelled to a single year

376   (2010), which may differ by up to four years from when lung function was measured. We

377   made a reasonable assumption that the spatial contrast in air pollution exposures will

378   have been relatively stable in the UK over these years[41], but cannot exclude the

379   possibility of exposure misclassification. Finally, the cross-sectional relationship between

380   air pollution and lung function and COPD demonstrated in our study show associations

381   but are prone to the influence of confounders and do not allow us to examine temporal

382   patterns between air pollution exposure and respiratory outcomes. Longitudinal analyses

383   of future follow-up data in large cohorts such as UK Biobank are needed to strengthen

384   inferences regarding causal relationships between air pollution and respiratory disease,

385   particularly among vulnerable subpopulations.

386

387   In conclusion, this is one of the largest analyses to date to examine associations between

388   ambient air pollution and lung function and COPD. Air pollutant concentrations were

389   clearly associated with lower lung function and increased COPD prevalence with higher

390   impacts in males, individuals from lower income households, those in occupations with

391   adverse respiratory exposures and those who were obese.

392

393   **Acknowledgments**

400   DD, KdH & AH proposed the study, all authors contributed to development of the study
401   design, DD conducted the statistical analyses and wrote the first draft of the paper, all
402   authors commented on results and contributed to the manuscript.
403

404   **Competing Financial Interest Declaration**
405   The authors declare they have no actual or potential competing financial interests.
406

References

1. Götschi T, Heinrich J, Sunyer J, Künzli N. Long-Term Effects of Ambient Air Pollution on Lung Function: A Review. *Epidemiology* 2008: 19(5): 690-701.

2. Schikowski T, Mills IC, Anderson HR, Cohen A, Hansell A, Kauffmann F, Krämer U, Marcon A, Perez L, Sunyer J, Probst-Hensch N, Künzli N. Ambient air pollution: a cause of COPD? *European Respiratory Journal* 2014: 43(1): 250-263.

3. Rice MB, Ljungman PL, Wilker EH, Dorans KS, Gold DR, Schwartz J, Koutrakis P, Washko GR, O'Connor GT, Mittleman MA. Long-Term Exposure to Traffic Emissions and Fine Particulate Matter and Lung Function Decline in the Framingham Heart Study. *American Journal of Respiratory and Critical Care Medicine* 2015: 191(6): 656-664.

4. Guo C, Zhang Z, Lau AKH, Lin CQ, Chuang YC, Chan J, Jiang WK, Tam T, Yeoh E-K, Chan T-C, Chang L-Y, Lao XQ. Effect of long-term exposure to fine particulate matter on lung function decline and risk of chronic obstructive pulmonary disease in Taiwan: a longitudinal, cohort study. *The Lancet Planetary Health* 2018: 2(3): e114-e125.

5. Adam M, Schikowski T, Carsin AE, Cai Y, Jacquemin B, Sanchez M, Vierkötter A, Marcon A, Keidel D, Sugiri D, Al Kanani Z, Nadif R, Siroux V, Hardy R, Kuh D, Rochat T, Bridevaux P-O, Eeftens M, Tsai M-Y, Villani S, Phuleria HC, Birk M, Cyrys J, Cirach M, de Nazelle A, Nieuwenhuijsen MJ, Forsberg B, de Hoogh K, Declerq C, Bono R, Piccioni P, Quass U, Heinrich J, Jarvis D, Pin I, Beelen R, Hoek G, Brunekreef B, Schindler C, Sunyer J, Krämer U, Kauffmann F, Hansell AL, Künzli N, Probst-Hensch N. Adult lung function and long-term air pollution exposure. ESCAPE: a multicentre cohort study and meta-analysis. *European Respiratory Journal* 2015: 45(1): 38-50.

6. Schikowski T, Adam M, Marcon A, Cai Y, Vierkötter A, Carsin AE, Jacquemin B, Al Kanani Z, Beelen R, Birk M, Bridevaux P-O, Brunekeef B, Burney P, Cirach M, Cyrys J, de Hoogh K, de Marco R, de Nazelle A, Declercq C, Forsberg B, Hardy R, Heinrich J, Hoek G, Jarvis D, Keidel D, Kuh D, Kuhlbusch T, Migliore E, Mosler G, Nieuwenhuijsen MJ, Phuleria H, Rochat T, Schindler C, Villani S, Tsai M-Y, Zemp E, Hansell A, Kauffmann F, Sunyer J, Probst-Hensch N, Krämer U, Künzli N. Association of ambient air pollution with the prevalence and incidence of COPD. *European Respiratory Journal* 2014: 44(3): 614-626.

7. Atkinson RW, Carey IM, Kent AJ, van Staa TP, Anderson HR, Cook DG. Long-term exposure to outdoor air pollution and the incidence of chronic obstructive pulmonary disease in a national English cohort. *Occupational and Environmental Medicine* 2014.

8. Fisher JA, Puett RC, Hart JE, Camargo CA, Varraso R, Yanosky JD, Laden F. Particulate matter exposures and adult-onset asthma and COPD in the Nurses' Health Study. *European Respiratory Journal* 2016: 48(3): 921-924.

9. UK Biobank. Protocol for a large-scale prospective epidemiological resource. 2007 [cited; Available from: http://www.ukbiobank.ac.uk/wp-content/uploads/2011/11/UK-Biobank-Protocol.pdf

10. Allen N, Sudlow C, Downey P, Peakman T, Danesh J, Elliott P, Gallacher J, Green J, Matthews P, Pell J, Sprosen T, Collins R. UK Biobank: Current status and what it means for epidemiology. *Health Policy and Technology* 2012: 1(3): 123-126.

11. De Matteis S, Jarvis D, Hutchings S, Darnton A, Fishwick D, Sadhra S, Rushton L, Cullinan P. Occupations associated with COPD risk in the large population-based UK Biobank cohort study. *Occupational and Environmental Medicine* 2016: 73(6): 378-384.

12. Quanjer PH, Stanojevic S, Cole TJ, Baur X, Hall GL, Culver BH, Enright PL, Hankinson JL, Ip MSM, Zheng J, Stocks J. Multi-ethnic reference values for spirometry for the 3–95-yr age range: the global lung function 2012 equations. *European Respiratory Journal* 2012: 40(6): 1324-1343.

