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Particulate matter air pollution components and risk for lung cancer

O. Raaschou-Nielsen [a,b,*], R. Beelen [c], M. Wang [c], G. Hoek [c], Z.J. Andersen [a,d], B. Hoffmann [e,f], M. Stafoggia [g], E. Samoli [h], G. Weinmayr [e,f,i], K. Dimakopoulou [h], M. Nieuwenhuijsen [j], W.W. Xun [k], P. Fischer [l], K.T. Eriksen [a], M. Sørensen [a], A. Tjønneland [a], F. Ricceri [m], K. de Hoogh [k,n,o], T. Key [p], M. Eeftens [c,n,o], P.H. Peeters [q,r], H.B. Bueno-de-Mesquita [s,t,u,v], K. Meliefste [c], B. Oftedal [w], P.E. Schwarze [w], P. Nafstad [w,x], C. Galassi [m], E. Migliore [m], A. Ranzi [y], G. Cesaroni [g], C. Badaloni [g], F. Forastiere [g], J. Penell [z], U. De Faire [z], M. Korek [z], N. Pedersen [aa], C.-G. Östenson [ab], G. Pershagen [z], L. Fratiglioni [ac], H. Concin [ad], G. Nagel [i,ad], A. Jaensch [i], A. Ineichen [ae], A. Naccarati [ae], M. Katsoulis [af], A. Trichpoulou [af], M. Keuken [ag], A. Jedynska [ag], I.M. Kooter [ag], J. Kukkonen [ah], B. Brunekreef [c,q], R.S. Sokhi [ai], K. Katsouyanni [h,aj], P. Vineis [k]

[a] Danish Cancer Society Research Center, Copenhagen, Denmark
[b] Department of Environmental Science, Aarhus University, Roskilde, Denmark
[c] Institute for Risk Assessment Sciences, Utrecht University, Utrecht, The Netherlands
[d] Center for Epidemiology and Screening, Department of Public Health, University of Copenhagen, Copenhagen, Denmark
[e] IUF–Leibniz Research Institute for Environmental Medicine, Düsseldorf, Germany
[f] University of Düsseldorf, Düsseldorf, Germany
[g] Department of Epidemiology, Lazio Regional Health Service, Local Health Unit ASL RME, Rome, Italy
[h] Department of Hygiene, Epidemiology and Medical Statistics, Medical School, National and Kapodistrian University of Athens, Athens, Greece
[i] Institute of Epidemiology and Medical Biometry, Ulm University, Ulm, Germany
[j] Center for Research in Environmental Epidemiology, Parc de Recerca Biomèdica de Barcelona, Barcelona, Spain
[k] MRC-HPA Centre for Environment and Health, Department of Epidemiology and Biostatistics, Imperial College London, London, United Kingdom
[l] National Institute for Public Health and the Environment, Center for Sustainability and Environmental Health, Bilthoven, The Netherlands
[m] Unit of Cancer Epidemiology, AO Citta' della Salute e della Scienza, University of Turin and Center for Cancer Prevention, Turin, Italy
[n] Swiss Tropical and Public Health Institute, Basel, Switzerland
[o] University of Basel, Basel, Switzerland
[p] Cancer Epidemiology Unit, Nuffield Department of Population Health, University of Oxford, Oxford, United Kingdom
[q] Julius Center for Health Sciences and Primary Care, University Medical Centre Utrecht, Utrecht, The Netherlands
[r] School of Public Health, Imperial College London, London, United Kingdom
[s] Department for Determinants of Chronic Diseases, National Institute for Public Health and the Environment, Bilthoven, The Netherlands
[t] Department of Gastroenterology and Hepatology, University Medical Centre, Utrecht, The Netherlands
[u] Department of Epidemiology and Biostatistics, School of Public Health, Imperial College London, London, United Kingdom
[v] Department of Social and Preventive Medicine, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia
[w] Norwegian Institute of Public Health, Oslo, Norway
[x] Institute of Health and Society, University of Oslo, Oslo, Norway
[y] Environmental Health Reference Centre, Regional Agency for Environmental Prevention of Emilia-Romagna, Modena, Italy
[z] Institute of Environmental Medicine, Karolinska Institute, Stockholm, Sweden
[aa] Department of Medical Epidemiology and Biostatistics, Karolinska Institute, Stockholm, Sweden
[ab] Department of Molecular Medicine and Surgery, Karolinska Institute, Karolinska University Hospital, Stockholm, Sweden
[ac] Aging Research Centre, Department of Neurobiology, Care Sciences and Society, Karolinska Institute and Stockholm University, Stockholm, Sweden
[ad] Agency for Preventive and Social Medicine, Bregenz, Austria
[ae] Human Genetics Foundation, Molecular and Genetic Epidemiology Unit, Turin, Italy
[af] Hellenic Health Foundation, Athens, Greece
[ag] Netherlands Organisation for Applied Scientific Research, Utrecht, The Netherlands
[ah] Finnish Meteorological Institute, Helsinki, Finland
[ai] Centre for Atmospheric and Instrumentation Research, University of Hertfordshire, College Lane, Hatfield, United Kingdom
[aj] Department of Primary Care and Public Health Sciences and Environmental Research Group, King's College London, United Kingdom

