The Abdus Salam
International Centre for Theoretical Physics

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Workshop on Aerosol Impact in the Environment: from Air Pollution to Climate Change

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Spatial heterogeneity of chemical constituents of fine particulates: implications for epidemiological and exposure research

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Italy

The Abdus Salam
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Workshop on Aerosol Impact in the Environment:

from Air Pollution to Climate Change

Spatial heterogeneity of chemical constituents of fine particulates: implications for epidemiological and exposure research.

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[b]Aerosol d.o.o., Ljubljana, Slovenia

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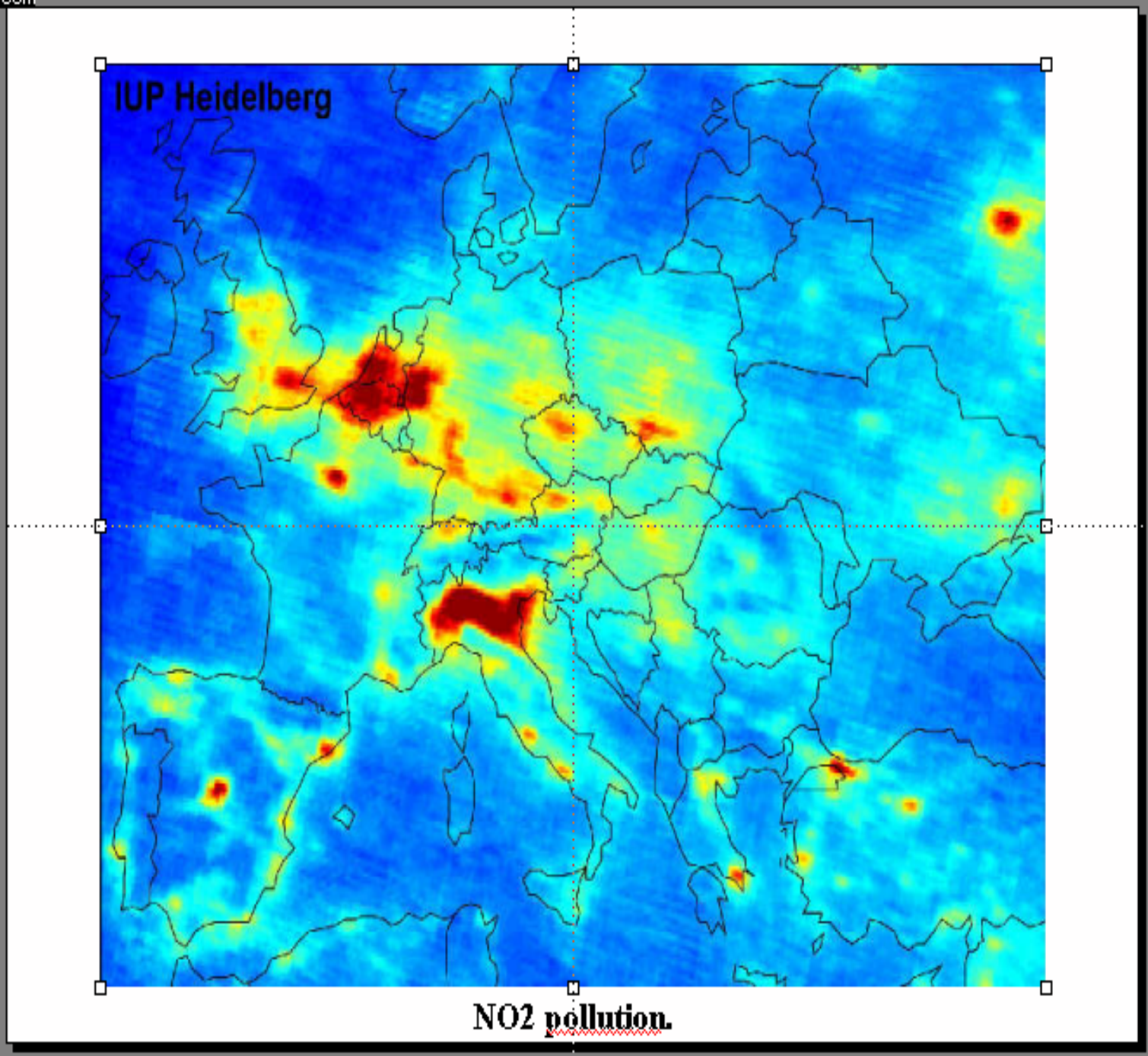
SIMG
Società Italiana
di Medicina Generale

Pollution is not a problem of the modern times: also pre-industrial cultures suffered from smoke produced by burning wood for cooking and heating.