452   13.   European Respiratory Society. Spirometry Equation Tools - R Macro. e-learning ressources 2017
453   [cited 2018 15 January]; Available from: http://www.ers-education.org/guidelines/global-lung-function-
454   initiative/spirometry-tools/r-macro.aspx
455   14.   Global Initiative for Chronic Obstructive Lung Disease. Global strategy for the diagnosis,
456   management, and prevention of chronic obstructive pulmonary disease; 2018.
457   15.   Beelen R, Hoek G, Vienneau D, Eeftens M, Dimakopoulou K, Pedeli X, Tsai M-Y, Künzli N,
458   Schikowski T, Marcon A, Eriksen KT, Raaschou-Nielsen O, Stephanou E, Patelarou E, Lanki T, Yli-Tuomi T,
459   Declercq C, Falq G, Stempfelet M, Birk M, Cyrys J, von Klot S, Nádor G, Varró MJ, Dėdelė A,
460   Gražulevičienė R, Mölter A, Lindley S, Madsen C, Cesaroni G, Ranzi A, Badaloni C, Hoffmann B,
461   Nonnemacher M, Krämer U, Kuhlbusch T, Cirach M, de Nazelle A, Nieuwenhuijsen M, Bellander T, Korek
462   M, Olsson D, Strömgren M, Dons E, Jerrett M, Fischer P, Wang M, Brunekreef B, de Hoogh K.
463   Development of NO2 and NOx land use regression models for estimating air pollution exposure in 36
464   study areas in Europe – The ESCAPE project. *Atmospheric Environment* 2013: 72(0): 10-23.
465   16.   Eeftens M, Beelen R, de Hoogh K, Bellander T, Cesaroni G, Cirach M, Declercq C, Dėdelė A, Dons
466   E, de Nazelle A, Dimakopoulou K, Eriksen K, Falq G, Fischer P, Galassi C, Gražulevičienė R, Heinrich J,
467   Hoffmann B, Jerrett M, Keidel D, Korek M, Lanki T, Lindley S, Madsen C, Mölter A, Nádor G,
468   Nieuwenhuijsen M, Nonnemacher M, Pedeli X, Raaschou-Nielsen O, Patelarou E, Quass U, Ranzi A,
469   Schindler C, Stempfelet M, Stephanou E, Sugiri D, Tsai M-Y, Yli-Tuomi T, Varró MJ, Vienneau D, Klot Sv,
470   Wolf K, Brunekreef B, Hoek G. Development of Land Use Regression Models for PM2.5, PM2.5
471   Absorbance, PM10 and PMcoarse in 20 European Study Areas; Results of the ESCAPE Project.
472   *Environmental Science & Technology* 2012: 46(20): 11195-11205.
473   17.   Gulliver J, de Hoogh K. Environmental exposure assessment: modelling air pollution
474   concentrations. *In:* Detels R, Gulliford M, Karim Q, Tan C, eds. Oxford textbook of global health. Oxford
475   University Press, Oxford, 2015.
476   18.   Doiron D, de Hoogh K, Probst-Hensch N, Mbatchou S, Eeftens M, Cai Y, Schindler C, Fortier I,
477   Hodgson S, Gaye A, Stolk R, Hansell A. Residential Air Pollution and Associations with Wheeze and
478   Shortness of Breath in Adults: A Combined Analysis of Cross-Sectional Data from Two Large European
479   Cohorts. *Environmental Health Perspectives* 2017: 125(9): 097025.
480   19.   Office for National Statistics. Median gross income, all households 1977 to financial year ending
481   2016. *In:* Statistics OfN, ed. Office for National Statistics, 2017.
482   20.   de Jong K, Vonk JM, Zijlema WL, Stolk RP, van der Plaat DA, Hoek G, Brunekreef B, Postma DS,
483   Boezen HM. Air pollution exposure is associated with restrictive ventilatory patterns. *European*
484   *Respiratory Journal* 2016: 48(4): 1221-1224.
485   21.   R Core Team. R: A language and environment for statistical computing. *In:* R Foundation for
486   Statistical Computing, ed., Vienna, Austria., 2018.
487   22.   Young RP, Hopkins R, Eaton TE. Forced expiratory volume in one second: not just a lung function
488   test but a marker of premature death from all causes. *European Respiratory Journal* 2007: 30(4): 616-
489   622.
490   23.   The Lancet Respiratory Medicine. New strategy for clean air in the UK—is it enough? *The Lancet*
491   *Respiratory Medicine* 2019: 7(3): 187.
492   24.   de Hoogh K, Korek M, Vienneau D, Keuken M, Kukkonen J, Nieuwenhuijsen MJ, Badaloni C,
493   Beelen R, Bolignano A, Cesaroni G, Pradas MC, Cyrys J, Douros J, Eeftens M, Forastiere F, Forsberg B,
494   Fuks K, Gehring U, Gryparis A, Gulliver J, Hansell AL, Hoffmann B, Johansson C, Jonkers S, Kangas L,
495   Katsouyanni K, Künzli N, Lanki T, Memmesheimer M, Moussiopoulos N, Modig L, Pershagen G, Probst-
496   Hensch N, Schindler C, Schikowski T, Sugiri D, Teixidó O, Tsai M-Y, Yli-Tuomi T, Brunekreef B, Hoek G,
497   Bellander T. Comparing land use regression and dispersion modelling to assess residential exposure to
498   ambient air pollution for epidemiological studies. *Environment International* 2014: 73: 382-392.