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ABSTRACT

Background: Particulate matter (PM) air pollution is a human lung carcinogen; however, the components responsible have not been identified. We assessed the associations between PM components and lung cancer incidence.
Methods: We used data from 14 cohort studies in eight European countries. We geocoded baseline addresses and

* Corresponding author at: Danish Cancer Society Research Center, Strandboulevarden 49, 2100 Copenhagen Ø, Denmark.
E-mail address: ole@cancer.dk (O. Raaschou-Nielsen).

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assessed air pollution with land-use regression models for eight elements (Cu, Fe, K, Ni, S, Si, V and Zn) in size fractions of $PM_{2.5}$ and PM_{10}. We used Cox regression models with adjustment for potential confounders for cohort-specific analyses and random effect models for meta-analysis.
Results: The 245,782 cohort members contributed 3,229,220 person–years at risk. During follow-up (mean, 13.1 years), 1878 incident cases of lung cancer were diagnosed. In the meta-analyses, elevated hazard ratios (HRs) for lung cancer were associated with all elements except V; none was statistically significant. In analyses restricted to participants who did not change residence during follow-up, statistically significant associations were found for $PM_{2.5}$ Cu (HR, 1.25; 95% CI, 1.01–1.53 per 5 ng/m^3), PM_{10} Zn (1.28; 1.02–1.59 per 20 ng/m^3), PM_{10} S (1.58; 1.03–2.44 per 200 ng/m^3), PM_{10} Ni (1.59; 1.12–2.26 per 2 ng/m^3) and PM_{10} K (1.17; 1.02–1.33 per 100 ng/m^3). In two-pollutant models, associations between PM_{10} and $PM_{2.5}$ and lung cancer were largely explained by $PM_{2.5}$ S.
Conclusions: This study indicates that the association between PM in air pollution and lung cancer can be attributed to various PM components and sources. PM containing S and Ni might be particularly important.

1. Introduction

We recently reported from the European Study of Cohorts for Air Pollution Effects (ESCAPE) that particulate matter (PM) in air pollution with diameters of <10 μm (PM_{10}) and 2.5 μm ($PM_{2.5}$) is associated with a risk for the development of lung cancer (Raaschou-Nielsen et al., 2013). This result, among others, formed the basis for classification of outdoor air pollution and PM in outdoor air as carcinogenic to humans in a recent Monograph of the International Agency for Research on Cancer (Loomis et al., 2013). Most knowledge about associations between air pollution and risk for lung cancer is based on measures of exposure to PM as a whole (Hamra et al., 2014), sulfur oxide-related pollution (Dockery et al., 1993; Pope et al., 2002), oxides of nitrogen (Nafstad et al., 2003; Raaschou-Nielsen et al., 2011) or cruder indicators such as proximity to traffic (Beelen et al., 2008; Hystad et al., 2013). PM is a complex mixture of particles from different sources with different composition. Little is known about the associations between specific components of PM and risk for cancer, although this could be of major importance in choosing the most efficient strategies for reducing the exposure of populations to carcinogenic air pollution.