Ancient Roman had even words in their Latin language to define the pollution: they called it “gravioris caeli” (heavy sky) or “infamis aer” (infamous air).

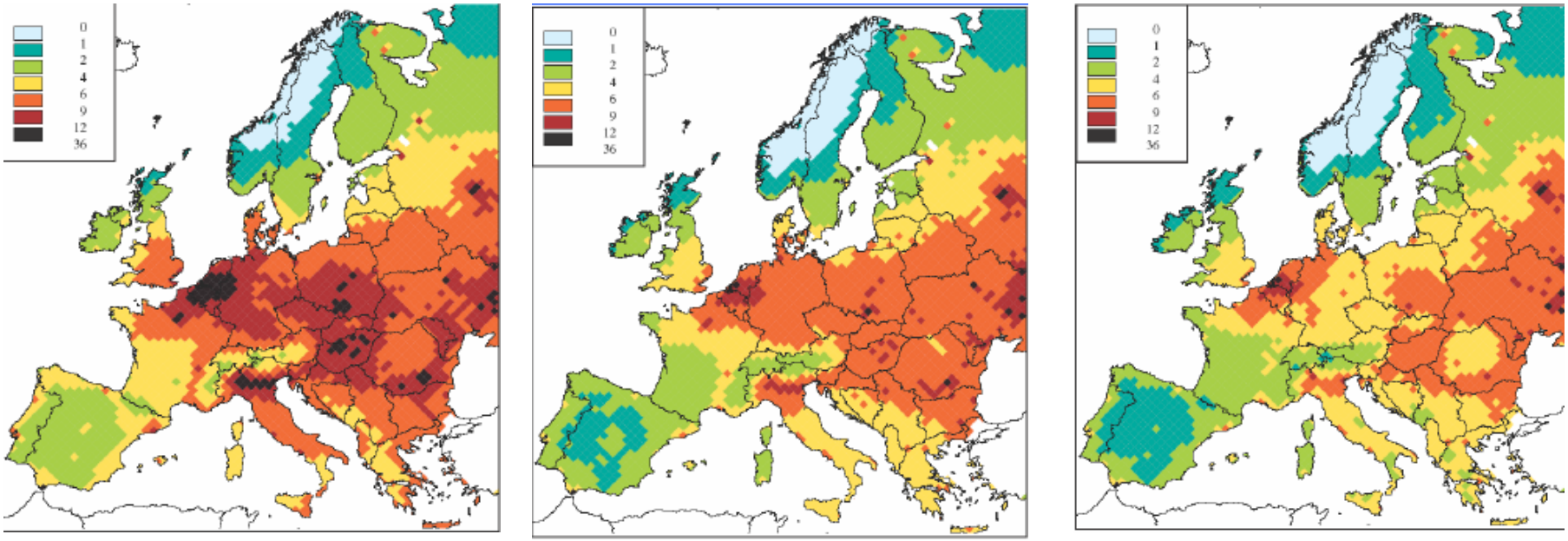
And there is evidence that these “infamous aer” was a problem, as reported by the great phylosopher Seneca, which was probably suffering of asthma, in one of the Letters to Lucilio:

Ut primum gravitatem urbis ecessi et illum odorem culinarum fumantium quae motae quidquid pestiferi vaporis sorbuerunt cum pulvere effundunt, protinus mutatam valetudinem sensis. **(as soon as I left the heavy Rome air and that smell of smoking kitchens which, once they are working, deliver with the dust all that pestilential steam they have absorbed, immediately I felt a change in my health conditions)**.



NO2 pollution.

Why atmospheric aerosols are so important?



2000 2010 2020

Even with reduced emissions: statistical life loss still around **5 months average in EU in 2020**!

Epidemiology of atmospheric pollution

The health burden of particle exposure

Estimating the National Public Health Burden Associated with Exposure to Ambient PM(2.5) and Ozone.

Fann N, Lamson AD, Anenberg SC, Wesson K, Risley D, Hubbell BJ.

Risk Anal. **2011**

U.S. Environmental Protection Agency, Office of Air Quality Planning and Standards, Research Triangle Park, NC, USA.

