Session 8: Health effects, Talk

Beyond current air quality standards: studies of ambient ultrafine air pollution and its effects on mortality and hospital admissions in Germany

M. Schwarz[1], A. Schneider[1], J. Cyrys[1], S. Bastian[2], S. Breitner-Busch[1,3], A. Peters[1, 3, 4, 5]

[1]Institute of Epidemiology, Helmholtz Zentrum München GmbH - German Research Center for Environmental Health, Neuherberg, Germany, [2]Saxon State Office for Environment, Agriculture and Geology (LfULG), Dresden, Germany, [3] Institute for Medical Information Processing, Biometry and Epidemiology, Medical Faculty, Ludwig-Maximilians-Universität München, Munich, Germany, [4]Department of Environmental Health, Harvard T.H. Chan School of Public Health, Boston, MA, USA , [5] Munich Heart Alliance, German Center for Cardiovascular Research (DZHK e.V.), Munich, Germany

Background: Ambient air pollution has been identified as a major threat to human health. Numerous studies have consistently shown associations between several air pollutants (e.g., fine particulate matter with diameters ≤2.5 µm; $PM_{2.5}$) and cause-specific morbidity and mortality. Consequently, national and international air quality standards and limit values have been established to guide exposure reductions, prevent premature deaths, and improve public health. However, not all air pollutants are subject to regulation. For instance, ultrafine particles (particles with diameters ≤ 100 nm □ 0.1 µm; UFP) remain unregulated due to limited monitoring, few multicenter epidemiological studies, and conflicting epidemiological evidence. Therefore, the objective of our study was to conduct a multicenter time-series analysis to examine the short-term health effects of UFP exposure on cause-specific mortality and hospital admissions in Germany.

Material and methods: We obtained daily counts of cause-specific cardiorespiratory mortality and hospital admission endpoints between 2010 and 2017 in the three German cities Dresden, Leipzig, and Augsburg. Daily averages of UFP number concentrations (10-100 nm) and size-fractionated particle number concentrations (e.g., total particle number concentration, PNC, 10-800 nm) were measured at six fixed monitoring sites, in addition to $PM_{2.5}$, nitrogen dioxide (NO_2), and black carbon (BC). We applied station-specific confounder-adjusted Poisson regression models to assess immediate (lag 0-1), delayed (lag 2-4, lag 5-7), and cumulative (lag 0-7) effects and used a novel multi-level meta-analytical approach to obtain pooled risk estimates. We performed two-pollutant models to investigate interdependencies between pollutants and examined possible effect modification by age, sex, and season.

Results: We found that elevated UFP concentrations were associated with a delayed increased risk of respiratory mortality five to seven days after UFP exposure (4.46% [95% confidence interval, 1.52% to 7.48%] per 3,223 particles/cm^3). Moreover, particles of the smallest size mode, the nucleation mode (10-30 nm), showed larger risks compared to larger particles. Comparable results were observed for both the warm and cold seasons and across different age groups; however, larger effects were seen for women. In contrast, UFP number concentrations did not show a clear association with cause-specific hospital admissions, suggesting a delayed pattern of an increased risk of respiratory hospital admissions two to four days after exposure (0.69% [95% confidence interval, -0.28% to 1.67%] per 3,220 particles/cm^3). However, larger particle size fractions, such as accumulation mode particles (100-800 nm), exhibited consistent and more pronounced effects. The findings indicated a higher risk for children as well as in cold seasons, while the risk for men and women was comparable. In general, no significant change was observed after adjusting for particulate pollutants. However, the additional adjustment for NO_2 resulted in wider confidence intervals and null findings.

Conclusion: Our study provides evidence that ultrafine air pollution is associated with adverse health effects, particularly in the respiratory system, and independently of other particulate air pollutants such as $PM_{2.5}$. Furthermore, the observed effects may vary by particle size and, to a certain extent, by exposure setting. Further multicenter studies are needed using harmonized and size- and source-specific UFP measurements to draw definite conclusions on the health effects of UFP. Finally, the revised EU Ambient Air Quality Directive mandates the monitoring of ultrafine particles at so-called "monitoring supersites" to support the scientific understanding of the UFP effects on human health and the environment.