As the concentrations of specific components of PM in air are often correlated, it is difficult to single out the specific components responsible for observed associations with health effects. A specific issue in air pollution epidemiology is to assess whether associations for specific components are stronger than associations for particle mass (Mostofsky et al., 2012). Particle mass is used in air quality regulations. Associations with lung cancer have been indicated in studies of exposure to the PM components elemental Carbon (Garshick et al., 2012; Steenland et al., 1998) and polycyclic aromatic hydrocarbons (Yuan et al., 2014), but, to our knowledge, no work on associations between exposure to other elements of PM and risk for lung cancer in general populations has been published. PM elements in air can serve as indicators of air pollution from different sources, but their compounds may also be carcinogenic for the lung per se, as seen for nickel International Agency for Research on Cancer Monograph Working Group, I, 2012.

Within the European study of Transport-related Air Pollution and Health Impacts—Integrated Methodologies for Assessing Particulate Matter (TRANSPHORM; www.transphorm.eu/), we analyzed data from the 14 cohort of the ESCAPE (www.escapeproject.eu/) study on lung cancer where PM air pollution was measured to determine associations between elementary components of PM air pollution at the residence and risk for lung cancer. A secondary aim was to investigate whether any particular elementary component could explain the previously observed association between PM air pollution and lung cancer.

2. Methods

2.1. Study design and participants

We conducted a prospective study of data collected within the ESCAPE and TRANSPHORM projects. The 14 cohorts were in Sweden (European Prospective Investigation into Cancer and Nutrition [EPIC]-Umeå, Swedish National Study on Aging and Care in Kungsholmen [SNAC-K], Stockholm Screening Across the Lifespan Twin Study and TwinGene [SALT], Stockholm 60 years old and IMPROVE study [60-y/IMPROVE], Stockholm Diabetes Prevention Program [SDPP]), Norway (Oslo Health Study [HUBRO]), Denmark (Diet, Cancer and Health Study [DCH]), The Netherlands (EPIC-Monitoring Project on Risk Factors and Chronic Diseases in The Netherlands [MORGEN], EPIC-PROSPECT), the UK (EPIC-Oxford), Austria (Vorarlberg Health Monitoring and Prevention Programme [VHM&PP]), Italy (EPIC-Turin, Italian Studies of Respiratory Disorders in Childhood and Environment [SIDRIA]-Turin and Rome, and Greece (EPIC-Athens); Fig. 1). Most of the study areas were large cities and the surrounding suburban or rural communities, as specified in Table 1 and in the online Appendix (pp. 2–15). Information on lifestyle etc. among cohort participants was obtained by questionnaires or interviews at enrolment (see online Appendix, Table S1). The use of cohort data was approved by the local ethical and data protection authorities. All participants signed informed consent forms at inception of the studies.

2.2. Procedures and lung cancer definition

Exposure was assessed in each area separately by standardized procedures. The association between long-term exposure to air pollution and incidence of lung cancer was analyzed in each cohort separately at the local center by common standardized protocols for outcome definition, confounder models and statistical analysis. Cohort-specific effect estimates were subsequently combined in a meta-analysis centrally. A pooled analysis of all cohort data was not possible because of data-transfer and privacy issues. We included cancers located in the bronchus and the lung (ICD10/ICDO3: C34.0–C34.9) and only primary cancers (i.e. not metastases); lymphomas in the lung (ICDO3 morphology codes 9590/3–9729/3) were not included. The cohort members were followed up for cancer incidence in national or local cancer registries, except in the SIDRIA cohorts in Italy and Athens. In the SIDRIA cohorts, hospital discharge and mortality register data were used. In Athens, cases were identified by active follow-up using questionnaires and telephone interviews with participants or next-of-kin, followed by verification of the cancer case through pathology records, medical records, discharge diagnosis or death certificates (online Appendix, Table S1).

2.3. Exposure assessment

Air pollution concentrations at the baseline residential addresses of study participants were estimated by Land Use Regression (LUR) models following a standardized procedure that has been described elsewhere (de Hoogh et al., 2013; Eeftens et al., 2012a). In brief, air pollution monitoring campaigns were performed between October 2008 and May 2011 in all study areas. Three two-week measurements of particles with aerodynamic diameters of <2.5 μm ($PM_{2.5}$) and <10 μm (PM_{10}) were performed at 20 sites in each cohort area. The three