Abstract. Ground-level ozone (O(3)) and fine particulate matter (PM(2.5)) are associated with increased risk of mortality. We quantify the burden of modeled 2005 concentrations of O(3) and PM(2.5) on health in the United States. We use the photochemical Community Multiscale Air Quality (CMAQ) model in conjunction with ambient monitored data to create fused surfaces of summer season average 8-hour ozone and annual mean PM(2.5) levels at a 12 km grid resolution across the continental United States. Using PM(2.5) and O(3) mortality risk coefficients drawn from the long-term American Cancer Society (ACS) cohort study and National Mortality and Morbidity Air Pollution Study (NMMAPS), respectively, **we estimate 130,000 PM(2.5) -related deaths** and 4,700 ozone-related deaths to result from 2005 air quality levels.

Among populations aged 65-99, we estimate nearly 1.1 million life years lost from PM(2.5) exposure and approximately 36,000 life years lost from ozone exposure.

Among the 10 most populous counties, the percentage of deaths attributable to PM(2.5) and ozone ranges from 3.5% in San Jose to 10% in Los Angeles. These results show that despite significant improvements in air quality in recent decades, recent levels of PM(2.5) and ozone still pose a non trivial risk to public health.

The health burden of particle exposure

Short term health effects of PM exposure
(daily mortality, all cause)

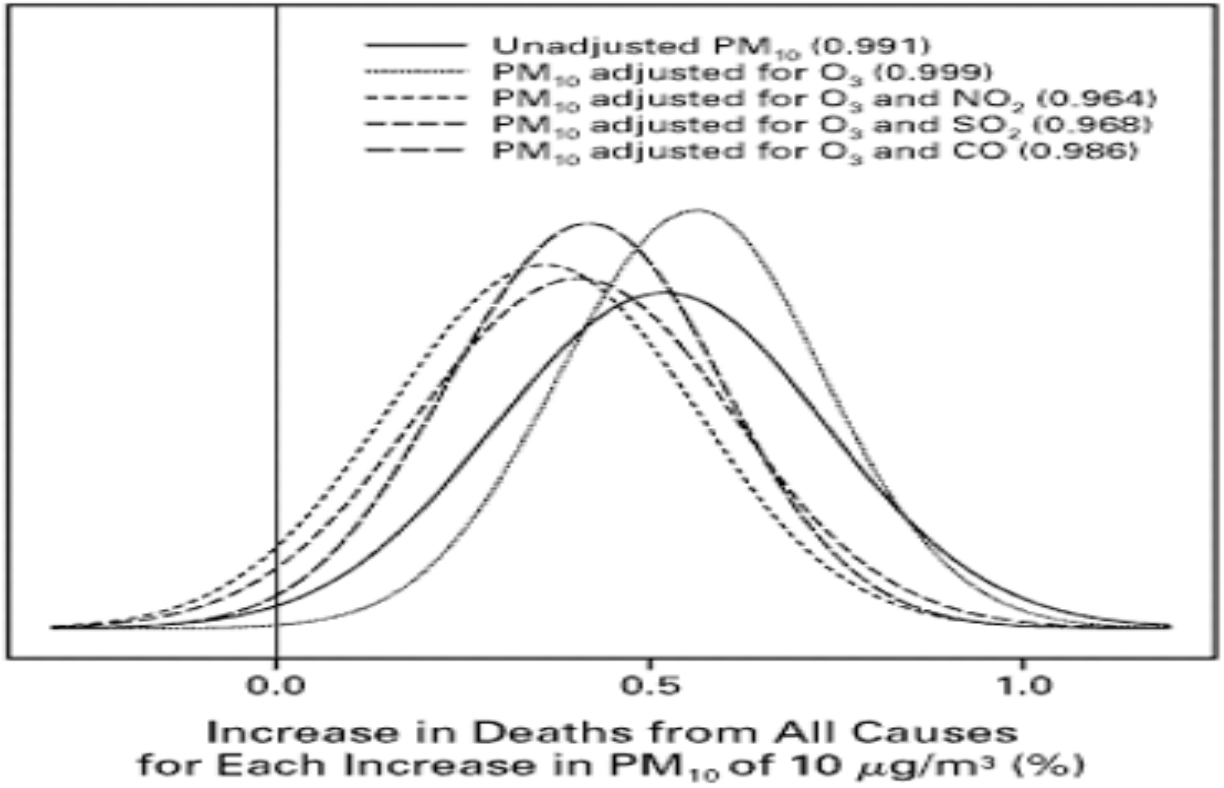
FINE PARTICULATE AIR POLLUTION AND MORTALITY IN 20 U.S.CITIES,1987 –1994

JONATHAN SAMET,M.D., FRANCESCADOMINICI,PH.D., FRANK CURRIERO,PH.D., IVAN COURSAC,M.S., AND SCOTT L.ZEGER,PH.D.

