Environ Health Perspect, DOI: 10.1289/ehp16554, Accepted 5/19/2025

Source-specific air pollution and risk of chronic obstructive pulmonary disease: A pooled cohort study

Manuella Lech Cantuaria,[1,2] Aslak Harbo Poulsen,[1] Ole Raaschou-Nielsen,[1,3] Étienne Audureau,[4,5] Ralph Epaud,[4,6,7] Sophie Lanone,[4] Jørgen Brandt,[3,8] Lise Marie Frohn,[3] Matthias Ketzel,[3] Anja Olsen,[9,10] Lau Caspar Thygesen,[11] Mette Sørensen[1,12]

[1] Work, Environment and Cancer, Danish Cancer Institute, Copenhagen, Denmark

[2] Department of Clinical Research, University of Southern Denmark, Odense, Denmark

[3] Department of Environmental Science, Aarhus University, Roskilde, Denmark

[4] University Paris-Est Créteil, INSERM, IMRB, Creteil, France

[5] Public Health Department, Clinical Research Unit (URC), Hôpital Henri-Mondor, Assistance Publique Hôpitaux de Paris (APHP), Créteil, France

[6] Department of General Pediatrics, Centre Hospitalier Intercommunal de Créteil, Créteil, France

[7] Center for Rare Lung Diseases (RESPIRARE), Créteil, France

[8] iClimate - Interdisciplinary Centre for Climate Change, Aarhus University, Roskilde, Denmark

[9] Diet, Cancer and Health, Danish Cancer Institute, Copenhagen, Denmark

[10] Department of Public Health, University of Aarhus, Aarhus, Denmark

[11] National Institute of Public Health, University of Southern Denmark, Copenhagen, Denmark

[12] Department of Natural Science and Environment, Roskilde University, Roskilde, Denmark

Corresponding author: Manuella Lech Cantuaria; Phone number: +45 2721-1181; Work address: Strandboulevarden 49, 2100 København. Email: mlc@cancer.dk

Conflict of interest: The authors declare they have no conflicts of interest related to this work to disclose.

Abstract

Background:
The evidence linking long-term exposure to air pollution and development of chronic obstructive pulmonary disease (COPD) is still controversial. Furthermore, most studies have investigated associations with particulate matter (PM) and nitrogen dioxide (NO_2), disregarding their emission source and other relevant air pollutants, such as ultrafine particles (UFP) and elemental carbon (EC).

Objectives:
This study aimed to assess associations between long-term residential exposure to $PM_{2.5}$, NO_2, UFP, and EC and risk of COPD, distinguishing the effects of air pollution from local traffic and other sources.

Methods:
We pooled data from two large Danish cohorts - the Diet, Cancer, and Health cohort and the Danish National Health Survey. For all participants (N = 159,769), we estimated long-term air pollution exposure to total, local traffic, and other contributions, based on complete address histories. We used Cox proportional hazards models to estimate associations between 10-year time-weighted averaged air pollution and incident COPD, adjusting for demographic, socioeconomic, and lifestyle factors, including smoking. We evaluated possible modification of these associations by sex, smoking status, and previous asthma diagnosis.

Results:
Long-term exposures to $PM_{2.5}$, NO_2, UFP, and EC were associated with higher risk of COPD. The highest hazard ratio (HR) per interquartile range of total contributions was observed for $PM_{2.5}$ (HR: 1.11 [95% confidence interval: 1.05, 1.17]), followed by NO_2 (1.08 [1.04, 1.13]), UFP (1.05 [0.99, 1.11]), and EC (1.02 [1.00, 1.05]), after full adjustment. $PM_{2.5}$ from other sources than local traffic was more strongly associated with COPD than $PM_{2.5}$ from local traffic, while for UFP and EC, the contributions from local traffic seemed most harmful. Effect modification analyses showed stronger associations among women, never smokers, and those with an asthma diagnosis.

Discussion:
Our findings suggest that air pollution from local traffic and other sources contribute to COPD risk, with variations depending on the pollutant type. Further research is needed to validate these findings across different populations and geographical settings.

1. Introduction

Chronic obstructive pulmonary disease (COPD) is a highly prevalent and debilitating condition characterized by persistent airflow obstruction and progressive, heterogeneous respiratory symptoms. The global number of COPD cases is expected to increase by 23% over the next 15 years, reaching nearly 600 million patients worldwide by 2050.[1] COPD therefore places an increasingly heavy burden on the healthcare system.

While smoking is the primary risk factor for COPD, ambient air pollution is also believed to play a significant role in its pathogenesis, by triggering airway inflammation and oxidative stress in bronchial epithelial cells.[2] Many studies have investigated respiratory health effects of acute increases in air pollution levels, such as short-term peaks caused by wildfires and extreme weather events.[3,4] These studies have consistently demonstrated that short-term exposure to air pollution is linked to an increased risk of COPD exacerbation,[5,6] hospitalization,[6–8] and mortality.[6,7]

The evidence on long-term air pollution exposure and development of COPD, however, is still limited and in general more challenging to establish.[3] A meta-analysis covering six prospective studies found that a 10 μg/m³ increase in particulate matter (PM) with an aerodynamic diameter of 2.5 μm or less ($PM_{2.5}$) was associated with an 18% increase in COPD incidence (95% confidence interval (CI): 13%, 23%).[9] This meta-analysis furthermore found suggestions of an association with nitrogen dioxide (NO_2), although these results are based on a limited number of studies.[9] Other cohort studies not included in this meta-analysis showed quite inconsistent results for both $PM_{2.5}$ and NO_2.[10–15]

Previous studies suggested that the adverse health effects of PM exposure can vary depending on the type of PM and its characteristics, such as size, density, and composition.[16,17] Ultrafine particles (UFPs), a subset of PM with diameters less than 0.1 μm, can penetrate deeper into the lungs compared to larger particles like $PM_{2.5}$ and PM_{10}, allowing them to reach the alveoli more easily and remain in the lungs for extended periods.[18] Elemental carbon (EC) refers to the pure carbon component present in PM. It is typically formed from incomplete combustion processes and serves as an indicator of local combustion sources, such as traffic, industry, and wood-burning, therefore being a relevant indicator of air quality.[19] The few studies that have investigated EC (or black carbon) in relation to COPD showed inconsistent results.[12,14,20] To our knowledge, only one longitudinal study assessed long-term UFP exposure and incident COPD, finding indications of an association.[21]

The impact of particulate air pollution on health, including the respiratory system, may vary depending on the emission source, as particles from different sources have been shown to differ in chemical composition, particle size, and toxicity.[22,23] For instance, traffic-related particles tend to have high oxidative potential, likely due to metals from engine and brake abrasion,[22] which may enhance their inflammatory effects in the lungs. PM from wood combustion appears to have a stronger impact on respiratory health than on cardiovascular health, possibly due to its role in impairing lung immune defense.[22,24,25] Furthermore, a global ecological study suggested that secondary aerosols were the strongest contributors to chronic respiratory diseases, including COPD. Therefore, evaluating associations based on emission sources, such as those from traffic versus non-traffic sources, can enhance our understanding of which air pollution constituents contribute to

COPD. Such information may be an important input in designing more effective policy measures. However, very few epidemiological studies have conducted a comparative analysis of the impact of air pollution from different sources on COPD development, e.g. Hendryx et al. (2019).[26]

We aimed to investigate associations between long-term residential exposure to different types of PM ($PM_{2.5}$, EC and UFP) and NO_2 and risk of COPD using pooled, harmonized data from two large, questionnaire-based Danish cohorts. For all air pollutants, we assessed associations with total, local traffic, and other contributions (i.e. non-traffic sources and non-local traffic sources).

2. Methods

Study population

This study was based on two large Danish cohorts: The Diet, Cancer, and Health (DCH) cohort and the Danish National Health Survey (DNHS).

The DCH cohort recruited residents from the two largest cities in Denmark, Aarhus and Copenhagen, between 1993 and 1997.[27] Participants had to be born in Denmark, cancer free at the time of recruitment, and aged 50-64 years old. In total, 57,053 persons (response proportion of 35%) were enrolled into the study and completed a comprehensive self-administered, interviewer-checked questionnaire on diet, lifestyle (e.g. current and previous smoking habits, physical activity, alcohol intake), and health upon study entry. The study was conducted according to the Declaration of Helsinki and approved by local ethical authorities, and all participants provided informed consent.

In the DNHS, conducted in 2010 and 2013, around 300,000 adults (≥16 years) were invited each year to participate by completing a detailed questionnaire on lifestyle and physical and mental health, using a mixed-mode (paper/web) approach.[28] The participants were randomly selected from each of Denmark's five administrative regions, along with a nationwide sample, resulting in six distinct and exclusive subsamples covering the entire country. Response proportions were 60% and 54% for 2010 and 2013, respectively, resulting in 339,922 respondents. Individuals who responded to the questionnaire in both 2010 and 2013 were included only once in our study, with their responses from 2010 considered as their baseline information. To align with the population characteristics of the DCH cohort, we have in the present study only included DNHS respondents aged 55 years and older. The study was approved by the Danish Data Protection Agency.