499   25.   Forbes LJL, Kapetanakis V, Rudnicka AR, Cook DG, Bush T, Stedman JR, Whincup PH, Strachan
500   DP, Anderson HR. Chronic exposure to outdoor air pollution and lung function in adults. *Thorax* 2009:
501   64(8): 657-663.
502   26.   Ackermann-Liebrich U, Leuenberger P, Schwartz J, Schindler C, Monn C, Bolognini G, Bongard JP,
503   Brandli O, Domenighetti G, Elsasser S, Grize L, Karrer W, Keller R, Keller-Wossidlo H, Kunzli N, Martin
504   BW, Medici TC, Perruchoud AP, Schoni MH, Tschopp JM, Villiger B, Wuthrich B, Zellweger JP, Zemp E.
505   Lung function and long term exposure to air pollutants in Switzerland. Study on Air Pollution and Lung
506   Diseases in Adults (SAPALDIA) Team. *Am J Respir Crit Care Med* 1997: 155(1): 122-129.
507   27.   Schikowski T, Sugiri D, Ranft U, Gehring U, Heinrich J, Wichmann H-E, Krämer U. Long-term air
508   pollution exposure and living close to busy roads are associated with COPD in women. *Respiratory*
509   *Research* 2005: 6(1): 152.
510   28.   Schikowski T, Ranft U, Sugiri D, Vierkötter A, Brüning T, Harth V, Krämer U. Decline in air
511   pollution and change in prevalence in respiratory symptoms and chronic obstructive pulmonary disease
512   in elderly women. *Respiratory Research* 2010: 11(1): 113.
513   29.   Wheeler BW, Ben-Shlomo Y. Environmental equity, air quality, socioeconomic status, and
514   respiratory health: a linkage analysis of routine data from the Health Survey for England. *Journal of*
515   *epidemiology and community health* 2005: 59(11): 948-954.
516   30.   Forastiere F, Stafoggia M, Tasco C, Picciotto S, Agabiti N, Cesaroni G, Perucci CA. Socioeconomic
517   status, particulate air pollution, and daily mortality: differential exposure or differential susceptibility.
518   *American journal of industrial medicine* 2007: 50(3): 208-216.
519   31.   Hegewald MJ, Crapo RO. Socioeconomic Status and Lung Function. *Chest* 2007: 132(5): 1608-
520   1614.
521   32.   Krewski D, Burnett RT, Goldberg M, Hoover K, Siemiatycki J, Abrahamowicz M, Villeneuve PJ,
522   White W. Reanalysis of the Harvard Six Cities Study, Part II: Sensitivity Analysis. *Inhalation Toxicology*
523   2005: 17(7-8): 343-353.
524   33.   Clougherty JE. A growing role for gender analysis in air pollution epidemiology. *Environmental*
525   *health perspectives* 2010: 118(2): 167-176.
526   34.   Abbey DE, Burchette RJ, Knutsen SF, McDonnell WF, Lebowitz MD, Enright PL. Long-term
527   Particulate and Other Air Pollutants and Lung Function in Nonsmokers. *American Journal of Respiratory*
528   *and Critical Care Medicine* 1998: 158(1): 289-298.
529   35.   Galizia A, Kinney PL. Long-term residence in areas of high ozone: associations with respiratory
530   health in a nationwide sample of nonsmoking young adults [dsee comments]. *Environmental health*
531   *perspectives* 1999: 107(8): 675-679.
532   36.   Kan H, Heiss G, Rose KM, Whitsel E, Lurmann F, London SJ. Traffic exposure and lung function in
533   adults: the Atherosclerosis Risk in Communities study. *Thorax* 2007: 62(10): 873-879.
534   37.   Jedrychowski W, Krzyzanowski M. Ventilatory lung function and chronic chest symptoms among
535   the inhabitants of urban areas with various levels of acid aerosols: prospective study in Cracow.
536   *Environmental Health Perspectives* 1989: 79: 101-107.
537   38.   Dubowsky SD, Suh H, Schwartz J, Coull BA, Gold DR. Diabetes, Obesity, and Hypertension May
538   Enhance Associations between Air Pollution and Markers of Systemic Inflammation. *Environmental*
539   *Health Perspectives* 2006: 114(7): 992-998.
540   39.   Zeka A, Sullivan JR, Vokonas PS, Sparrow D, Schwartz J. Inflammatory markers and particulate air
541   pollution: characterizing the pathway to disease. *International Journal of Epidemiology* 2006: 35(5):
542   1347-1354.
543   40.   Cai Y, Schikowski T, Adam M, Buschka A, Carsin A-E, Jacquemin B, Marcon A, Sanchez M,
544   Vierkötter A, Al-Kanaani Z, Beelen R, Birk M, Brunekreef B, Cirach M, Clavel-Chapelon F, Declercq C, de
545   Hoogh K, de Nazelle A, Ducret-Stich RE, Valeria Ferretti V, Forsberg B, Gerbase MW, Hardy R, Heinrich J,
546   Hoek G, Jarvis D, Keidel D, Kuh D, Nieuwenhuijsen MJ, Ragettli MS, Ranzi A, Rochat T, Schindler C, Sugiri

547 D, Temam S, Tsai M-Y, Varraso R, Kauffmann F, Krämer U, Sunyer J, Künzli N, Probst-Hensch N, Hansell
548 AL. Cross-sectional associations between air pollution and chronic bronchitis: an ESCAPE meta-analysis
549 across five cohorts. *Thorax* 2014: 69(11): 1005-1014.
550 41.   Department for Environment FRA. Emissions of air pollutants in the UK, 1970 to 2017; 2019 15
551 February, 2019.

552

553

554

Table 1: Population characteristics

Characteristic	Lung function (FEV$_1$ and FVC) and NO$_2$ population n=299 537 *	Lung function (FEV$_1$ and FVC) and PM population n=278 228 †	Excluded from analyses due to incomplete data (for lung function and NO$_2$ population) n=203 082	Difference p-Value
Sex, %				
Male	47.1 (n=140 977)	47.2 (n=131 257)	43.4 (n= 88 187)	<.001
Female	52.9 (n=158 560)	52.8 (n=146 971)	56.6 (n= 114 895)	
Age, mean (SD)	56 (8.05)	56 (8.05)	57.3 (8.1)	<.001
Age, %				
<65 years	83.2 (n=249 067)	83.1 (n=231 221)	77.6 (n=157 526)	<.001
≥65 years	16.8 (n=50 470)	16.9 (n=47 007)	22.4 (n=45 556)	
BMI, mean (SD)	27.4 (4.68)	27.4 (4.69)	27.6 (4.97) NA= 3 105	<.001
BMI, %				
Normal (<25 kg/m2)	33.3 (n=99 832)	33.3 (n=92 673)	32.7 (n=65 350)	
Overweight (25 to 29.9 kg/m2)	43.2 (n=129 271)	43.1 (n=120 024)	41.4 (n=82 872)	<.001
Obese (≥30 kg/m2)	23.5 (n=70 434)	23.6 (n=65 531)	25.9 (n=51 755) NA= 3 105	
Education level, %				
A, O or CSEs level	51.3 (n=153 657)	51.9 (n=144 504)	61.7 (n= 119 076)	<.001
College, university, NVQ or Other professional qualifications	48.7 (n=145 880)	48.1 (n=133 724)	38.3 (n=73 864) NA= 10 142	
Household income, %				
Less than £ 31,000	44.2 (n=132 527)	44.6 (n=124 097)	57.9 (n=72 891)	<.001
£ 31,000 and above	55.8 (n=167 010)	55.4 (n=154 131)	42.1 (n=52 993) NA= 77 198	
Smoking status, %				
Never smoker	59.0 (n=176 817)	58.8 (n=163 686)	48.4 (n=96 773)	
Former smoker	38.1 (n=114 249)	38.3 (n=106 658)	29.4 (n=58 842)	<.001
Current smoker	2.8 (n=8 471)	2.8 (n=7 884)	22.2 (n=44 515) NA= 2 952	
Passive smoking exposure at home	94.7 (n= 283 521)	94.8 (n=263 679)	93.6 (n=142 028)	<.001
None	5.3 (n= 16 016)	5.2 (n=14 549)	6.4 (n=9 781)	
Any			NA= 51 273	
Asthma, %				
Never had asthma	89.4 (n=267 490)	89.3 (n=248 232)	89.3 (n=179 670)	
Ever had asthma	10.6 (n=31 818)	10.7 (n=29 779)	10.7 (n=21 498)	0.53
	NA= 229	NA= 217	NA= 1 914	
Occupational status, %				
Non "at-risk" occupation	98.2 (n=206 506)	98.2 (n=192 826)	96.4 (n=112 765)	
"At-risk" occupation	1.8 (n=3 724)	1.8 (n=3 552)	3.6 (n=4 165)	<.001
	NA= 89 307	NA= 81 850	NA= 86 152	
FEV$_1$, mean (SD)	2.9 (0.78)	2.9 (0.78)	2.6 (0.77) NA=116 641	<.001
FVC, mean (SD)	3.8 (1.00)	3.8 (1.00)	3.5 (0.98) NA=116 641	<.001
FEV$_1$/FVC, mean (SD)	0.8 (0.07)	0.8 (0.07)	0.8 (0.08) NA=116 641	<.001
COPD, %				
No	92.7 (n=276 948)	92.6 (n=257 089)	87.9 (n=74 762)	
Yes	7.3 (n=21 900)	7.4 (n=20 478)	12.1 (n=10 267)	<.001
	NA= 689	NA= 661	NA=118 053	

Definition of abbreviations: FEV$_1$ = forced expiratory volume in 1 second, FVC = forced vital capacity, NO$_2$ = nitrogen dioxide, PM = particulate matter, SD = standard deviation, BMI = body mass index, COPD = chronic obstructive pulmonary disease

* Descriptive statistics shown are for participants with complete data for FEV$_1$ and FVC, age, sex, BMI, education level, household income, smoking status, passive smoking exposure at home, and residential NO$_2$ exposure.