N Engl J Med 2000;343:1742-9

The health burden of particle exposure

Short term health effects of PM exposure (daily mortality, all cause)



The health burden of particle exposure

Short term health effects of PM exposure (daily mortality, all cause)

Public Health and Air Pollution in Asia (PAPA): coordinated Studies of Short-Term Exposure to Air Pollution and Daily Mortality in Two Indian Cities
HEI Public Health and Air Pollution in Asia Program HEALTH EFFECTS INSTITUTE Report Number 157 March 2011

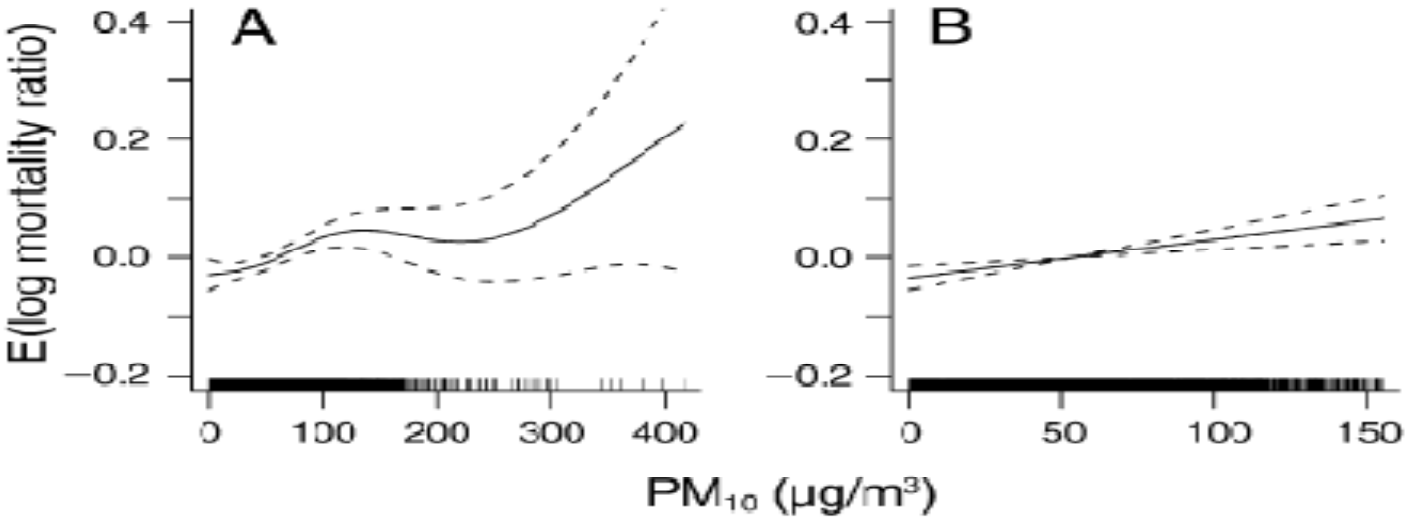


Figure 22. Sensitivity analysis: Dose response curves for PM_{10} using version 1.3-24 of the mgcv package in R and the estimated degrees of freedom for each model. A) The estimated curve from the full data set (4 *df*); **B)** The estimated curve after deleting outlying exposures (1 *df*). E(log mortality ratio) indicates expectation of log mortality ratio.

Relative risk (RR) for nonaccidental, all-cause mortality of 1.004 (95% confidence interval [CI] = 1.002 to 1.007) per 10-µg/m3 increase in PM10 concentration on the previous day, Chennai, India.

Public Health and Air Pollution in Asia (PAPA): coordinated Studies of Short-Term Exposure to Air Pollution and Daily Mortality in Two Indian Cities

HEI Public Health and Air Pollution in Asia Program

HEALTH EFFECTS INSTITUTE Report Number 157 March 2011

“There is broad general consistency of the results of the two Indian studies described here and in other Asian time-series studies of mortality with those in Europe and North America.”

Increase in mortality rates associated to a long term increase of 10 mcg/m^3 $PM_{2.5}$

- **All causes 4%**
- **Cardiopulmonary 6%**
- **Lung cancer 8%**

Pope CA et al.: JAMA 2002; 287:1132-41.

The health burden of particle exposure

Short term health effects of PM exposure (daily mortality, all cause)

Exposure-response for cardiovascular risk is non linear both for ambient PM and tobacco smoking

- Relatively low levels of fine particulate exposure from either air pollution or secondhand cigarette smoke are sufficient to induce adverse biological responses increasing the risk of cardiovascular disease mortality.
- The exposure-response relationship between cardiovascular disease mortality and fine particulate matter is relatively steep at low levels of exposure and flattens out at higher exposures.