Efficacy of HEPA air purifiers at reducing blood pressure for near highway residents

D. Brugge[1], M. Eliasziw[2], V. Kuchhal[3], C. Morson[4], T. Vazquez-Dodero[1], W. Goldstein-Gelb[5], S. Kunwar[1], H. Gates[1], F. Majluf[3], W. Zamore[6]*, S. Oakley Hersey[3]*

[1]University of Connecticut, [2]Tufts University, [3]Olin College, [4]University of Connecticut , [5]The Welcome Project, [6] Somerville Transportation Equity Partnership

Background: Airborne particulate matter pollution (PM) emanating from motor vehicles is a leading cause of cardiovascular risk and illness. Blood pressure (BP) is one indicator of the effects of and risk from exposure to PM, including near highway ultrafine and black carbon PM.

Objectives: To assess efficacy of in-home air purifiers to reduce BP in healthy adults living next to highways.

Methods: We conducted a double blind, randomized crossover trial with one month each of high efficiency particulate arrestance (HEPA) vs. sham filtration that was completed by 156 participants. Indoor/outdoor air monitoring was conducted at a subset of homes. Brachial and central BP were measured at the start and end of each month. Linear mixed models were used to compare the mean change in BP between the HEPA and sham filtration periods. We included a random intercept to account for within-participant correlation of repeated BP measurements, sequence and period effects. Models were adjusted for participant's age, sex, BP measurement at start of each intervention period, number of hours spent indoors a week prior to the BP measurement, and outdoor temperature and perceived stress score at the time of the BP measurement.

Results: $PM_{2.5}$ and UFP were reduced during HEPA compared to sham filtration periods. The overall results yielded no significant differences in BP between the HEPA and sham filtration periods. However, in a pre-planned subgroup analysis, participants who had an elevated SBP (i.e., brachial $\geq$ 120 or central $\geq$ 110 mmHg) at the start of the intervention period had a significant 3.2 mmHg difference in favor of HEPA filtration ($P = 0.03$). A similar 3.1 mmHg net difference was observed for central SBP ($P = 0.02$). In contrast, only small, clinically unimportant, reductions in DBP were observed that were not statistically significant.

Conclusions: In this randomized crossover trial that effectively controlled for most time invariant and time varying confounders, we showed that air purifier use can result in a clinically meaningful reduction in SBP for people with elevated SBP. Thus, air purifiers may be a viable intervention for at risk populations living near high volumes of motor vehicle traffic.

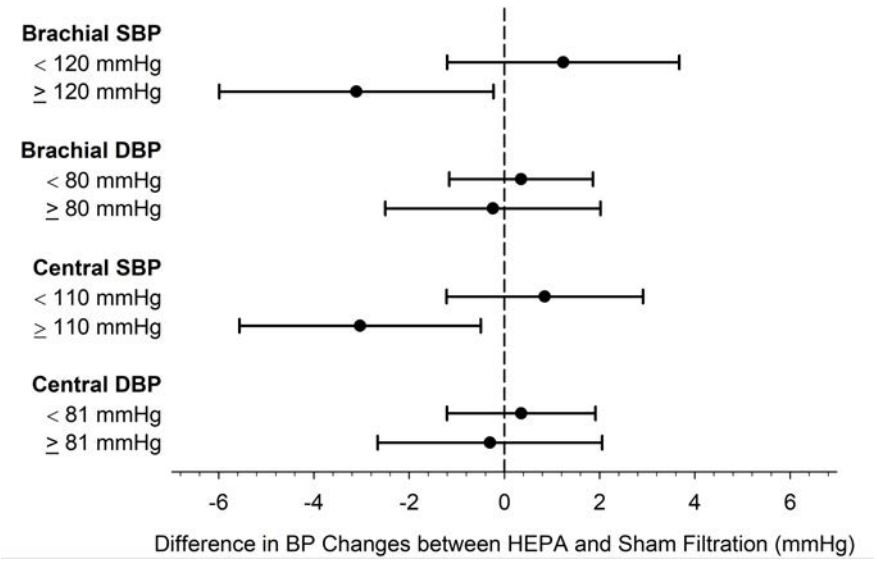

Figure. Difference in BP Changes between HEPA and Sham Filtration. Mean differences with 95% confidence intervals of changes in BPs between HEPA and sham filtration.