† Descriptive statistics shown are for participants with complete data for FEV$_1$ and FVC, age, sex, BMI, education level, household income, smoking status, passive smoking exposure at home, and residential PM exposure.

Table 2: Pollutant descriptive statistics and correlation matrix *

Pollutant	N	Mean (SD), μg/m^3	Minimum, μg/m^3	Maximum, μg/m^3	IQR, μg/m^3	Pearson correlation coefficients			
						PM$_{2.5}$	PM$_{10}$	PM$_{coarse}$	NO$_2$
PM$_{2.5}$	278 228	9.94 (1.04)	8.17	19.89	1.27	1	0.53	0.21	0.87
PM$_{10}$	278 228	16.18 (1.90)	11.78	31.39	1.77		1	0.81	0.50
PM$_{coarse}$	278 228	6.41 (0.90)	5.57	12.82	0.77			1	0.19
NO$_2$	299 537	26.31 (7.49)	12.93	108.49	9.70				1

Definition of abbreviations: SD = standard deviation, IQR = interquartile range, PM$_{2.5}$ = fine particulate matter with diameter <2.5 μm, PM$_{10}$ = particulate matter with diameter <10 μm, PM$_{coarse}$ = coarse particulate matter with diameter between 2.5 μm and 10 μm, NO$_2$ = nitrogen dioxide

* Descriptive statics shown are for participants with complete data for FEV$_1$ and FVC, age, sex, BMI, education level, household income, smoking status, passive smoking exposure at home

Table 3: Associations of lung function and ambient air pollution exposure*

Exposure	N	FEV$_1$ (mL) Beta [95% CI]	FVC (mL) Beta [95% CI]	FEV$_1$/FVC Beta [95% CI]
PM$_{2.5}$ (per 5 µg/m^3)	278 228	**-83.13** **[-92.50, -73.75]**	**-62.62** **[-73.91, -51.32]**	**-9.68** **[-10.81, -8.56]**
PM$_{10}$ (per 10 µg/m^3)	278 228	**-94.41** **[-104.59, -84.22]**	**-122.95** **[-135.22, -110.68]**	-0.34 [-1.56, 0.89]
PM$_{coarse}$ (per 5 µg/m^3)	278 228	**-68.61** **[-79.37, -57.85]**	**-96.69** **[-109.65, -83.73]**	**1.34** **[0.04, 2.63]**
NO$_2$ (per 10 µg/m^3)	299 537	**-33.85** **[-36.34, -31.36]**	**-33.47** **[-36.47, -30.46]**	**-2.27** **[-2.57, -1.96]**

Definition of abbreviations: FEV$_1$ = forced expiratory volume in 1 second, FVC = forced vital capacity, CI = confidence interval, PM$_{2.5}$ = fine particulate matter with diameter <2.5 µm, PM$_{10}$ = particulate matter with diameter <10 µm, PM$_{coarse}$ = coarse particulate matter with diameter between 2.5 µm and 10 µm, NO$_2$ = nitrogen dioxide

* Adjusted for age (continuous), age-squared, sex, height, BMI (Kg/m^2), household income (less than £ 31,000 / £ 31,000 and above), education level (lower vocational or less / higher vocational or more), smoking status (never / former / current), and passive smoking exposure at home (none / any)

Table 4: Associations of COPD and ambient air pollution exposure*

Exposure	No. cases / non-cases⁺	OR [95% CI]
PM$_{2.5}$ (per 5 µg/m^3)	20 478 / 257 089	**1.52 [1.42, 1.62]**
PM$_{10}$ (per 10 µg/m^3)	20 478 / 257 089	**1.08 [1.00, 1.16]**
PM$_{coarse}$ (per 5 µg/m^3)	20 478 / 257 089	0.99 [0.91, 1.07]
NO$_2$ (per 10 µg/m^3)	21 900 / 276 948	**1.12 [1.10, 1.14]**

Definition of abbreviations: OR = odds ratio, CI = confidence interval, PM$_{2.5}$ = fine particulate matter with diameter <2.5 µm, PM$_{10}$ = particulate matter with diameter <10 µm, PM$_{coarse}$ = coarse particulate matter with diameter between 2.5 µm and 10 µm, NO$_2$ = nitrogen dioxide

* Adjusted for age (continuous), sex, BMI (Kg/m^2), household income (less than £ 31,000 / £ 31,000 and above), education level (lower vocational or less / higher vocational or more), smoking status (never / former / current), passive smoking exposure at home (none / any)