We excluded all participants who had COPD at baseline, who had incomplete (i.e. more than 20% missing) address history and/or exposure information before study entry, and those with missing covariate data.

Questionnaire information from the two cohorts (collected at baseline) were harmonized and pooled. Participants in the pooled cohort were subsequently linked to national administrative and health registries using unique personal identification numbers that all residents in Denmark have.[29]

Outcome definition

We identified COPD cases through linkage with the National Patient Register, which holds nationwide information on inpatient diagnoses since 1977 as well as outpatient diagnoses since

1994.[30] We defined cases of COPD as individuals who received a primary or secondary diagnosis coded as 491 or 492 according to the International Classification of Diseases, Eighth Edition (ICD-8), or as J42, J43, or J44 according to the Tenth Edition (ICD-10). All persons with a COPD diagnosis before baseline were considered prevalent cases and excluded from our study population.

Exposure

We retrieved residential address-history for all participants in the pooled cohort from 1990 until censoring using the Danish Civil Registration System.[29] For all corresponding addresses, we modelled outdoor air pollution concentrations of $PM_{2.5}$, NO_2, UFP, and EC using the Danish DEHM/UBM/AirGIS modelling system.[31–33] This system calculates air pollution concentrations at the individual address level based on three different models, covering different geographical scales: 1) regional background, calculated using the Danish Eulerian Hemispheric Model (DEHM) to assess long-range transport of air pollution on the Northern Hemisphere. The DEHM is based on detailed atmospheric chemistry and deposition processes, as well as input data on emissions inventories and meteorological aspects;[34] 2) local background, simulated using the Urban Background Model (UBM) on a 1 km x 1 km grid resolution covering the entire Denmark. Together with the DEHM, the UBM relies on meteorological data generated by the Weather Research and Forecasting model,[35] which is routinely executed alongside DEHM and UBM as part of the modeling framework;[36,37] and 3) local street-level pollution, simulated using the Operational Street Pollution Model (OSPM), which incorporates factors such as traffic and street characteristics, building layouts, emission rates, and meteorological conditions.[31,32] The DEHM/UBM/AirGIS modelling system have been validated, showing correlation coefficients ranging from 0.67 to 0.85 for $PM_{2.5}$, 0.77 to 0.79 for EC, and 0.60 to 0.80 for NO_2 when comparing modeled and observed concentrations across various locations and measurement periods.[38,39]

For all Danish addresses, the hourly concentrations of $PM_{2.5}$, NO_2, and EC were subsequently aggregated as monthly averages over the period of 1990-2017. Recently, modelling of particle number concentrations was added to the modelling system, therefore providing an estimate of UFP address-level concentrations covering the entire period from 1990 to 2017.[40,41] This was done by extending the DEHM/UBM/AirGIS modelling system with the M7 particle dynamics module (Vignati et al., 2004), which simulates key physical transformation processes such as nucleation, coagulation, and condensation.[42] Modelled UFP concentrations were validated against measured UFP concentrations for annual averages, showing Pearson correlation coefficients of 0.86 for UFP at a regional-scale station, 0.87 for an urban-scale station and 0.95 for a street-scale station.[41]

Using comprehensive inventories for Denmark based on standardized, internationally recognized emission categories denominated as Selected Nomenclature for Air Pollution (SNAP) codes, we disaggregated total air pollution concentrations into source-specific contribution.[43] An overview of the SNAP categories used in Danish emission inventories is provided in Table S1. Emissions from local road traffic (i.e. SNAP code 07 and up to a distance of 25 km from the address location) were used to calculate the "traffic contribution"; whereas emissions from non-traffic sources and secondary long-range transported traffic emissions were used to calculate the "non-traffic contribution",

including e.g. industrial activities, agriculture, non-industrial combustion plants, waste treatment, traffic from more than 25 km distance and other mobile sources such as shipping.[44]

Monthly address-specific air pollutant concentrations ($PM_{2.5}$, NO_2, UFP, and EC) were linked to individual address histories for the entire study population. For each cohort member, we calculated time-weighted 10-year running means, considering exposure at all addresses and accounting for the exact duration each individual resided at each address. We calculated both total, local traffic and non-traffic concentrations for all four pollutants.

Covariates

Covariates were selected based on: 1) existing literature, taking into consideration plausible risk factors for COPD (e.g. socioeconomics and education,[45] dietary patterns,[46,47] smoking,[48] and physical activity,[49] that are also linked to air pollution exposure;[50–52] and 2) the data availability after harmonization across the two cohorts.

From the registers at Statistics Denmark, we obtained annual, time-varying information for both cohorts across all study years on the following individual-level covariates: cohabiting status (married/cohabiting, single/widow/divorced); highest-attained education (mandatory, secondary/vocational, medium/long); income (based on quintiles defined for the entire Danish population, stratified by sex and year, i.e. low (Q1); medium (Q2-Q4); high (Q5); and occupational status (white collar, blue collar, unemployed/retired). We also gathered information on three area-level covariates calculated for all 2,160 parishes in Denmark, i.e. proportion of the population in each parish with low income (1st quartile), with only basic education, and with criminal record (given in percentage). All variables obtained from Statistics Denmark were time-dependent (i.e. subject to change over time), updated annually, and available for all study years.

Lifestyle information was retrieved from the baseline questionnaire used for each cohort. Since the questionnaires were different for both cohorts, the data collected was harmonized. Table S2 shows the original questions and how variables resulted after harmonization. After harmonization of questionnaire data, the following covariates were used: smoking status (never, former, current); smoking intensity among current smokers (g tobacco/day), alcohol intake (g/day), alcohol abstainers (yes, no), fruit and vegetable intake (no intake/very low, low, medium, high), and physical activity (none/low, medium, high).

Statistical analysis

We followed the DCH cohort from January 1, 2000, enabling at least 10-years of exposure history for all participants. For the DNHS cohort, follow-up started from collection of questionnaire data (January 2010 or January 2013) or 55 years of age, whichever came later. Follow-up ended at COPD diagnosis, missing address, emigration, death, or 31 December 2017, whichever came first (Figure S1). We used Cox proportional hazards models with age as underlying time to assess the association between 10-year time-weighted averaged exposure to air pollution and risk of incident COPD. The time-weighted 10-years running means were entered as time-varying variables into the Cox model. Risk estimates were calculated per interquartile range (IQR) increase in total, traffic, and non-traffic contributions of each air pollutant ($PM_{2.5}$, NO_2, UFP, and EC) to allow for direct comparison of risk

estimates across pollutants. The calculation of IQRs were based on the 10-year running averages estimated for each cohort participant over the entire study period, i.e. from beginning of follow-up until censoring.

We calculated hazard ratios (HR) between COPD and air pollution using four models with increasing level of adjustment: Model 1, adjusted for sex (male, female), age (years), calendar year (categorical variable with two-year intervals) and cohort (strata); Model 2, further adjusted for socio-demographic information (cohabiting status, education, income, occupation and area-level covariates); Model 3, further adjusted for smoking information (smoking status and smoking intensity); Model 4, further adjusted for lifestyle (alcohol intake, alcohol abstinence, fruit intake, vegetable intake, and physical activity). All socio-demographic variables, except for sex, were included as time-varying variables, being updated every year. In contrast, smoking and lifestyle information, collected only at baseline, remained constant in our models throughout follow-up. Model 4 was selected *a priori* as our primary model as it includes the most comprehensive adjustment for potential confounders, reducing the risk of residual confounding and strengthening causal interpretation. This model was used in the subsequent described analyses.

We evaluated the shape of the associations between each air pollutant (total, traffic, and non-traffic contributions) and COPD, by fitting natural cubic splines with three degrees of freedom. We disregarded the upper and lower 5% of the exposure range, since CIs for extreme exposures were too wide to provide reliable insights. In addition to reporting results per IQR increase, we also assessed associations per fixed increment, where exposure variables were scaled by predefined fixed units to facilitate comparison with previous studies. The specific increments used were 5 and 10 $\mu g/m^3$ for $PM^{2.5}$, 10 $\mu g/m^3$ for NO^2, 10,000 particles/cm^3 for UFP, and 1 $\mu g/m^3$ for EC. We also performed a sensitivity analysis in which COPD cases were identified exclusively based on a specific COPD diagnosis (ICD-10 code J44).

We also assessed the associations between COPD and $PM_{2.5}$, NO_2, UFP, and EC using two-pollutant models, testing combinations of pollutants within the same source category (i.e. total, traffic, and non-traffic).We performed effect modification analyses to investigate whether the association between $PM_{2.5}$, NO_2, UFP, and EC (total, traffic, and non-traffic contributions) and COPD differed according to sex, smoking status (never smoker, previous smoker, and current smoker) or a previous diagnosis for asthma. This analysis was done by the including an interaction term between each exposure variable and these three covariates. We identified asthma diagnoses in the National Patient Register,[30] using the codes 493 (ICD-8) or J45 (ICD-10). We followed up for diagnosis of asthma throughout the entire study period, with individuals classified as cases from their first recorded diagnosis onward. Persons with an asthma diagnosis before baseline were considered cases from the start of follow-up.