Associations between Short-Term Exposure to Ambient Ultrafine and Fine Particulate Matter and Biomarkers of Inflammation and Coagulation in Seniors in the German CorPuScula Study

M. L. Jakobi[1], K. Ogurtsova[1], P. Thoelke[1], S. Lucht[1,2], L. Glaubitz[1], P. Höppe[3], D. Nowak[3], C. Herder[4,5], P. Angerer[1], B. Hoffmann[1]

[1]Institute for Occupational Social and Environmental Medicine, Heinrich Heine University Düsseldorf, [2]Real-World Evidence & Insights, Cardinal Health, Dublin, OH, United States, [3]Institute for Occupational, Social and Environmental Medicine, Ludwig-Maximilians-University Munich, [4]Institute for Clinical Diabetology, German Diabetes Center, [5] Department of Endocrinology and Diabetology, Heinrich Heine University Düsseldorf

Introduction. The current evidence on the short-term effects of ultrafine particles (UFP) on biomarkers remains inconclusive, as only a limited number of studies have accounted for co-pollutants or analyzed multiple time points. In this study, we analyzed the associations between short-term exposure to ambient ultrafine and fine particulate matter and biomarkers of inflammation and coagulation in elderly institutionalized participants of the CorPuScula panel study.

Methods. Participants were recruited at the senior retirement home Wohnstift Augustinum Munich-North in the year 2000. Inclusion criteria were: (1) age >55 years and (2) availability to participate during the study period. Exclusion criteria were: (1) physical health conditions preventing measurements, (2) current smoking, (3) presence of a pacemaker, (4) diagnosis of a blood disorder, and (5) use of anticoagulant medication. At baseline, the participants completed a questionnaire on demographics, lifestyle factors, chronic illnesses, medications, and allergies. Venous blood samples were drawn repeatedly between May 2000 and July 2001.

UFP concentrations were measured using a condensation particle counter (TSI 3022A, detecting particles >7 nm), located 3 km from the retirement home. Particulate matter concentrations (PM_{10} and $PM_{2.5}$) were measured using a Low Volume Sampler (LVS3; Leckel) positioned in the garden of the retirement home, 30 m from the residential road. Data on co-pollutants (NO□, O_3) and meteorological conditions were gathered at a state urban background monitoring station and at the Meteorological Institute in Munich. Hourly mean values were used to calculate individual exposures for 24-, 12-, 3- and 1-hour periods before venopuncture, as well as lagged exposures for lags 0, 1, and 2 calendar days. Biomarkers of inflammation and coagulation, including C-reactive protein (CRP), fibrinogen, von Willebrand factor (VWF), plasminogen activator inhibitor-1 (PAI-1) and factor VIII (FVIII), were analyzed. Associations between short-term exposure to air pollutants (UFP, $PM_{2.5}$, and PM_{10}) and these biomarkers were assessed using linear mixed-effects regression models adjusted for environmental and individual confounders. Two-pollutant and multipollutant models adjusted for NO□ and O□. For UFP models, additional adjustments were made for $PM_{2.5}$ levels.

Results. The study included 50 participants (mean age at baseline: 76.9 years; 51% female) with 576 total observations (mean 11.5 per person) and identified positive associations between UFP, PM_{10}, and $PM_{2.5}$ and CRP with specific time points for each pollutant. Additionally, UFP was positively associated with PAI-1. Negative associations were observed between UFP, PM_{10}, and $PM_{2.5}$ and fibrinogen, FVIII, and vWF for various lagged time periods. Associations of UFP and fine PM with fibrinogen were not robust to adjustment for NO□, O□, or $PM_{2.5}$ in multi-pollutant models, whereas associations for other biomarkers remained largely consistent.

Discussion. Short-term exposure to concentrations of ambient UFP and fine particulate matter was associated with several biomarkers of inflammation and coagulation in a panel study involving residents of a senior retirement home, and most associations remained robust after co-pollutants adjustment.

Studying adverse effects of diesel exhaust particles on human intestine tissue in vitro

G. Gunasingam[1], R. He[1], A. Petri-Fink[1,2], B. Rothen-Rutishauser[1]*

[1]Adolphe Merkle Institute, University of Fribourg, Chemin des Verdiers 4, 1700 Fribourg, Switzerland, [2]Chemistry Department, University of Fribourg, Chemin du Musée 8, 1700 Fribourg, Switzerland

Traffic-borne pollutants represent a major proportion of ambient air pollution and are known to contribute to adverse human health effects. Fractions of these particles can be deposited within the respiratory tract upon inhalation. Ultrafine particles (UFPs) can even translocate from the alveoli across the air-blood tissue barrier into the bloodstream and accumulate in secondary organs beyond the lungs, such as the brain, liver, kidneys, and intestines. Understanding the impacts of UFPs on secondary organs remains an area of active investigation.