Table 5: Lung function subgroup analyses for $PM_{2.5}$ and NO_2*

	FEV$_1$ (mL)				FVC (mL)				FEV1 / FVC			
	PM$_{2.5}$ (per 5 µg/m³)		NO$_2$ (per 10 µg/m³)		PM$_{2.5}$ (per 5 µg/m³)		NO$_2$ (per 10 µg/m³)		PM$_{2.5}$ (per 5 µg/m³)		NO$_2$ (per 10 µg/m³)	
Group	Beta [95% CI]	Inter. p-value	Beta [95% CI]	Inter. p-value	Beta [95% CI]	Inter. p-value	Beta [95% CI]	Inter. p-value	Beta [95% CI]	Inter. p-value	Beta [95% CI]	Inter. p-value
Sex		**<.001**		**<.001**		**<.001**		**<.001**		.928		.883
Male	-102.32 [-118.16, -86.48]		-41.22 [-45.44, -37.00]		-78.48 [-97.42, -59.54]		-40.85 [-45.89, -35.81]		-9.52 [-11.25, -7.80]		-2.27 [-2.73, -1.80]	
Female	-68.14 [-78.68, -57.59]		-28.01 [-30.82, -25.21]		-50.47 [-63.28, -37.67]		-27.66 [-31.06, -24.26]		-9.79 [-11.26, -8.32]		-2.25 [-2.65, -1.86]	
Age		.574		.113		.187		**.014**		**<.001**		**<.001**
<65 years	-83.63 [-93.85, -73.40]		-32.55 [-37.27, -31.83]		-65.06 [-77.40, -52.71]		-34.86 [-38.15, -31.58]		-8.92 [-10.11, -7.73]		-2.04 [-2.36, -1.72]	
≥65 years	-85.32 [-108.62, -62.01]		-31.64 [-37.82, -25.47]		-54.05 [-81.85, -26.25]		-27.41 [-34.78, -20.05]		-13.73 [-16.91, -10.54]		-3.50 [-4.35, -2.65]	
Obesity		.068		**.003**		.460		.082		**.005**		**.005**
Non-obese	-78.68 [-89.31, -68.04]		-31.69 [-34.51, -28.87]		-58.93 [-71.78, -46.08]		-31.65 [-35.05, -28.24]		-9.07 [-10.36, -7.79]		-2.07 [-2.41, -1.73]	
Obese	-95.53 [-115.24, -75.82]		-40.36 [-45.68, -35.04]		-76.78 [-100.30, -53.27]		-40.78 [-47.12, -34.45]		-10.99 [-13.32, -8.67]		-2.61 [-3.24, -1.98]	
Smoking status		.388		**<.001**		**<.001**		**<.001**		**<.001**		**<.001**
Never smoker	-84.49 [-96.74, -72.25]		-38.11 [-41.37, -34.85]		-76.56 [-91.51, -61.60]		-41.89 [-45.87, -37.91]		-6.91 [-8.35, -5.47]		-1.61 [-2.00, -1.23]	
Current or past smoker	-87.08 [-101.61, -72.55]		-30.42 [-34.28, -26.56]		-49.66 [-66.87, -32.46]		-24.42 [-28.99, -19.85]		-13.80 [-15.59, -12.00]		-3.31 [-3.79, -2.83]	
Household income		**<.001**		**<.001**		**<.001**		**<.001**		**<.001**		**<.001**
Less than £ 31,000	-78.85 [-93.56, -64.13]		-35.76 [-39.79, -31.73]		-95.83 [-112.86, -78.79]		-46.92 [-51.58, -42.25]		-13.70 [-15.49, -11.91]		-3.46 [-3.96, -2.97]	
£ 31,000 and above	-39.12 [-52.30, -25.94]		-21.81 [-25.24, -18.37]		-31.69 [-46.76, -16.62]		-22.15 [-26.08, -18.23]		-6.38 [-7.82, -4.95]		-1.41 [-1.78, -1.03]	
Asthma status		**.002**		**.033**		.094		.319		**.013**		.113
Never had asthma	-84.84 [-94.61, -75.08]		-33.93 [-36.53, -31.33]		-63.17 [-75.10, -51.24]		-33.21 [-36.38, -30.04]		-9.78 [-10.92, -8.64]		-2.27 [-2.57, -1.96]	
Ever had asthma	-70.01 [-99.76, -40.26]		-33.13 [-41.08, -25.17]		-54.57 [-89.32, -19.81]		-34.12 [-43.40, -24.85]		-9.25 [-13.30, -5.21]		-2.43 [-3.51, -1.34]	
Occupational status		**.001**		**<.001**		**.002**		**<.001**		.431		.594
Non "at-risk" occupation	-71.88 [-83.25, -60.51]		-30.88 [-33.87, -27.89]		-57.95 [-71.67, -44.24]		-32.20 [-35.81, -28.59]		-6.94 [-8.25, -5.62]		-1.57 [-1.92, -1.22]	
"At-risk" occupation	-183.85 [-271.13, -96.56]		-77.71		-192.19 [-296.36, -88.01]		-91.28		-9.18 [-19.57, 1.20]		-1.81 [-4.71, 1.09]	

	[-101.86, -53.57]		[-120.11, -62.46]

Definition of abbreviations: FEV$_1$ = forced expiratory volume in 1 second, FVC = forced vital capacity, CI = confidence interval, PM$_{2.5}$ = fine particulate matter with diameter <2.5 µm, PM$_{10}$ = particulate matter with diameter <10 µm, PM$_{coarse}$ = coarse particulate matter with diameter between 2.5 µm and 10 µm, NO$_2$ = nitrogen dioxide

* Adjusted for age (continuous), age-squared, sex, height, BMI (Kg/m^2), household income (less than £ 31,000 / £ 31,000 and above), education level (lower vocational or less / higher vocational or more), smoking status (never / former / current), passive smoking exposure at home (none / any)

Table 6: COPD subgroup analyses for $PM_{2.5}$ and NO_2*

Group	PM$_{2.5}$ (per 5 µg/m³)			NO$_2$ (per 10 µg/m³)		
	No. cases / non-cases	OR [95% CI]	Interaction p-value	No. cases / non-cases	OR [95% CI]	Interaction p-value
Sex			**.024**			.101
Male	10 615 / 120 233	1.40 [1.27, 1.54]		11 279 / 129 269	1.10 [1.07, 1.13]	
Female	9 863 / 136 856	1.64 [1.49, 1.81]		10 621 / 147 679	1.13 [1.10, 1.16]	
Age			.128			.260
<65 years	16 685 / 214 004	1.49 [1.38, 1.60]		17 854 / 230 661	1.11 [1.09, 1.13]	
≥65 years	3 793 / 43 085	1.64 [1.40, 1.92]		4 046 / 46 287	1.13 [1.09, 1.18]	
Obesity			**.002**			**.002**
Non-obese	16 508 / 195 722	1.44 [1.34, 1.56]		17 646 / 210 967	1.10 [1.08, 1.12]	
Obese	3 970 / 61 367	1.80 [1.55, 2.09]		4 254 / 65 981	1.17 [1.12, 1.22]	
Smoking status			**.009**			.181
Never smoker	10 574 / 152 753	1.39 [1.26, 1.53]		11 319 / 165 120	1.10 [1.07, 1.13]	
Current or past smoker	9 904 / 104 336	1.69 [1.53, 1.85]		10 581 / 111 828	1.14 [1.11, 1.17]	
Household income			**<.001**			**<.001**
Less than £ 31,000	10 090 / 113 656	1.85 [1.69, 2.04]		10 700 / 121 462	1.19 [1.15, 1.22]	
£ 31,000 and above	10 388 / 143 433	1.25 [1.14, 1.38]		11 200 / 155 486	1.06 [1.03, 1.09]	
Asthma status			**<.001**			**<.001**
Never had asthma	14 484 / 233 176	1.66 [1.53, 1.79]		15 510 / 251 382	1.14 [1.12, 1.17]	
Ever had asthma	5 967 / 23 729	1.24 [1.08, 1.42]		6 362 / 25 371	1.06 [1.02, 1.10]	
Occupational status			.742			.725
Non "at-risk" occupation	13 512 / 178 876	1.37 [1.26, 1.49]		14 354 / 191 700	1.09 [1.06, 1.11]	
"At-risk" occupation	381 / 3 161	1.46 [0.89, 2.39]		399 / 3 314	1.11 [0.97, 1.27]	

Definition of abbreviations: OR = odds ratio, $PM_{2.5}$ = fine particulate matter with diameter <2.5 µm, PM_{10} = particulate matter with diameter <10 µm, PM_{coarse} = coarse particulate matter with diameter between 2.5 µm and 10 µm, NO_2 = nitrogen dioxide

* Adjusted for age (continuous), sex, BMI (Kg/m²), household income (less than £ 31,000 / £ 31,000 and above), education level (lower vocational or less / higher vocational or more), smoking status (never / former / or current), passive smoking exposure at home (none / any)

Figure 1: Study population, exclusions and missing data

Definition of abbreviations: FEV_1 = forced expiratory volume in 1 second, FVC = forced vital capacity, COPD = chronic obstructive pulmonary disease, NO_2 = nitrogen dioxide, PM = particulate matter