Analyses were performed in SAS (version 9.4, SAS Institute Inc.), apart from natural splines and correlation matrix, which were built in R (version 4.3.2).

3. Results

Out of the 57,053 DCH participants and 339,922 DNHS respondents, the pooled study population comprised 159,769 individuals, of whom 8,456 developed COPD during follow-up. The inclusion and exclusion criteria for the DCH and DNHS cohorts are detailed in Figure 1, which illustrates the selection of the final study population.

Pearson's correlation coefficients between $PM_{2.5}$, NO_2, UFP, and EC (total, traffic and non-traffic contributions) ranged from 0.28 to 0.99 (Figure 2). We found strong correlations between the air pollutants (total concentrations) and their source-specific contributions. The traffic contributions were also strongly correlated with each other.

Table 1 presents the baseline sociodemographic characteristics and air pollution exposure for the pooled study population and for each cohort separately. Compared to the DCH cohort, DNHS respondents were generally older, had lower income, smoked less, drank less, exercised more, and consumed more fruits. Air pollution levels, especially from traffic, were lower in DNHS. Across all pollutants, non-traffic-related levels were generally higher than traffic-related levels, with the most pronounced differences observed for $PM_{2.5}$ (Table 1 and Figure S2).

Results from the fully adjusted model (Model 4) showed that all air pollutants (total contribution) were associated with a higher risk of COPD, with HRs per interquartile range (IQR) of: 1.11 (95% CI: 1.05, 1.17) per 2.33 $\mu g/m^3$ of $PM_{2.5}$; 1.08 (1.04, 1.13) per 9.25 $\mu g/m^3$ of NO_2; 1.05 (0.99, 1.11) per 5,737 particles/m^3 of UFP; and 1.02 (1.00, 1.05) per 0.34 $\mu g/m^3$ of EC (Table 2). HRs remained virtually unchanged when COPD cases were defined exclusively by the specific ICD-10 code J44 (Table S3). When comparing HRs across the adjustment models, we found that adjustment for sociodemographic covariates generally resulted in modest changes in HRs, but with no clear pattern regarding the direction of the change. In contrast, further adjustment for smoking status and intensity lowered HRs, while further adjustment for lifestyle information had little impact on the HRs. HRs per fixed increment are shown in Table S4.

In multi-pollutant models (Tables S5–S7), $PM_{2.5}$ and NO_2 emerged as the strongest contributors to increased COPD risk. NO_2 was the predominant pollutant in traffic-related contributions (Table S6), while $PM_{2.5}$ played the main role in non-traffic-related exposure (Table S7). However, it is important to note that these pollutants are highly correlated, which makes interpretation difficult and furthermore may affect the stability of the models. The associations approached linearity for total $PM_{2.5}$ and NO_2, showing higher HRs with increased exposure levels and a slight levelling-off observed for higher exposures (Figure 3A and Figure 3D). Although associations were weaker, both total UFP and EC followed a near-linear trend (Figure 3G and Figure 3J).

We found that both traffic and non-traffic $PM_{2.5}$ were associated with a higher risk of COPD, but HRs for non-traffic $PM_{2.5}$ were substantially higher than HRs for traffic $PM_{2.5}$ (Table 2). The associations with non-traffic $PM_{2.5}$ followed an inverted U-shape, showing a reduction in risk at higher exposure levels, while the associations with traffic $PM_{2.5}$ remained largely leveled off across most of the exposure range (Figure 3B-C). For NO_2, we observed that both traffic and non-traffic contributions were associated with higher COPD risk, with similar size HRs per IQR (Table 2) but considerably different HRs per fixed increase (Table S4). Findings for NO_2 revealed monotonic exposure-response relationships, although for non-traffic NO_2, there were indications of a levelling off at higher exposure

levels (Figure 3E-F). For UFP and EC, we observed that the traffic contributions were associated with a higher risk of COPD following a monotonic exposure-response relationship, though for EC the associations levelled off at higher concentrations (Figure 3H and 3K). In contrast, no associations were observed for non-traffic UFP and EC contributions (Table 2).

Effect modification analyses showed stronger associations between air pollution (all four pollutants) and COPD among females (Figure 4) and among never and current smokers, whereas among former smokers either no association or risk estimates below 1 were observed (Figure 4, total contributions; similar results were observed for the traffic and non-traffic contributions Figure S3). Furthermore, we observed higher HRs between air pollution and COPD among individuals with a previous asthma diagnosis compared to those without an asthma diagnosis (Figure 4 and Figure S4). Precise HRs and test for interactions are shown in Tables S8-S10.

4. Discussion

In this pooled cohort study, long-term exposure to air pollution was associated with a higher risk of COPD. The highest risk estimates per IQR were observed for $PM_{2.5}$, followed by NO_2, UFP, and EC. For UFP and EC, the higher COPD risk was primarily attributed to air pollution from local traffic, while for $PM_{2.5}$, the contributions from other sources yielded the highest risk estimates per IQR change. Adjusting for smoking status and intensity lowered HRs, highlighting the importance of considering smoking when investigating the effects of air pollution on COPD. We found stronger associations for people with a previous asthma diagnosis and among former smokers no association was observed.

A 2021 meta-analysis on air pollution and incident COPD reported a pooled RR of 1.18 (95% CI: 1.13, 1.23) per 10 $\mu g/m^3$ increase in $PM_{2.5}$ based on six cohort studies.[9] We observed a considerably higher risk estimate, with a HR of 1.58 (95% CI: 1.25, 2.00) per 10 $\mu g/m^3$ $PM_{2.5}$ increase. The stronger associations observed in our study may be attributed to the high temporal and spatial resolution of our exposure assessment methodology, which likely results in more precise modelled exposure levels. Our cohort also comprises an older population compared to other studies,[11,21,53,54] and several studies have demonstrated that PM exposure has a greater effect on increasing hospital admissions for respiratory diseases in the elderly compared to younger individuals.[8,55,56] Moreover, Denmark is characterized by having low-level air pollution, as well as other Scandinavian countries. A meta-analysis of $PM_{2.5}$ and mortality have indicated a supralinear relationship, with a steeper risk increase at lower exposure levels,[57] and one could speculate that a similar shape exposure-response relationship exists for $PM_{2.5}$ and COPD, which would explain the higher risk estimates in our study. Interestingly, a study pooling data from three Scandinavian cohorts (ELAPSE study), including the DCH cohort, found a HR of 1.17 (95% CI: 1.06, 1.29) per 5 $\mu g/m^3$ increase in $PM_{2.5}$, thus more comparable to the HR of 1.26 per 5 $\mu g/m^3$ observed in the present study.[12]

PM consists of a complex mixture of particles with different physical and chemical properties, and therefore its composition and toxicity can be largely dependent on the emission source.[22,23] We found a stronger association with COPD for $PM_{2.5}$ originated from non-traffic and regional sources compared to local traffic sources, suggesting a need to prioritize mitigation strategies targeting non-

traffic emissions., e.g. residential wood burning and industrial activities Additionally, although results from two-pollutant models should be interpreted with caution, we found $PM_{2.5}$ to be the predominant pollutant in non-traffic contributions. $PM_{2.5}$ non-traffic constitutes the major fraction of total $PM_{2.5}$ emissions in Denmark. Since this study includes participants living across Denmark including rural areas, long-range transported air pollution, which primarily originates from non-traffic sources, plays a dominant role in overall exposure (Figure S2), with nearly all study participants exposed to concentrations exceeding 5 μg/m³—the WHO air quality guideline for $PM_{2.5}$. The primary contributors for non-traffic emissions include non-industrial combustion plants, such as biomass burning for residential heating, as well as other mobile and machinery sources, including shipping.[58,59] In agreement, Penning et al. reported that $PM_{2.5}$ from biomass burning was associated with increased emergency department visits for respiratory conditions, including COPD, while no positive associations were observed for traffic-related sources (i.e., gasoline and diesel-fueled vehicles).[60] A British study also found no association between $PM_{2.5}$ originating from traffic and incident COPD.[13] However, other studies have reported opposite results, indicating associations between traffic-related emissions and hospitalizations for COPD.[61,62] Additionally, several studies have linked short-term exposure to traffic-related PM with worsening symptoms and lung function decline in COPD patients,[4,63,64] still highlighting potential adverse effects of traffic PM on the respiratory system.

Based on five cohort studies, the 2021 meta-analysis found a RR of 1.07 (1.00, 1.16) per 10 μg/m³ increase in NO_2 [9] which is in line with the results obtained in the ELAPSE study (HR: 1.11; CI: 1.06, 1.16 per 10 μg/m^3 NO_2), as well as the results of the present study (HR: 1.09 per 10 μg/m³ NO_2).[12] Attributing effects to specific air pollutants is challenging due to their high correlations with one another. NO_2 is often considered a proxy for traffic-related air pollution, e.g. UFP, and it is unclear whether NO_2 in itself affects the risk of COPD, though potential mechanisms underlying NO_2 exposure include inflammatory responses, with increased mucus production and development of airspace enlargement, which could contribute to the progressive loss of lung function.[65] Unlike PM, the composition of NO_2 is not dependent on the emission source, so similar risk estimates would be expected for all emission sources. We observed, however, different HRs per fixed unit of traffic and non-traffic NO_2 (i.e. 1.08 (CI: 1.04, 1.13) and 1.29 (CI: 1.10, 1.52), respectively), thus suggesting NO_2 may also be a proxy for other urban pollutants.