This study aims to evaluate the effects of standard diesel exhaust particles (DEPs) on human intestine tissue *in vitro*. Direct exposure to DEPs simulates particles that are swallowed after being cleared by the airway mucociliary activity after inhalation and deposition in the airways. Indirect exposure simulates the components, including translocated particles from the lungs and lung-derived mediators, circulating by the blood circulation to the secondary organs. Human intestinal tissues composed of human enterocytes, and mucus-producing cells were cultured for 21 days, and then macrophages were added to investigate these effects. Direct exposure involved treating intestinal tissues with DEPs at 5, 20, and 80 µg/mL concentrations for 24, 48, and 72 hours. Indirect exposure used conditioned media from DEP-treated human lung tissues. Biological responses, including inflammatory reactions, xenobiotic metabolism, and genotoxicity of the intestine tissue, were analyzed.

We found that direct exposure to DEPs predominantly accentuated xenobiotic metabolism with the upregulation of genes encoding for proteins such as aryl hydrocarbon receptor (AhR) and Cytochrome P450 monooxygenase, but no inflammatory reactions. Indirect exposure with conditioned media primarily triggered inflammatory responses in intestinal cells, with an increased release of the pro-inflammatory chemokine interleukin-8 (IL-8), suggesting that mediators originating from the lungs are likely pivotal contributors to the observed secondary tissue effects. Furthermore, genes involved in DNA damage and repair pathways - specifically *ATR*, *CHEK2*, and *GADD45A* - were upregulated in both direct and indirect exposure scenarios, implicating DEPs in the potential induction of genotoxicity in intestinal cells.

Our findings reveal that DEPs adverse effects on human intestine tissue depending on the route of exposure and that lung-mediated- pro-inflammatory mediators could influence the homoeostatic conditions of the tissue. Building on these insights, we advocate for the indirect exposure approach in our further study utilizing conditioned media from advanced human lung tissue cultures exposed to real-world engine emissions.

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Associations between PM2.5 components, brake and tyre wear markers, ultrafine particles, and childhood cancers in Canada

E. Lavigne[1], S. Weichenthal[2], M. Cloutier[1]

[1]Environmental Health Science and Research Bureau, Health Canada, Ottawa, Ontario, Canada, [2]Department of Epidemiology, Biostatistics, and Occupational Health, McGill University, Montreal, Quebec, Canada

Background: Prenatal exposure to fine particulate matter ($PM_{2.5}$) and ultrafine particles (UFPs) is linked to childhood cancers, but the role of its components, especially brake and tyre wear particles, are unclear. The objective of this study was to examine the associations between early life $PM_{2.5}$ components exposure and childhood cancer risk.

Methods: This was a retrospective epidemiological cohort study including over 6 million singleton live births across Canada from 2000 to 2022, with follow-up until age 5 for cancer incidence. Early life exposure to $PM_{2.5}$ components (black carbon, dust, ammonium, nitrate, organic matter, sulfate, sea salt and metal components) as well as UFPs were assessed from conception to 36 weeks as well as during childhood using residential address at birth to assign exposures. $PM_{2.5}$ concentrations and UFPs were estimated from satellite data, a chemical transport model, and ground-based measurements. The primary outcome was cancer diagnosis by age 5 and subtypes included leukemia, non-Hodgkin lymphoma and astrocytoma. Cox proportional hazards models assessed the associations between the exposures and cancer incidence.

Results: Among over 6 million births, prenatal exposure to sulfate (SO_4), Barium [Ba] as a marker of brake dust and UFPs were associated with the risk of astrocytoma, a type of brain tumor. The effects were particularly observed during the second trimester of pregnancy exposure. Effects of SO_4 were found for the impact on acute lymphoblastic leukemia. Effects appeared more pronounced among more deprived socioeconomic status populations.

Conclusions and Relevance: Prenatal $PM_{2.5}$ components, UFPs and a specific marker of brake dust wear were associated with specific types of childhood cancers. These findings underscore the need for further research to understand components of particle's role in the development of cancers in children.