Figure 2: Air pollution exposure, FEV_1 (a), FVC (b), and COPD (c): comparison with other studies using ESCAPE air pollution estimates*

Definition of abbreviations: FEV_1 = forced expiratory volume in 1 second, FVC = forced vital capacity, COPD = chronic obstructive pulmonary disease, $PM_{2.5}$ = fine particulate matter with diameter <2.5 µm, PM_{10} = particulate matter with diameter <10 µm, PM_{coarse} = coarse particulate matter with diameter between 2.5 µm and 10 µm, NO_2 = nitrogen dioxide

* Cohorts included in each study:
Adam *et al.* [3]: European Community Respiratory Health Survey (ECRHS), French Epidemiological study on Genetics and Environment of Asthma (EGEA), National Survey of Health and Development (NSHD), Study on the influence of Air pollution on Lung function, Inflammation and Aging (SALIA) and Swiss cohort Study on Air Pollution and Lung and Heart Diseases in Adults (SAPALDIA)
De Jong *et al.* [18]: Lifelines Cohort Study
Schikowski *et al.* [4]: European Community Respiratory Health Survey (ECRHS), National Survey of Health and Development (NSHD), Study on the influence of Air pollution on Lung function, Inflammation and Aging (SALIA) and Swiss cohort Study on Air Pollution and Lung and Heart Diseases in Adults (SAPALDIA)

Supplementary Material

Air pollution, lung function and COPD: results from the population-based UK Biobank study

Authors: Dany Doiron[1,2,3], Kees de Hoogh[2,3], Nicole Probst-Hensch[2,3], Isabel Fortier[1], Yutong Cai[4,5], Sara De Matteis[6], Anna L Hansell[4,7]

[1]Research Institute of the McGill University Health Centre, Montreal, Quebec, Canada
[2]Swiss Tropical and Public Health Institute, Basel, Switzerland
[3]University of Basel, Basel, Switzerland
[4]Department of Epidemiology and Biostatistics, School of Public Health, Imperial College London, London, UK
[5]Department of Analytical, Environmental and Forensic Sciences, School of Population Health and Environmental Sciences, King's College London, London, UK
[6]National Heart & Lung Institute, Imperial College London, London, UK
[7]Centre for Environmental Health and Sustainability, University of Leicester, Leicester, UK

Table S1: ESCAPE project Southeast England area (London/Oxford) LUR models*

Pollutant	Predictor variables in final model [†]	Final LUR model	R^2 of model	R^2 cross validation
$PM_{2.5}$	• Product of inverse distance to the nearest road and nearest major road and traffic intensity on this road (INTMAJORINVDIST)[‡] • 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%
PM_{10}	• Inverse distance to the nearest road of the central road network (DISTINVMAJORC1)[§] • 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%
PM_{coarse}	• Inverse distance and inverse squared distance to the nearest major road in local road network (DISTINVMAJOR1)[‡] • Heavy-duty traffic intensity on nearest major road (HEAVYTRAFMAJOR)[‡]	$5.36 +$ 33.08*DISTINVMAJOR1 $+ 7.98 \times 10^{-4} \times$ HEAVYTRAFMAJOR	68%	57%
NO_2	• Total traffic load of major roads in a 50-meter buffer (sum of (traffic intensity * length of all segments)) (TRAFMAJORLOAD_50)[‡] • 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%

Definition of abbreviations: $PM_{2.5}$ = fine particulate matter with diameter <2.5 µm, PM_{10} = particulate matter with diameter <10 µm, PM_{coarse} = coarse particulate matter with diameter between 2.5 µm and 10 µm, NO_2 = nitrogen dioxide
* Information extracted from Eeftens *et al.* [1] and Beelen *et al.* [2]; validation data shown in this table is not specific to the study area included in the present analysis
[†] 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
[‡] Major roads for local road network are road with traffic intensity > 5,000 mvh/24h
[§] Major roads for central road network are classes 0, 1, and 2 (+ classes 3 and 4 based on local knowledge and decision)

Table S2: List of 14 occupations showing a moderate increased risk of COPD (prevalence ratio ≥ 1.30) *

SOC code, version 2000	Occupation
8217	Seafarers; barge, lighter and boat operatives
8122	Coal mine operatives
9132	Industrial cleaning process occupations
5313	Roofers, roof tilers and slaters
9134	Packers, bottlers, canners, fillers
5112	Horticultural trades
8111	Food, drink and tobacco process operatives
9233	Cleaners, domestics
5322	Floorers and wall tilers
8114	Chemical and related process operatives
9211	Postal workers, mail sorters, messengers, couriers
9121	Labourers in building and woodworking trades
9244	School mid-day assistants
9223	Kitchen and catering assistants

Definition of abbreviations: SOC = Standard Occupational Classification

* Information extracted from: De Matteis *et al.* [3]

Table S3: Associations of lung function and ambient air pollution exposure, per interquartile range (IQR)*

Exposure	N	FEV$_1$ (mL) Beta [95% CI]	FVC (mL) Beta [95% CI]	FEV$_1$/FVC Beta [95% CI]
PM$_{2.5}$ (per IQR = 1.27 μg/m^3)	278 228	**-21.11** **[-23.50, -18.73]**	**-15.90** **[-18.77, -13.03]**	**-2.46** **[-2.75, -2.17]**
PM$_{10}$ (per IQR = 1.77 μg/m^3)	278 228	**-16.71** **[-18.51, -14.91]**	**-21.76** **[-23.93, -19.59]**	-0.06 [-0.28, 0.16]
PM$_{coarse}$ (per IQR = 0.77 μg/m^3)	278 228	**-10.57** **[-12.22, -8.91]**	**-14.89** **[-16.89, -12.89]**	**0.21** **[0.01, 0.40]**
NO$_2$ (per IQR = 9.70 μg/m^3)	299 537	**-32.83** **[-35.25, -30.41]**	**-32.46** **[-35.38, -29.55]**	**-2.20** **[-2.49, -1.91]**

Definition of abbreviations: FEV$_1$ = forced expiratory volume in 1 second, FVC = forced vital capacity, CI = confidence interval, PM$_{2.5}$ = fine particulate matter with diameter <2.5 μm, PM$_{10}$ = particulate matter with diameter <10 μm, PM$_{coarse}$ = coarse particulate matter with diameter between 2.5 μm and 10 μm, NO$_2$ = nitrogen dioxide

* Adjusted for age (continuous), age-squared, sex, height, BMI (Kg/m^2), household income (less than £ 31,000 / £ 31,000 and above), education level (lower vocational or less / higher vocational or more), smoking status (never / former / current), and passive smoking exposure at home (none / any)

Table S4: Associations of COPD and ambient air pollution exposure, per interquartile range (IQR)*

Exposure	No. cases / non-cases$^+$	OR [95% CI]
PM$_{2.5}$ (per IQR = 1.27 μg/m^3)	20 478 / 257 089	**1.11 [1.09, 1.13]**
PM$_{10}$ (per IQR = 1.77 μg/m^3)	20 478 / 257 089	**1.01 [1.00, 1.03]**
PM$_{coarse}$ (per IQR = 0.77 μg/m^3)	20 478 / 257 089	1.00 [0.99, 1.01]
NO$_2$ (per IQR = 9.70 μg/m^3)	21 900 / 276 948	**1.11 [1.09, 1.13]**