Due to their small size, UFPs can penetrate deep into the lungs and be retained over longer period, and may therefore pose greater risks to human health than larger particles.[16,18] However, only one Canadian cohort study has investigated the impact of long-term UFP exposure on COPD incidence.[21] This study found an association between UFP exposure and COPD; however, the association did not remain after adjusting for NO_2. Similarly, a Dutch birth cohort study found UFP exposure to be associated with reduced lung function measurements, such as forced expiratory volume in the first second (FEV1) and forced vital capacity (FVC); however, these associations did not persist after adjusting for NO_2 or $PM_{2.5}$.[66] We found an association between local traffic-related UFP and COPD, whereas no associations were observed for non-traffic UFP. Since traffic UFP and traffic NO_2 are strongly correlated ($R_{Pearson}$ of 0.96), a model including both pollutants would likely be very unstable. It is thus not possible in the present study to separate effects of local traffic UFP and NO_2, making it

unclear whether UFP, NO_2 or both are harmful in relation to COPD development. More sophisticated UFP exposure models need to be developed to enable separation of the effect of the two exposures in cohort studies.

Carbonaceous particles are among the most toxic components of PM, potentially contributing to COPD through mechanisms such as oxidative stress and inflammation.[67] However, in our study, we found only weak associations between EC and COPD, and notably, no statistically significant associations with non-traffic-related EC, which contrasts with the results observed for $PM_{2.5}$. Research on long-term exposure to EC or black carbon (BC) and development of COPD is limited and yields contradictory results. For instance, the ELAPSE study reported consistent associations between BC and COPD that remained significant even after adjusting for $PM_{2.5}$,[12] whereas another study indicated no association.[14]

Our findings revealed stronger associations between air pollutants and COPD among females, aligning with previous studies.[53,68] A possible explanation for higher HRs among women is that they may spend more time at home, making residential air pollution exposure estimates more accurate for this group. Additionally, biological differences between males and females, such as higher airway reactivity in women,[68] have been suggested as potential explanation.

Consistent with previous studies,[68–70] we found higher risk estimates among never smokers compared to former and current smokers for all air pollutants, although the difference in HRs between never and current smokers in our study was small. Since smoking is a major factor in lung damage, any additional impact of air pollution on pulmonary function in smokers may be less pronounced or more difficult to detect.[54,68] Nevertheless, we still observed positive associations among current smokers, aligning with a previous study that suggest air pollution exacerbates smoking-induced lung function decline in COPD patients.[71] No associations were found among former smokers, and the reason remains unclear. It could be speculated that this group includes individuals who chose to quit smoking, indicating a greater concern for their health. This group may, therefore, be more likely to adopt lifestyle changes that offer some protection against the effects of air pollution on the respiratory system.

For all four exposures (including total, traffic, and non-traffic contributions), we observed much stronger associations with COPD risk among individuals with a prior asthma diagnosis. This is likely due to the increased susceptibility among those with chronic respiratory conditions, such as asthma, to the harmful effects of air pollution.[72,73] In contrast to our findings, Doiron et al. found stronger associations in non-asthmatic patients.[68] However, this is a cross-sectional study, making it difficult to establish the temporal relationship between asthma and COPD diagnoses, and to confirm whether asthma preceded the development of COPD. Another study observed no effect modification by asthma status (assessed at baseline).[12]

A key strength of our study was the use of two large Danish cohorts with comprehensive lifestyle data, including smoking, the primary risk factor for COPD. Some studies on air pollution and COPD did not adjust for smoking,[20,21] which increases the risk for residual confounding, as indicated in our study, where we found that adjustment for smoking attenuated the HRs, even after individual-level

adjustment for key SES variables, like education and income. Moreover, the prospective design and access to high-quality national registers allowed for collection of detailed SES information and identification of COPD cases with demonstrated high positive predictive value (92%).[74]

Another strength of this study was the use of advanced and robust modeling techniques with high temporal and spatial resolution to assess time-varying exposure for all participants, taking into account their complete address history. This approach included estimates of UFP and EC, which have been less studied in relation to COPD. Nonetheless, uncertainties remain due to limitations in the Danish emission inventories, particularly for UFP in earlier years. Despite this, UFP modeling showed robust performance, with correlation coefficients of 0.86–0.87 compared to measurement station data.

To our knowledge, this is also the first study to specifically assess source-specific air pollution in relation to COPD development. Additionally, while the DCH cohort is predominantly living in urban areas, the DNHS cohort covers the entire country. Thus, the pooled study population provides a better representation of the air pollution levels in Denmark. Modelling residential exposures, however, may lead to exposure misclassification, as it does not capture exposures occurring away from the home address. Furthermore, we found very high correlations between some air pollutants and their source-specific contributions, highlighting that results from epidemiological models should be interpreted with caution, as the assessed pollutant may serve as a proxy for other correlated risk factors.

A limitation of our study is that COPD cases were identified through hospital-based records (i.e. inpatient and outpatient contacts). As a result, diagnoses made in primary care and frequent consultations with general practitioners, as well as medication prescriptions, were not captured. This approach may therefore primarily identify patients with more severe COPD and frequent exacerbations. The same limitation applies to asthma diagnosis used for the effect modification analysis. Additionally, we did not have access to spirometry or lung function data to confirm the COPD diagnoses or to examine lung function decline in relation to air pollution. However, Danish hospitals usually perform spirometry before discharging COPD patients.[75] This practice, along with the fact that diagnoses in the Danish Patient Register are often entered by a physician, helps to minimize the risk of outcome misclassification.[76] Recognizing the potential under-recording of COPD diagnoses in the Danish Patient Register,[74] we expanded our COPD definition to include other relevant codes, such as J42 (unspecified chronic bronchitis) and J43 (emphysema), as done in other studies.[77] Furthermore, the outcome misclassification is unlikely to be related to exposure status (i.e. non-differential), which would possibly bias the estimates towards the null.

Although our models were adjusted for a range of lifestyle and SES factors, the possibility of residual confounding cannot be entirely ruled out. For example, smoking information was only collected at baseline, and thus we lacked data on smoking status at the time of diagnosis and during follow-up. We also did not have data for passive smoking, smoking duration and time since smoking cessation for the entire cohort. Other relevant covariates, such as job-related exposures, were also not available, Lastly, since our study was conducted in Denmark, further research in different geographical settings - with varying air pollution sources, exposure degree, and genetic backgrounds - is strongly recommended.

In conclusion, this study reinforces the evidence that long-term exposure to PM and NO_2 is associated with a higher risk of COPD. Our investigation of contributions from different sources suggests that, for $PM_{2.5}$, the contribution from other sources than local traffic is most strongly associated with COPD, whereas for UFP, it is local traffic-related contributions that appear to be the most harmful. However, these results should be validated in future studies across different geographical and population settings including a broader range of air pollutants.

Acknowledgements

This work was funded by the European Union through the H2020 project REMEDIA (Impact of Exposome on the Course of Lung Diseases), grant no. 874753.

References

1. Boers, E. *et al.* Global Burden of Chronic Obstructive Pulmonary Disease Through 2050. *JAMA Netw Open* **6**, E2346598 (2023).
2. Kelly, F. J. & Fussell, J. C. Air pollution and airway disease. *Clinical and Experimental Allergy* **41**, 1059–1071 (2011).
3. Thurston, G. D. *et al.* Outdoor air pollution and new-onset airway disease: An official american thoracic society workshop report. *Ann Am Thorac Soc* **17**, 387–398 (2020).
4. Sin, D. D. *et al.* Air pollution and COPD: GOLD 2023 committee report. *European Respiratory Journal* **61**, 1–13 (2023).
5. Li, J. *et al.* Major air pollutants and risk of COPD exacerbations: A systematic review and meta-analysis. *International Journal of COPD* **11**, 3079–3091 (2016).
6. Sario, M. De, Katsouyanni, K. & Michelozzi, P. Climate change, extreme weather events, air pollution and respiratory health in Europe. *European Respiratory Journal* vol. 42 826–843 Preprint at https://doi.org/10.1183/09031936.00074712 (2013).
7. Li, M. H. *et al.* Short-term exposure to ambient fine particulate matter increases hospitalizations and mortality in COPD: A systematic review and meta-analysis. *Chest* **149**, 447–458 (2016).
8. Delavar, M. A. *et al.* Relationship between fine particulate matter (PM2.5) concentration and risk of hospitalization due to chronic obstructive pulmonary disease: a systematic review and meta-analysis. *BMC Public Health* **23**, 1–9 (2023).
9. Park, J., Kim, H. J., Lee, C. H., Lee, C. H. & Lee, H. W. Impact of long-term exposure to ambient air pollution on the incidence of chronic obstructive pulmonary disease: A systematic review and meta-analysis. *Environ Res* **194**, 1–8 (2021).
10. Shin, S. *et al.* Air pollution as a risk factor for incident chronic obstructive pulmonary disease and Asthma: A 15-year population-based cohort study. *Am J Respir Crit Care Med* **203**, 1138–1148 (2021).
11. Liu, S. *et al.* Long-term air pollution and road traffic noise exposure and COPD: The Danish Nurse Cohort. *European Respiratory Journal* **58**, (2021).
12. Liu, S. *et al.* Long-term exposure to low-level air pollution and incidence of chronic obstructive pulmonary disease: The ELAPSE project. *Environ Int* **146**, 1–8 (2021).
13. Carey, I. M. *et al.* Traffic pollution and the incidence of cardiorespiratory outcomes in an adult cohort in London. *Occup Environ Med* **73**, 849–856 (2016).