Pope CA 3rd, Burnett RT, Krewski D, Jerrett M, Shi Y, Calle EE, Thun MJ. Cardiovascular mortality and exposure to airborne fine particulate matter and cigarette smoke: shape of the exposure-response relationship.
***Circulation* 2009**

The exposure-response relationship between cardiovascular disease mortality and PM2.5: relatively steep at low levels of exposure and flattens out at higher exposures.

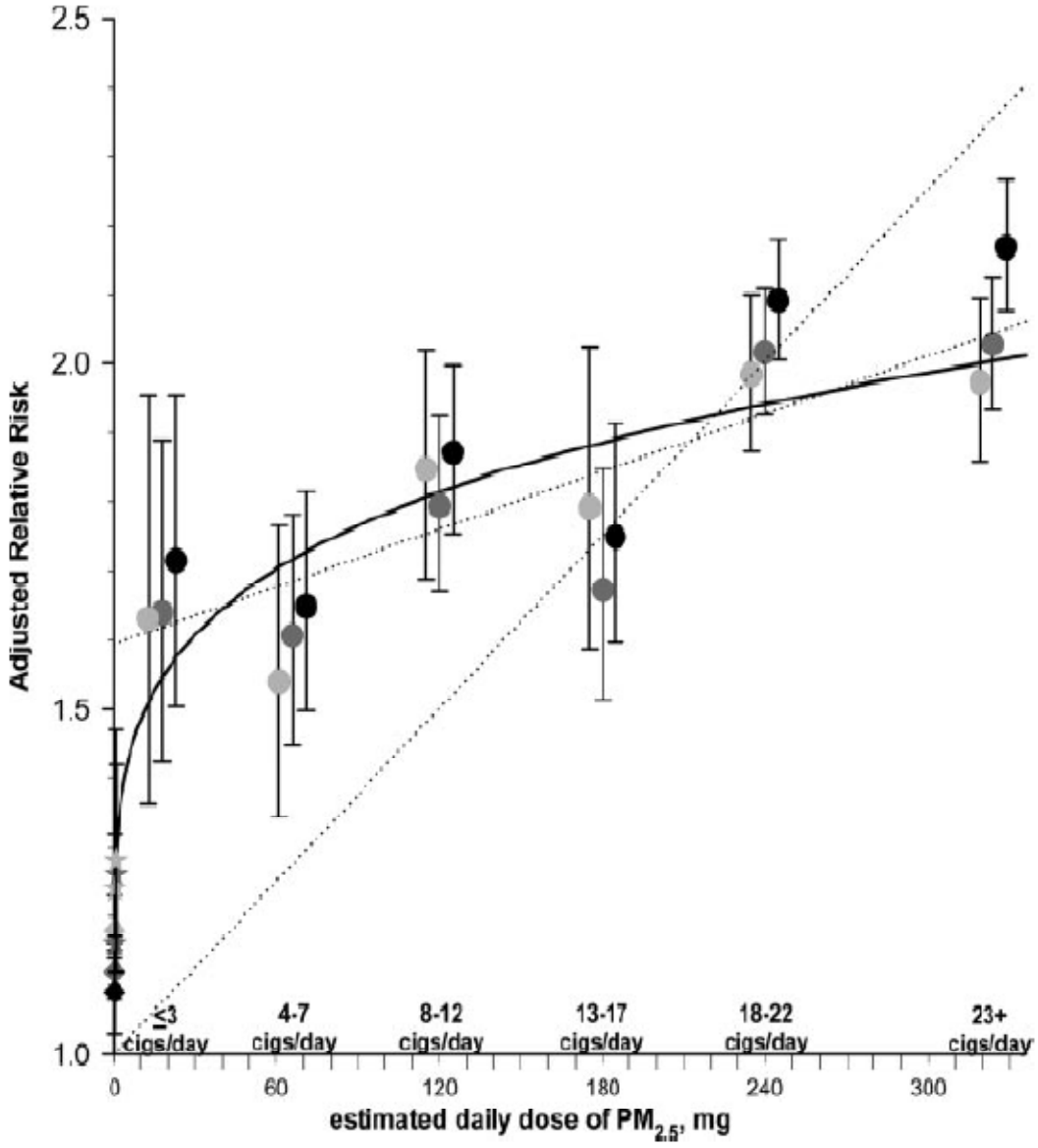
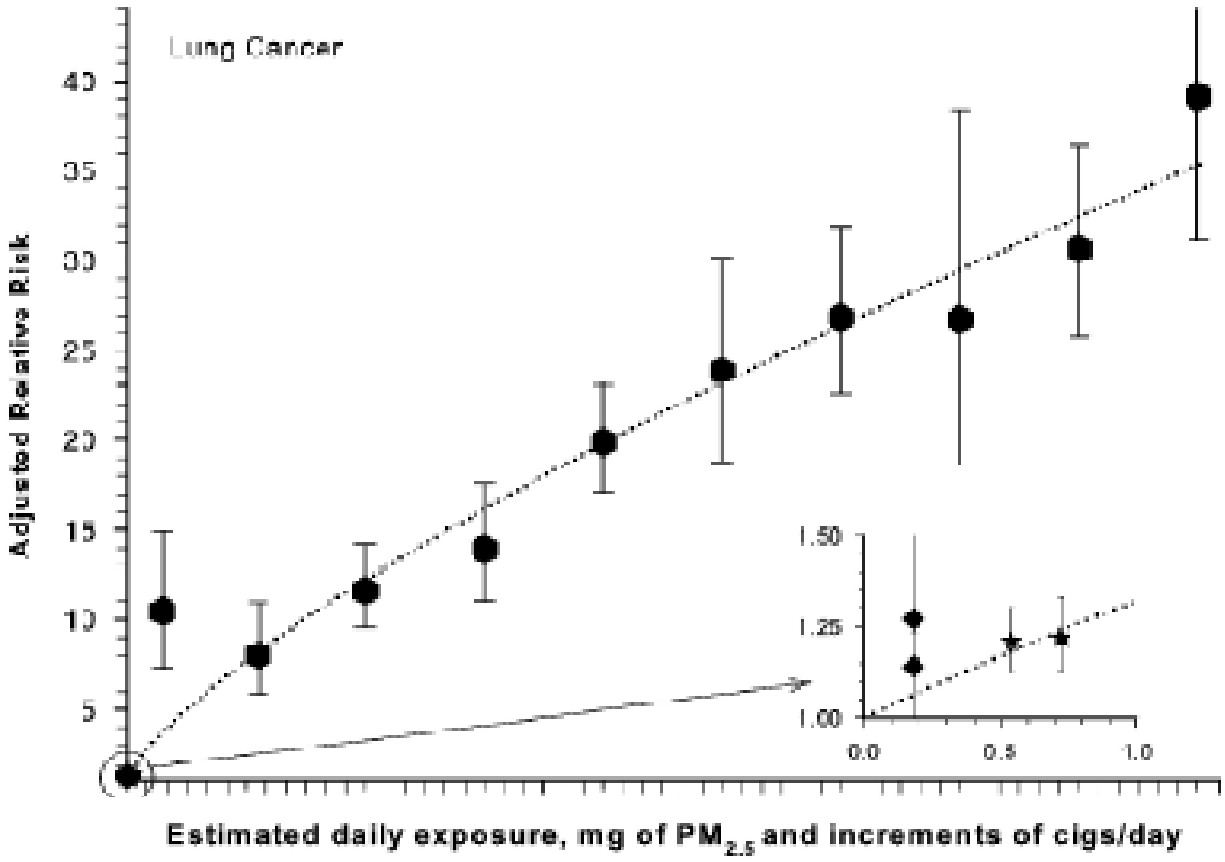