Definition of abbreviations: OR = odds ratio, CI = confidence interval, PM$_{2.5}$ = fine particulate matter with diameter <2.5 μm, PM$_{10}$ = particulate matter with diameter <10 μm, PM$_{coarse}$ = coarse particulate matter with diameter between 2.5 μm and 10 μm, NO$_2$ = nitrogen dioxide

* Adjusted for age (continuous), sex, BMI (Kg/m^2), household income (less than £ 31,000 / £ 31,000 and above), education level (lower vocational or less / higher vocational or more), smoking status (never / former / current), passive smoking exposure at home (none / any)

Table S5: Associations of COPD and lung function with PM$_{2.5}$, NO$_2$, smoking status and passive smoking exposure*

Exposure	FEV$_1$ (mL) Beta [95% CI]	FVC (mL) Beta [95% CI]	FEV$_1$/FVC Beta [95% CI]	COPD OR [95% CI]
PM$_{2.5}$ (per 5 μg/m^3)	**-83.13** **[-92.50, -73.75]**	**-62.62** **[-73.91, -51.32]**	**-9.68** **[-10.81, -8.56]**	**1.52** **[1.42, 1.62]**
NO$_2$ (per 10 μg/m^3)	**-33.85** **[-36.34, -31.36]**	**-33.47** **[-36.47, -30.46]**	**-2.27** **[-2.57, -1.96]**	**1.12** **[1.10, 1.14]**
Former smoker	**-127.13** **[-147.54, -106.73]**	**38.05** **[13.46, 62.64]**	**-47.17** **[-49.62, -44.72]**	**4.40** **[3.79, 5.11]**
Current smoker	**-283.98** **[-343.04, -224.93]**	-63.84 [-135.01, 7.33]	**-70.15** **[-77.24, -63.06]**	**9.95** **[6.80, 14.47]**
Passive smoking exposure at home	**-294.95** **[-338.68, -251.23]**	**-270.68** **[-323.37, -217.99]**	**-24.97** **[-30.22, -19.72]**	**2.81** **[2.09, 1.62]**

Definition of abbreviations: FEV$_1$ = forced expiratory volume in 1 second, FVC = forced vital capacity, CI = confidence interval, PM$_{2.5}$ = fine particulate matter with diameter <2.5 μm, PM$_{10}$ = particulate matter with diameter <10 μm, PM$_{coarse}$ = coarse particulate matter with diameter between 2.5 μm and 10 μm, NO$_2$ = nitrogen dioxide

* For FEV$_1$, FVC and FEV$_1$/FVC ratio: Adjusted for age (continuous), age-squared, sex, height, BMI (Kg/m^2), household income (less than £ 31,000 / £ 31,000 and above), education level (lower vocational or less / higher vocational or more), smoking status (never / former / current), and passive smoking exposure at home (none / any). Former smoker, current smoker and passive smoking exposure associations are adjusted for PM$_{2.5}$ exposure.

For COPD: Adjusted for age (continuous), sex, BMI (Kg/m^2), household income (less than £ 31,000 / £ 31,000 and above), education level (lower vocational or less / higher vocational or more), smoking status (never / former / current), and passive smoking

exposure at home (none / any). Former smoker, current smoker and passive smoking exposure associations are adjusted for $PM_{2.5}$ exposure.

Table S6: Lung function sensitivity analyses restricted to individuals having lived at the same address for 10 years or more*

Exposure	N	FEV_1 (mL) Beta [95% CI]	FVC (mL) Beta [95% CI]	FEV1/FVC Beta [95% CI]
$PM_{2.5}$ (per 5 µg/m³)	188 257	-75.20 [-86.76, -63.64]	-49.15 [-63.09, -35.21]	-10.86 [-12.27, -9.44]
PM_{10} (per 10 µg/m³)	188 257	-88.69 [-101.15, -76.23]	-112.60 [-127.62, -97.58]	-1.24 [-2.76, 0.28]
PM_{coarse} (per 5 µg/m³)	188 257	-63.13 [-76.15, -50.11]	-84.88 [-100.58, -69.19]	0.27 [-1.32, 1.86]
NO_2 (per 10 µg/m³)	203 041	-31.75 [-34.83, -28.67]	-29.89 [-33.60, -26.17]	-2.58 [-2.96, -2.21]

Definition of abbreviations: FEV_1 = forced expiratory volume in 1 second, FVC = forced vital capacity, CI = confidence interval, $PM_{2.5}$ = fine particulate matter with diameter <2.5 µm, PM_{10} = particulate matter with diameter <10 µm, PM_{coarse} = coarse particulate matter with diameter between 2.5 µm and 10 µm, NO_2 = nitrogen dioxide

*Adjusted for age (continuous), age-squared, sex, height, BMI (Kg/m²), household income (less than £ 31,000 / £ 31,000 and above), education level (lower vocational or less / higher vocational or more), smoking status (never, former, or current), passive smoking exposure at home (none / any)

Table S7: COPD sensitivity analyses restricted to individuals having lived at the same address for 10 years or more*

Exposure	No. cases / non-cases	OR [95% CI]
$PM_{2.5}$ (per 5 µg/m³)	13 564 / 174 236	1.56 [1.43, 1.70]
PM_{10} (per 10 µg/m³)	13 564 / 174 236	1.13 [1.03, 1.24]
PM_{coarse} (per 5 µg/m³)	13 564 / 174 236	1.04 [0.94, 1.15]
NO_2 (per 10 µg/m³)	14 535 / 188 026	1.13 [1.10, 1.15]

Definition of abbreviations: OR = odds ratio, CI = confidence interval, $PM_{2.5}$ = fine particulate matter with diameter <2.5 µm, PM_{10} = particulate matter with diameter <10 µm, PM_{coarse} = coarse particulate matter with diameter between 2.5 µm and 10 µm, NO_2 = nitrogen dioxide
* Adjusted for age (continuous), sex, BMI (Kg/m²), household income (less than £ 31,000 / £ 31,000 and above), education level (lower vocational or less / higher vocational or more), smoking status (never / former / or current), passive smoking exposure at home (none / any)

Table S8: Exposure estimate descriptive statistics for the five studies included in Adam *et al.* (2015) [4] meta-analysis