14. Xu, S. *et al.* Associations of long-term exposure to air pollution and greenness with incidence of chronic obstructive pulmonary disease in Northern Europe: The Life-GAP project. *Environ Res* **257**, 1–10 (2024).
15. Salimi, F. *et al.* Long-term exposure to low concentrations of air pollutants and hospitalisation for respiratory diseases: A prospective cohort study in Australia. *Environ Int* **121**, 415–420 (2018).
16. HEI. *Understanding the Health Effects of Ambient Ultrafine Particles - HEI Review Panel on Ultrafine Particles*. www.healtheffects.org (2013).
17. Pryor, J. T., Cowley, L. O. & Simonds, S. E. The Physiological Effects of Air Pollution: Particulate Matter, Physiology and Disease. *Front Public Health* **10**, 1–13 (2022).
18. Schraufnagel, D. E. The health effects of ultrafine particles. *Experimental and Molecular Medicine* vol. 52 311–317 Preprint at https://doi.org/10.1038/s12276-020-0403-3 (2020).
19. Janssen, N. A. H. *et al.* Black carbon as an additional indicator of the adverse health effects of airborne particles compared with pm10 and pm2.5. *Environ Health Perspect* **119**, 1691–1699 (2011).
20. Gan, W. Q., FitzGerald, J. M., Carlsten, C., Sadatsafavi, M. & Brauer, M. Associations of ambient air pollution with chronic obstructive pulmonary disease hospitalization and mortality. *Am J Respir Crit Care Med* **187**, 721–727 (2013).
21. Weichenthal, S. *et al.* Long-term exposure to ambient ultrafine particles and respiratory disease incidence in in Toronto, Canada: A cohort study. *Environ Health* **16**, 1–11 (2017).
22. Hime, N. J., Marks, G. B. & Cowie, C. T. A comparison of the health effects of ambient particulate matter air pollution from five emission sources. *Int J Environ Res Public Health* **15**, 1–24 (2018).
23. Zhang, X. *et al.* Ecological Study on Global Health Effects due to Source-Specific Ambient Fine Particulate Matter Exposure. *Environ Sci Technol* **57**, 1278–1291 (2023).
24. Naeher LP *et al.* Woodsmoke health effects: a review. *Inhal Toxicol* **19**, 67–106 (2007).

25. Zelikoff, J. T., Chen, L. C., Cohen, M. D. & Schlesinger, R. B. The Toxicology of Inhaled Woodsmoke. *J Toxicol Environ Health* **5**, 269–282 (2002).
26. Hendryx, M., Luo, J., Chojenta, C. & Byles, J. E. Air pollution exposures from multiple point sources and risk of incident chronic obstructive pulmonary disease (COPD) and asthma. *Environ Res* **179**, 1–6 (2019).
27. Tjønneland, A. *et al.* Study design, exposure variables, and socioeconomic determinants of participation in Diet, Cancer and Health: A population-based prospective cohort study of 57,053 men and women in Denmark. *Scand J Public Health* **35**, 432–441 (2007).
28. Christensen, A. I. *et al.* The Danish National Health Survey: Study design, response rate and respondent characteristics in 2010, 2013 and 2017. *Scand J Public Health* **50**, 180–188 (2022).
29. Schmidt, M., Pedersen, L. & Sørensen, H. T. The Danish Civil Registration System as a tool in epidemiology. *European Journal of Epidemiology* vol. 29 541–549 Preprint at https://doi.org/10.1007/s10654-014-9930-3 (2014).
30. Lynge, E., Sandegaard, J. L. & Rebolj, M. The Danish national patient register. *Scand J Public Health* **39**, 30–33 (2011).
31. Jensen, S. S. *et al.* High resolution multi-scale air quality modelling for all streets in Denmark. *Transportation Research Part D* **52**, 322–339 (2017).
32. Khan, J. *et al.* Development and performance evaluation of new AirGIS – A GIS based air pollution and human exposure modelling system. *Atmos Environ* **198**, 102–121 (2019).
33. Brandt, J. *et al.* Operational air pollution forecasts from European to local scale. *Atmos Environ* **1**, S91–S98 (2001).
34. Brandt, J. *et al.* An integrated model study for Europe and North America using the Danish Eulerian Hemispheric Model with focus on intercontinental transport of air pollution. *Atmos Environ* **53**, 156–176 (2012).
35. Skamarock, W. C. *et al. A Description of the Advanced Research WRF Version 3 - NCAR Technical Note*. (2008).
36. Brandt, J., Christensen, J. H., Frohn, L. M. & Berkowicz, R. Air pollution forecasting from regional to urban street scale- implementation and validation for two cities in Denmark. *Physics and Chemistry of the Earth* **28**, 335–344 (2003).

37. Frohn, L. M. *et al.* Evaluation of multidecadal high-resolution atmospheric chemistry-transport modelling for exposure assessments in the continental Nordic countries. *Atmos Environ* **290**, 1–20 (2022).
38. Hvidtfeldt, U. A. *et al.* Evaluation of the Danish AirGIS air pollution modeling system against measured concentrations of PM2.5, PM10, and black carbon. *Environmental Epidemiology* **2**, 1–11 (2018).
39. Ketzel, M., Berkowicz, R., Hvidberg, M., Jensen, S. S. & Raaschou-Nielsen, O. Evaluation of AirGIS: A GIS-based air pollution and human exposure modelling system. *Int J Environ Pollut* **47**, 226–238 (2011).
40. Frohn, L. M. *et al.* Modelling ultrafine particle number concentrations at address resolution in Denmark from 1979-2018 – Part 1: Regional and urban scale modelling and evaluation. *Atmos Environ* **264**, 1–17 (2021).
41. Ketzel, M. *et al.* Modelling ultrafine particle number concentrations at address resolution in Denmark from 1979 to 2018 - Part 2: Local and street scale modelling and evaluation. *Atmos Environ* **264**, 1–16 (2021).
42. Vignati, E., Wilson, J. & Stier, P. M7: An efficient size-resolved aerosol microphysics module for large-scale aerosol transport models. *Journal of Geophysical Research D: Atmospheres* **109**, 1–17 (2004).
43. Plejdrup, M. S., Nielsen, O.-K., Gyldenkærne, S. & Bruun, H. G. Spatial high-resolution distribution of emissions to air - Spread 2.0. Preprint at (2018).
44. Ole Raaschou-Nielsen *et al. Cardiometabolic Health Effects of Air Pollution, Noise, Green, and Socioeconomic: The HERMES Study*. (2024).
45. Grigsby, M. *et al.* Socioeconomic status and COPD among low-and middle-income countries. *International Journal of COPD* **11**, 2497–2507 (2016).
46. Scoditti, E., Massaro, M., Garbarino, S. & Toraldo, D. M. Role of diet in chronic obstructive pulmonary disease prevention and treatment. *Nutrients* vol. 11 1–32 Preprint at https://doi.org/10.3390/nu11061357 (2019).
47. Marín-Hinojosa, C. *et al.* Nutriepigenomics and chronic obstructive pulmonary disease: Potential role of dietary and epigenetics factors in disease development and management. *American Journal of Clinical Nutrition* vol. 114 1894–1906 Preprint at https://doi.org/10.1093/ajcn/nqab267 (2021).