Figure 1. Adjusted relative risks (and 95% CIs) of ischemic heart disease (light gray), cardiovascular disease (dark gray), and cardiopulmonary disease (black) mortality plotted over baseline estimated daily dose of $PM_{2.5}$ from different increments of current cigarette (cigs) smoking (relative to never smokers). Diamonds represent comparable mortality risk estimates for $PM_{2.5}$ from air pollution. Stars represent comparable pooled relative risk estimates associated with SHS exposure from the 2006 Surgeon General's report and from the INTERHEART study. The solid and dotted lines are fitted linear and nonlinear lines illustrating alternative monotonic exposure-response relationships.

Pope A et al, *Circulation* 2009

Exposure-response to urban PM and cigarette smoke for lung cancer risk is <u>linear</u> both for ambient PM and tobacco smoking



Lung Cancer and Cardiovascular Disease Mortality Associated with Ambient Air Pollution and Cigarette Smoke: Shape of the Exposure-Response Relationships.

Pope CA 3rd, Burnett RT, Turner MC, Cohen AJ, Krewski D, Jerrett M, Gapstur SM, Thun MJ.

Environ Health Perspect. 2011

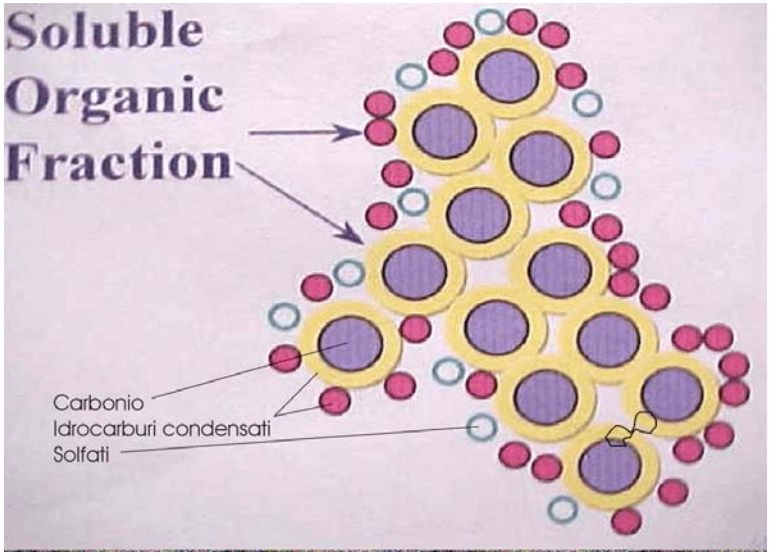
Airborn combustion particle composition

What do they carry on?

Airborn combustion particle morphology and composition

Veichle exhaust and wood smoke

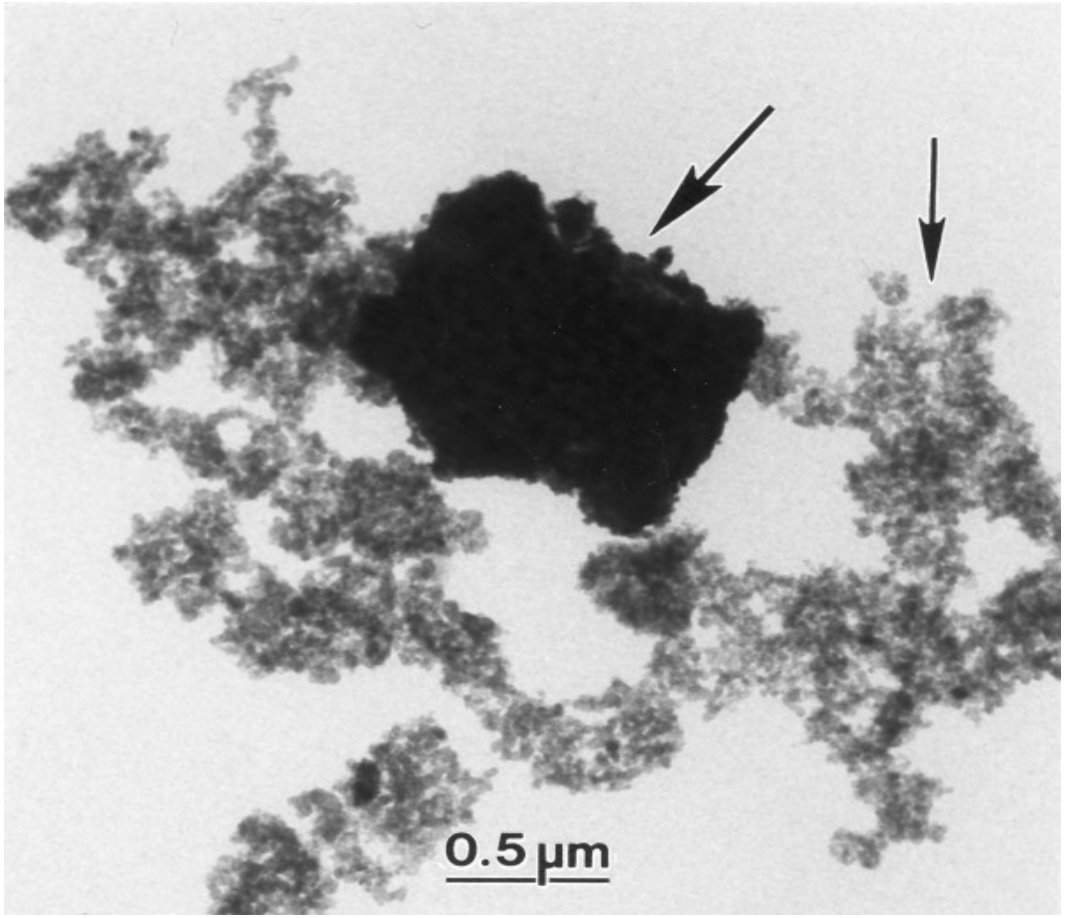
Schematic composition of a particle



Airborn combustion particle morphology and composition.