Study	Exposure	Mean ug/m3	Minimum ug/m3	Maximum ug/m3
European Community Respiratory Health Survey (ECRHS)	$PM_{2.5}$	15.9	8.2	34.4
	PM_{10}	25.8	11.9	55.2
	PM_{coarse}	10.3	3.9	25.4
	NO_2	28.9	0	115.5
French Epidemiological study on Genetics and Environment of Asthma (EGEA)	$PM_{2.5}$	15.3	10	22.3
	PM_{10}	25.1	18.6	36.2
	PM_{coarse}	9.4	3.9	17.1
	NO_2	27.4	9.3	98.5
National Survey of Health and Development (NSHD)	$PM_{2.5}$	9.5	8.2	13.5
	PM_{10}	15.7	11.8	26.2
	PM_{coarse}	6.4	5.6	9.7
	NO_2	22.4	12.9	62
Study on the influence of Air pollution on Lung function, Inflammation and Aging (SALIA)	$PM_{2.5}$	17.8	15.9	21.9
	PM_{10}	26.7	23.9	33.5
	PM_{coarse}	9.4	2.8	14.8
	NO_2	27.6	19.7	70.3
Swiss Cohort Study on Air Pollution and Lung and Heart Diseases in Adults (SAPALDIA)	$PM_{2.5}$	16.8	12.4	23.5
	PM_{10}	23.2	17.6	31.7
	PM_{coarse}	6.5	4.3	10.4
	NO_2	27	6.9	56.3

Table S9: Exposure estimate descriptive statistics for four studies in Schikowski *et al.* (2015) [5] meta-analysis

Study	Exposure	Mean ug/m3	Minimum ug/m3	Maximum ug/m3
European Community Respiratory Health Survey (ECRHS)	$PM_{2.5}$	16.13	8.17	34.37
	PM_{10}	25.88	11.91	55.17
	PM_{coarse}	10.2	3.89	25.37
	NO_2	28.95	0	115.52
National Survey of Health and Development (NSHD)	$PM_{2.5}$	9.52	8.17	13.49
	PM_{10}	15.73	11.79	26.2
	PM_{coarse}	6.37	5.57	9.71
	NO_2	22.39	12.93	61.99
Study on the influence of Air pollution on Lung function, Inflammation and Aging (SALIA)	$PM_{2.5}$	17.76	15.9	21.9
	PM_{10}	26.72	23.88	33.47
	PM_{coarse}	9.37	2.85	14.79
	NO_2	27.62	19.66	70.34
Swiss Cohort Study on Air Pollution and Lung and Heart Diseases in Adults (SAPALDIA)	$PM_{2.5}$	16.78	12.36	23.48
	PM_{10}	23.16	17.6	31.69
	PM_{coarse}	6.49	4.27	10.39
	NO_2	26.17	6.87	56.3

Table S10: Exposure estimate descriptive statistics in de Jong *et al.* (2016) [6]

Study	Exposure	Median ug/m3	Minimum ug/m3	Maximum ug/m3
LifeLines Cohort	$PM_{2.5}$	15.4	14.8	20.2
	PM_{10}	24	23.7	31.7
	NO_2	15.7	8.4	50.8

References

1.   Eeftens M, Beelen R, de Hoogh K, Bellander T, Cesaroni G, Cirach M, Declercq C, Dėdelė A, Dons E, de Nazelle A, Dimakopoulou K, Eriksen K, Falq G, Fischer P, Galassi C, Gražulevičienė R, Heinrich J, Hoffmann B, Jerrett M, Keidel D, Korek M, Lanki T, Lindley S, Madsen C, Mölter A, Nádor G, Nieuwenhuijsen M, Nonnemacher M, Pedeli X, Raaschou-Nielsen O, Patelarou E, Quass U, Ranzi A, Schindler C, Stempfelet M, Stephanou E, Sugiri D, Tsai M-Y, Yli-Tuomi T, Varró MJ, Vienneau D, Klot Sv, Wolf K, Brunekreef B, Hoek G. Development of Land Use Regression Models for PM2.5, PM2.5 Absorbance, PM10 and PMcoarse in 20 European Study Areas; Results of the ESCAPE Project. *Environmental Science & Technology* 2012: 46(20): 11195-11205.

2.   Beelen R, Hoek G, Vienneau D, Eeftens M, Dimakopoulou K, Pedeli X, Tsai M-Y, Künzli N, Schikowski T, Marcon A, Eriksen KT, Raaschou-Nielsen O, Stephanou E, Patelarou E, Lanki T, Yli-Tuomi T, Declercq C, Falq G, Stempfelet M, Birk M, Cyrys J, von Klot S, Nádor G, Varró MJ, Dėdelė A, Gražulevičienė R, Mölter A, Lindley S, Madsen C, Cesaroni G, Ranzi A, Badaloni C, Hoffmann B, Nonnemacher M, Krämer U, Kuhlbusch T, Cirach M, de Nazelle A, Nieuwenhuijsen M, Bellander T, Korek M, Olsson D, Strömgren M, Dons E, Jerrett M, Fischer P, Wang M, Brunekreef B, de Hoogh K. Development of NO2 and NOx land use regression models for estimating air pollution exposure in 36 study areas in Europe – The ESCAPE project. *Atmospheric Environment* 2013: 72(0): 10-23.

3.   De Matteis S, Jarvis D, Hutchings S, Darnton A, Fishwick D, Sadhra S, Rushton L, Cullinan P. Occupations associated with COPD risk in the large population-based UK Biobank cohort study. *Occupational and Environmental Medicine* 2016: 73(6): 378-384.

4.   Adam M, Schikowski T, Carsin AE, Cai Y, Jacquemin B, Sanchez M, Vierkötter A, Marcon A, Keidel D, Sugiri D, Al Kanani Z, Nadif R, Siroux V, Hardy R, Kuh D, Rochat T, Bridevaux P-O, Eeftens M, Tsai M-Y, Villani S, Phuleria HC, Birk M, Cyrys J, Cirach M, de Nazelle A, Nieuwenhuijsen MJ, Forsberg B, de Hoogh K, Declerq C, Bono R, Piccioni P, Quass U, Heinrich J, Jarvis D, Pin I, Beelen R, Hoek G, Brunekreef B, Schindler C, Sunyer J, Krämer U, Kauffmann F, Hansell AL, Künzli N, Probst-Hensch N. Adult lung function and long-term air pollution exposure. ESCAPE: a multicentre cohort study and meta-analysis. *European Respiratory Journal* 2015: 45(1): 38-50.

5.   Schikowski T, Adam M, Marcon A, Cai Y, Vierkötter A, Carsin AE, Jacquemin B, Al Kanani Z, Beelen R, Birk M, Bridevaux P-O, Brunekeef B, Burney P, Cirach M, Cyrys J, de Hoogh K, de Marco R, de Nazelle A, Declercq C, Forsberg B, Hardy R, Heinrich J, Hoek G, Jarvis D, Keidel D, Kuh D, Kuhlbusch T, Migliore E, Mosler G, Nieuwenhuijsen MJ, Phuleria H, Rochat T, Schindler C, Villani S, Tsai M-Y, Zemp E, Hansell A, Kauffmann F, Sunyer J, Probst-Hensch N, Krämer U, Künzli N. Association of ambient air pollution with the prevalence and incidence of COPD. *European Respiratory Journal* 2014: 44(3): 614-626.

6.	de Jong K, Vonk JM, Zijlema WL, Stolk RP, van der Plaat DA, Hoek G, Brunekreef B, Postma DS, Boezen HM. Air pollution exposure is associated with restrictive ventilatory patterns. *European Respiratory Journal* 2016: 48(4): 1221-1224.