48. Bartal, M. COPD and tobacco smoke. *Monaldi Archives for Chest Disease* **63**, 213–225 (2005).
49. Hansen, G. M. *et al.* Midlife cardiorespiratory fitness and the long-term risk of chronic obstructive pulmonary disease. *Thorax* **74**, 843–848 (2019).
50. Hajat, A., Hsia, C. & O'Neill, M. S. Socioeconomic Disparities and Air Pollution Exposure: A Global Review. *Current environmental health reports* vol. 2 440–450 Preprint at https://doi.org/10.1007/s40572-015-0069-5 (2015).
51. Tainio, M. *et al.* Air pollution, physical activity and health: A mapping review of the evidence. *Environ Int* **147**, 1–15 (2021).
52. Springmann, M. *et al.* The global and regional air quality impacts of dietary change. *Nat Commun* **14**, 1–8 (2023).
53. Schikowski, T. *et al.* Association of ambient air pollution with the prevalence and incidence of COPD. *European Respiratory Journal* **44**, 614–626 (2014).
54. Guo, C. *et al.* 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. *Lancet Planetary Health* **2**, 114–139 (2018).
55. Belleudi, V. *et al.* Impact of fine and ultrafine particles on emergency hospital admissions for cardiac and respiratory diseases. *Epidemiology* **21**, 414–423 (2010).
56. Renzi, M. *et al.* A nationwide study of air pollution from particulate matter and daily hospitalizations for respiratory diseases in Italy. *Science of the Total Environment* **807**, 1–9 (2022).
57. Chen, J. & Hoek, G. Long-term exposure to PM and all-cause and cause-specific mortality: A systematic review and meta-analysis. *Environ Int* **143**, 1–23 (2020).
58. Poulsen, A. H. *et al.* Source-Specific Air Pollution Including Ultrafine Particles and Risk of Myocardial Infarction: A Nationwide Cohort Study from Denmark. *Environ Health Perspect* **131**, 1–8 (2023).
59. Plejdrup, M., Nielsen, O.-K., Gyldenkærne, S. & Bruun, H. G. Spatial high-resolution distribution of emissions to air - Spread 3.0. Preprint at (2021).
60. Pennington, A. F. *et al.* Source-Apportioned PM2.5 and cardiorespiratory emergency department visits: Accounting for source contribution uncertainty. *Epidemiology* **30**, 789–798 (2019).

61. Chi, R. *et al.* Association of emergency room visits for respiratory diseases with sources of ambient PM2.5. *J Environ Sci (China)* **86**, 154–163 (2019).
62. Hopke, P. K. *et al.* Changes in the hospitalization and ED visit rates for respiratory diseases associated with source-specific PM2.5 in New York State from 2005 to 2016. *Environ Res* **181**, (2020).
63. Peacock, J. L. *et al.* Outdoor air pollution and respiratory health in patients with COPD. *Thorax* **66**, 591–596 (2011).
64. Sinharay, R. *et al.* Respiratory and cardiovascular responses to walking down a traffic-polluted road compared with walking in a traffic-free area in participants aged 60 years and older with chronic lung or heart disease and age-matched healthy controls: a randomised, crossover study. *The Lancet* **391**, 339–349 (2018).
65. Wegmann, M. *et al.* NO2-induced airway inflammation is associated with progressive airflow limitation and development of emphysema-like lesions in C57BL/6 mice. *Experimental and Toxicologic Pathology* **56**, 341–350 (2005).
66. Yu, Z. *et al.* Ultrafine particles, particle components and lung function at age 16 years: The PIAMA birth cohort study. *Environ Int* **157**, 1–8 (2021).
67. Wang, Q. & Liu, S. The Effects and Pathogenesis of PM2.5 and Its Components on Chronic Obstructive Pulmonary Disease. *International Journal of COPD* **18**, 493–506 (2023).
68. Doiron, D. *et al.* Air pollution, lung function and COPD: Results from the population-based UK Biobank study. *European Respiratory Journal* **54**, (2019).
69. Cai, Y. *et al.* Cross-sectional associations between air pollution and chronic bronchitis-an ESCAPE meta-analysis across five cohorts. *Thorax* **69**, 1005–1014 (2014).
70. Fisher, J. A. *et al.* Particulate matter exposures and adult-onset asthma and COPD in the Nurses' Health Study. *EuropeanRespiratoryJournal* **48**, 921–924 (2016).
71. Zhao, J. *et al.* Role of PM2.5 in the development and progression of COPD and its mechanisms. *Respir Res* **20**, 1–13 (2019).
72. Chen, T. *et al.* Acute respiratory response to individual particle exposure (PM1.0, PM2.5 and PM10) in the elderly with and without chronic respiratory diseases. *Environmental Pollution* **271**, 1–11 (2021).

73. Zanobetti, A., Schwartz, J. & Gold, D. Are There Sensitive Subgroups for the Effects of Airborne Particles? *Environ Health Perspect* **108**, 841–845 (2000).
74. Thomsen, R. W. *et al.* Validity and underrecording of diagnosis of COPD in the Danish National Patient Registry. *Respir Med* **105**, 1063–1068 (2011).
75. Ingebrigtsen, T. *et al.* Genetic influences on chronic obstructive pulmonary disease - A twin study. *Respir Med* **104**, 1890–1895 (2010).
76. Andersen, Z. J. *et al.* Chronic obstructive pulmonary disease and long-term exposure to traffic-related air pollution: A cohort study. *Am J Respir Crit Care Med* **183**, 455–461 (2011).
77. Gothe, H. *et al.* Algorithms to identify COPD in health systems with and without access to ICD coding: A systematic review. *BMC Health Serv Res* **19**, 1–4 (2019).

Table 1. Baseline sociodemographic characteristics and 10-year exposure levels among the study population (N = 159,769).

Baseline characteristics	**Entire study population (N = 159,769)**	**DCH cohort (N = 50,957)** [a]	**DNHS cohort (N = 108,812)**
Sex, women [%]	52.3	52.9	52.1
Age [mean ± SD]	63.5 ± 7.8	60.4 ± 4.4	64.9 ± 8.6
Cohabiting status, yes [%]	77.8	76.1	78.6
Individual income [%]			
Low (Q1)	24.2	18.9	26.7
Medium (Q2-Q4)	53.5	50.1	55.2
High (Q5)	22.3	31.0	18.2
Occupational status [%]			
White collar	26.0	32.5	22.9
Blue collar	23.6	25.4	22.7
Unemployed or retired	50.4	42.1	54.4
Highest attained education [%]			
Mandatory education	29.3	27.3	30.2
Secondary or vocational education	48.3	49.3	47.8
Medium or long education	22.4	23.4	22.0
Area-level factors [mean ± SD]			
% population with low income (1st quartile)	4.7 ± 2.2	4.7 ± 2.6	4.4 ± 2.0
% population with only basic education	9.1 ± 2.9	9.7 ± 3.1	8.9 ± 2.8
% population with criminal record	0.5 ± 0.3	0.6 ± 0.3	0.4 ± 0.3
Smoking status [%]			
Never	39.9	36.9	41.3
Former	35.7	28.0	39.3
Current	24.4	35.1	19.4
Smoking intensity, g/day [mean ± SD] [b]	15.7 ± 10.2	17.3 ± 10.3	14.3 ± 9.9
Alcohol intake, g/day [mean ± SD]	15.8 ± 19.9	20.2 ± 21.3	13.7 ± 18.8
Alcohol abstainers, yes [%]	7.8	2.1	10.5
Fruit intake [%]			
No or very low	15.2	18.7	13.5
Low	22.2	30.6	18.2
Medium	57.1	48.5	61.2
High	5.5	2.2	7.1
Vegetables intake [%]			
No or very low	19.1	12.7	22.1
Low	42.7	26.6	50.2
Medium	27.8	39.3	22.5
High	10.4	21.4	5.2
Physical activity [%]			
None or low	26.0	51.0	14.3
Medium	51.4	19.9	66.2
High	22.6	29.1	19.5
Air pollution levels (10-y mean) [mean ± SD] [c]			
Total $PM_{2.5}$ ($\mu g/m^3$)	11.6 ± 2.3	14.5 ± 1.4	10.3 ± 1.0
Traffic $PM_{2.5}$ ($\mu g/m^3$) [d]	0.6 ± 0.9	1.2 ± 1.3	0.3 ± 0.4
Non-traffic $PM_{2.5}$ ($\mu g/m^3$) [e]	11.0 ± 1.7	13.2 ± 0.2	10.0 ± 0.9
Total NO_2 ($\mu g/m^3$)	18.6 ± 7.7	26.3 ± 6.6	14.9 ± 5.1

Traffic NO_2 ($\mu g/m^3$) [c]	6.8 ± 5.9	11.7 ± 6.3	4.5 ± 4.0
Non-traffic NO_2 ($\mu g/m^3$) [d]	11.8 ± 2.5	14.6 ± 1.0	10.5 ± 1.9
Total UFP (particles/cm^3)	13,516 ± 4,753	19,097 ± 2,881	10,902 ± 2,806
Traffic UFP (particles/cm^3) [c]	2,448 ± 2,245	4,815 ± 2,089	1,340 ± 1,228
Non-traffic UFP (particles/cm^3) [d]	11,068 ± 2,888	14,283 ± 1,580	9,562 ± 1,993
Total EC ($\mu g/m^3$)	0.8 ± 0.4	1.2 ± 0.5	0.6 ± 0.2
Traffic EC ($\mu g/m^3$) [c]	0.3 ± 0.4	0.5 ± 0.5	0.1 ± 0.1
Non-traffic EC ($\mu g/m^3$) [d]	0.6 ± 0.2	0.7 ± 0.1	0.5 ± 0.2

[a] Including individuals (n = 3,743) who participated in both cohorts.

[b] Among current smokers.

[c] $PM_{2.5}$, particulate matter with a diameter <2.5 μm; NO_2, nitrogen dioxide; UFP, ultrafine particles; EC, elemental carbon.

[d] Local traffic sources.

[e] Non-traffic sources and non-local traffic sources.

Table 2. Associations between 10-year mean residential exposure to air pollution (per interquartile change) and risk for COPD (8,456 cases). Cohort study pooling data from two Danish cohorts (DCH, in Copenhagen and Aarhus from 2000-2017; and DNHS, nationwide from 2010/2013 - 2017).

Air pollutant exposure (per IQR) [a]	**IQR**	**Model 1** [a, b] **HR (95% CI)**	**Model 2** [a, c] **HR (95% CI)**	**Model 3** [a, d] **HR (95% CI)**	**Model 4** [a, e] **HR (95% CI)**
$PM_{2.5}$ ($\mu g/m^3$)					
Total	2.33	1.24 (1.18, 1.30)	1.19 (1.12, 1.25)	1.12 (1.06, 1.19)	1.11 (1.05, 1.17)
Traffic [f]	1.85	1.06 (1.05, 1.07)	1.03 (1.02, 1.05)	1.02 (1.00, 1.03)	1.01 (1.00, 1.03)
Non-traffic [g]	0.48	1.14 (1.06, 1.22)	1.20 (1.11, 1.29)	1.17 (1.08, 1.26)	1.17 (1.09, 1.26)
NO_2 ($\mu g/m^3$)					
Total	9.25	1.19 (1.15, 1.23)	1.15 (1.10, 1.19)	1.09 (1.05, 1.14)	1.08 (1.04, 1.13)
Traffic [f]	6.52	1.14 (1.11, 1.17)	1.10 (1.07, 1.13)	1.06 (1.03, 1.10)	1.05 (1.02, 1.09)
Non-traffic [g]	3.02	1.05 (1.02, 1.09)	1.12 (1.06, 1.17)	1.08 (1.03, 1.14)	1.08 (1.03, 1.14)
UFP (particles/cm^3)					
Total	5737	1.12 (1.07, 1.18)	1.12 (1.06, 1.18)	1.06 (1.01, 1.12)	1.05 (0.99, 1.11)
Traffic [f]	2570	1.18 (1.15, 1.23)	1.13 (1.09, 1.18)	1.08 (1.04, 1.13)	1.07 (1.03, 1.12)
Non-traffic [g]	3308	0.96 (0.92, 1.01)	1.01 (0.96, 1.06)	0.99 (0.94, 1.04)	0.98 (0.94, 1.03)
EC ($\mu g/m^3$)					
Total	0.34	1.06 (1.05, 1.08)	1.05 (1.03, 1.07)	1.03 (1.00, 1.05)	1.02 (1.00, 1.05)
Traffic [f]	0.22	1.07 (1.05, 1.09)	1.04 (1.02, 1.06)	1.02 (1.00, 1.04)	1.02 (1.00, 1.04)
Non-traffic [g]	0.12	0.97 (0.94, 1.00)	1.00 (0.98, 1.02)	1.00 (0.98, 1.03)	1.00 (0.98, 1.03)

[a] IQR, interquartile range; CI, confidence interval; HR, hazard ratio; $PM_{2.5}$, particulate matter with a diameter <2.5 µm; NO_2, nitrogen dioxide; UFP, ultrafine particles; EC, elemental carbon.

[b] Adjusted for age (by design), sex and calendar-year.

[c] Further adjusted for cohabiting status, education, income, occupational status, and area-level socioeconomic variables (i.e. percent population with low income, with only basic education, and with a criminal record).

[d] Further adjusted for smoking (smoking status and intensity (g tobacco/day) measured at baseline).

[e] Further adjusted for physical activity, dietary habits (i.e. intake of fruit and vegetable), and alcohol consumption (intake g/day and abstainers) measured at baseline.

[f] Local traffic sources.

[g] Non-traffic sources and non-local traffic sources.

Figure captions

Figure 1.

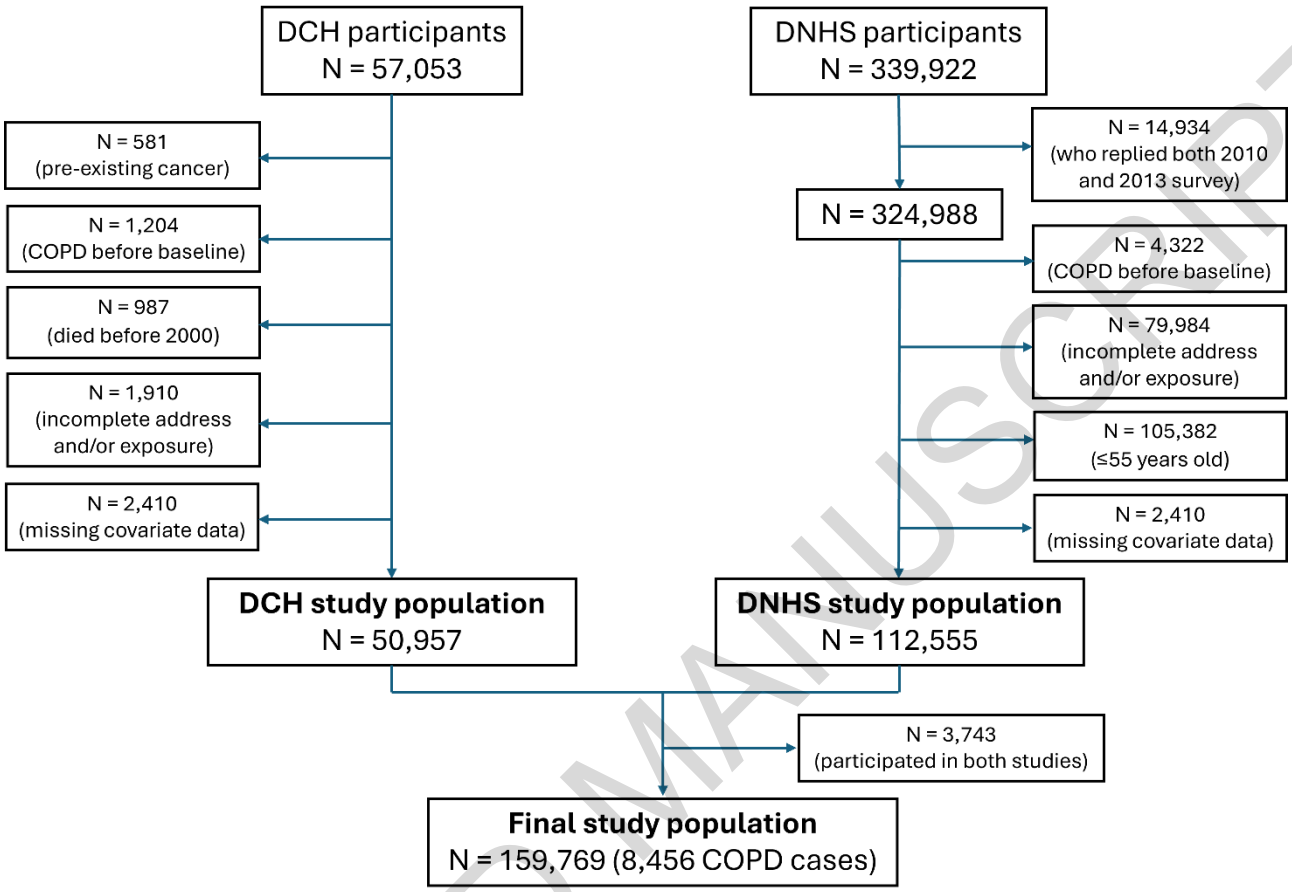

Figure 1. Flowchart illustrating participant selection in the DCH and DNHS cohorts.

Figure 2.

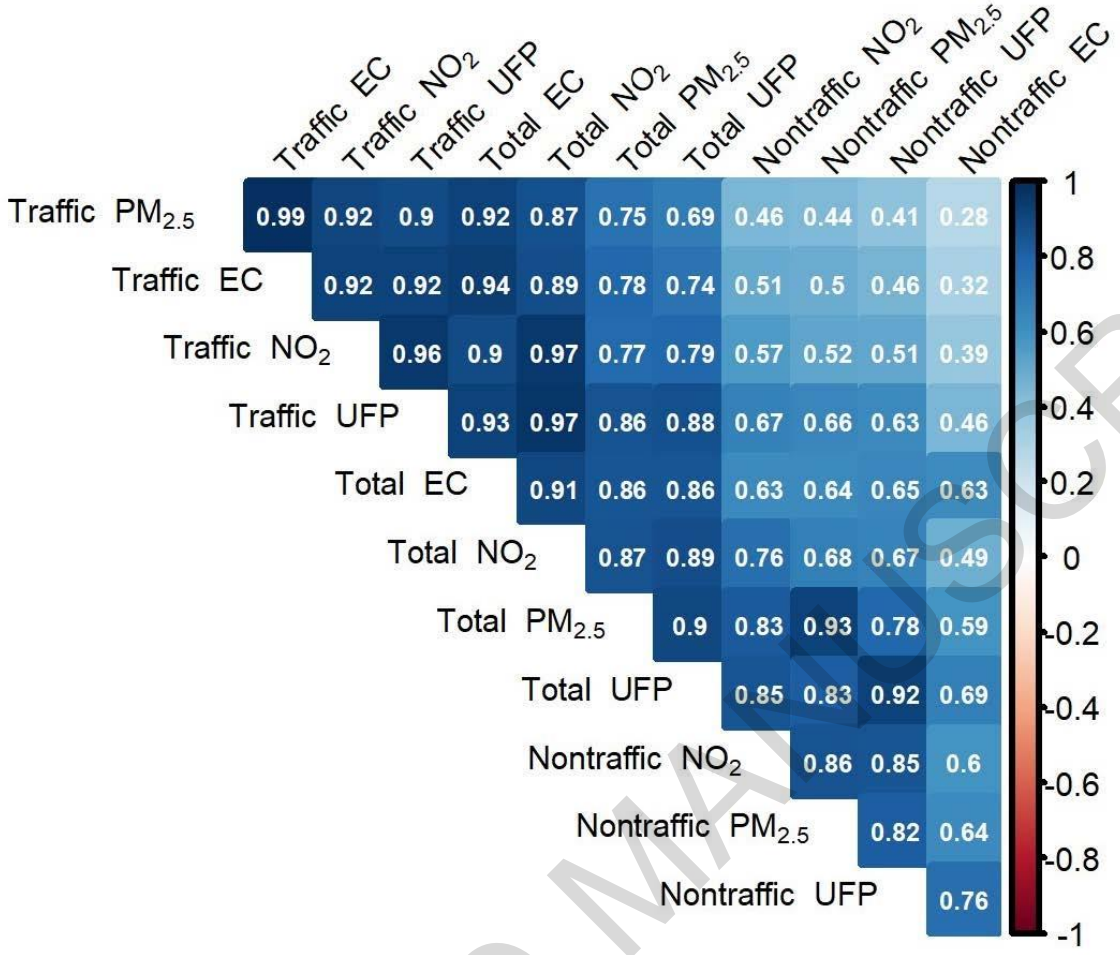

Figure 2. Pearson's correlation coefficients between 10-year time-weighted averaged air pollution exposures for the entire study population (N=159,769). Traffic contributions refer to air pollution generated from local traffic sources, whereas non-traffic contributions refer to air pollution generated from non-traffic sources and non-local traffic sources.

Figure 3.

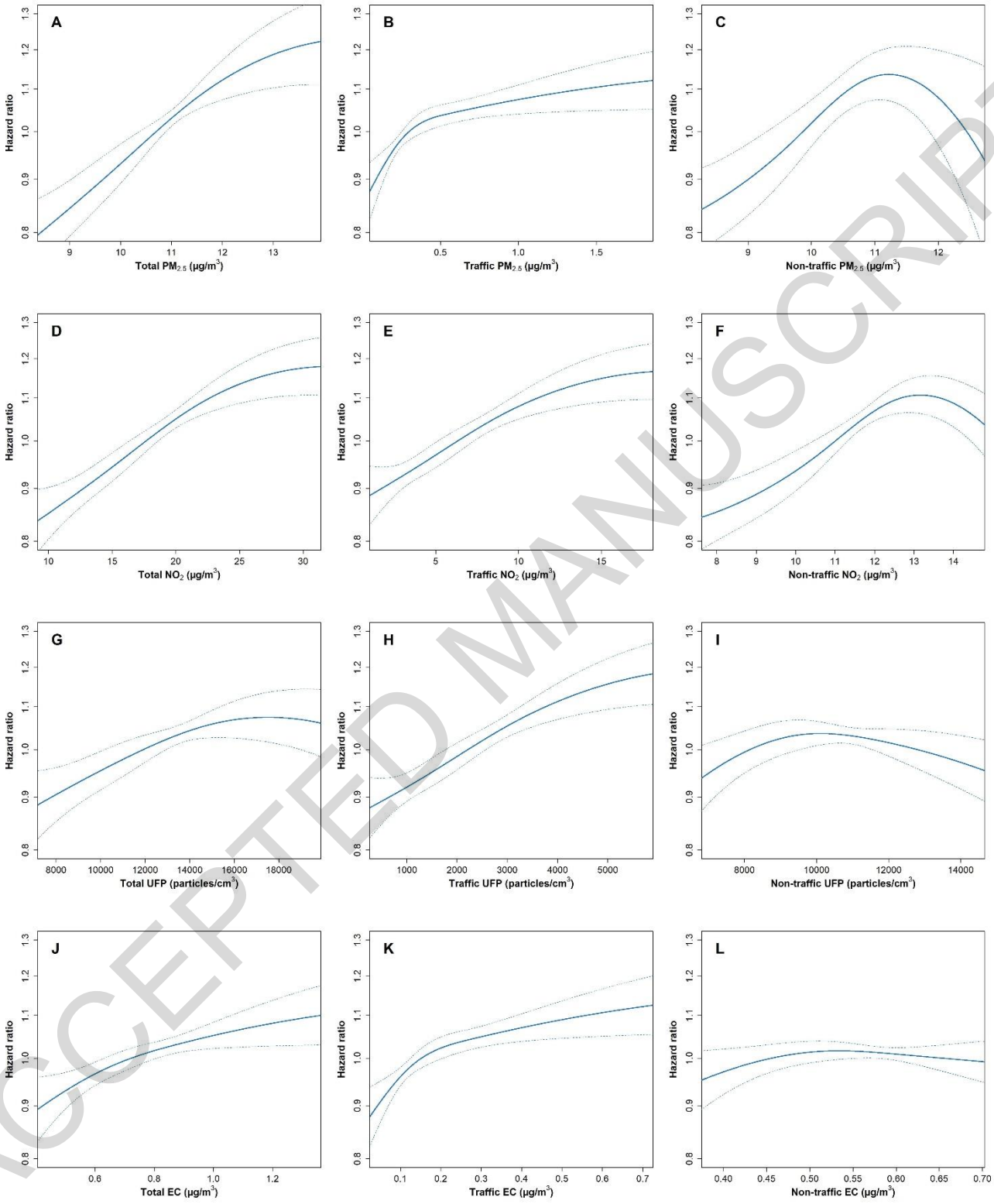

Figure 3. Association between 10-year mean residential exposure to: A) $PM_{2.5}$ (total contribution); B) $PM_{2.5}$ (traffic contribution); C) $PM_{2.5}$ (non-traffic contribution); D) NO_2 (total contribution); E)

NO_2 (traffic contribution); F) NO_2 (non-traffic contribution); G) UFP (total contribution); H) UFP (traffic contribution); I) UFP (non-traffic contribution); J) EC (total contribution); K) EC (traffic contribution); L) EC (non-traffic contribution), and risk for COPD using the fully adjusted model (i.e. Model 4). $PM_{2.5}$, particulate matter with a diameter <2.5 µm; NO_2, nitrogen dioxide; UFP, ultrafine particles; EC, elemental carbon. The plots display the exposure range from 5th to 95th percentile. Traffic contributions refer to air pollution generated from local traffic sources, whereas non-traffic contributions refer to air pollution generated from non-traffic sources and non-local traffic sources.

Figure 4.

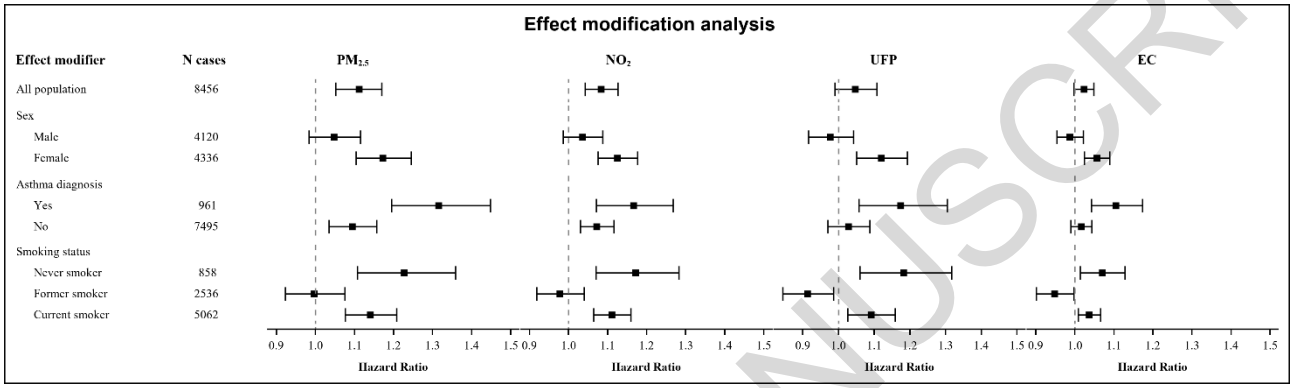

Figure 4. Effect modification analysis of linear associations between 10-year interquartile change exposure to air pollution (total contributions) and risk for COPD according to previous asthma diagnosis and smoking status. Risk estimates are based on the fully adjusted model (i.e. Model 4). $PM_{2.5}$, particulate matter with a diameter <2.5 µm; NO_2, nitrogen dioxide; UFP, ultrafine particles; EC, elemental carbon; CI, confidence interval; HR, hazard ratio.