Veichle exhaust and wood smoke

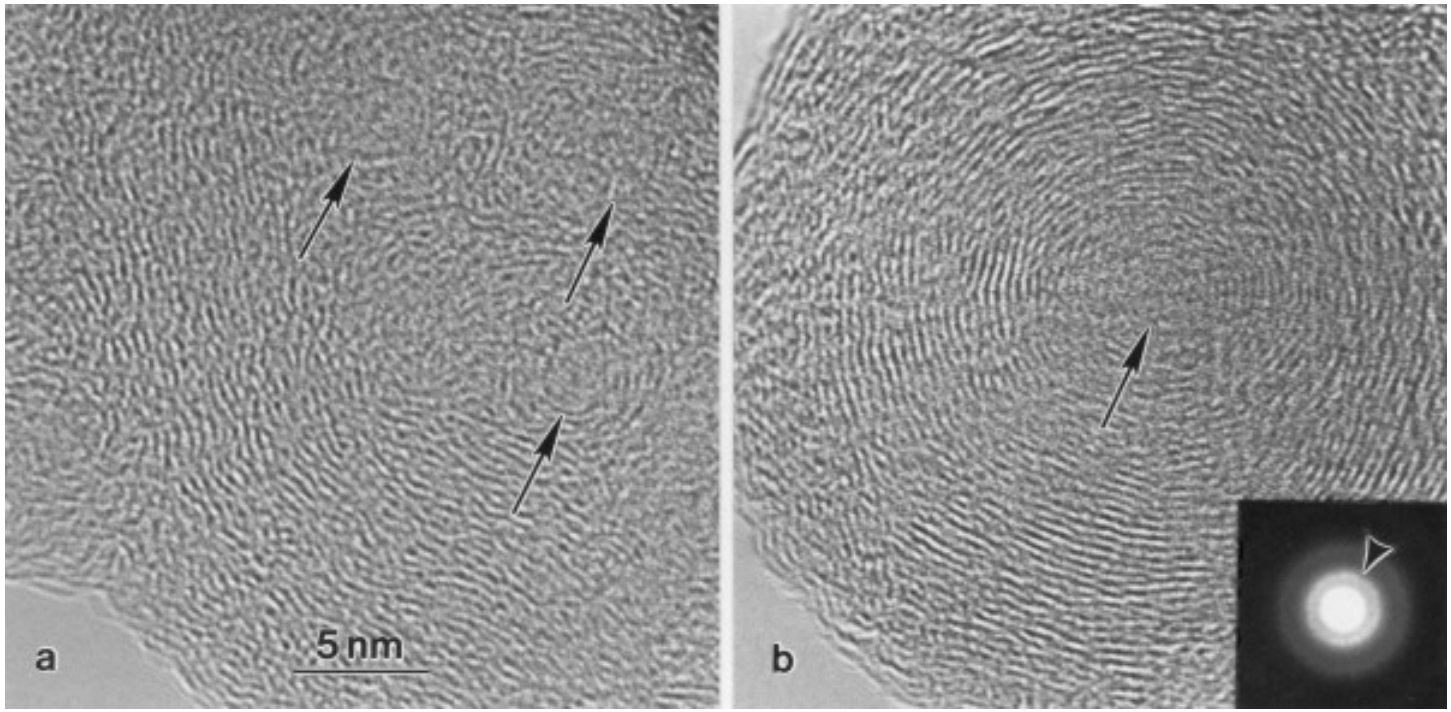
Particle morphology. TEM micrograph of a tunnel sample showing a mineral particle (large arrow) and carbon aggregates (small arrow).



Kocbach A, Li Y, Yttri KE, Cassee FR,[4] Per E Schwarze PE, Namork E.
Physicochemical characterisation of combustion particles from vehicle exhaust and residential wood smoke.
***Part Fibre Toxicol.* 2006**

Airborn combustion particle morphology and composition.

Vehicle exhaust and wood smoke



Turbostratic microstructure of primary carbon particles. TEM micrographs showing the turbostratic microstructures, consisting of concentric carbon layers surrounding a) several nuclei in vehicle exhaust (arrows), or b) a single nucleus in wood smoke (arrow). The inset shows a SAED pattern from a wood smoke particle. The arrowhead points at the ring corresponding to the 002 spacings in the turbostratic microstructure.

Kocbach A, Li Y, Yttri KE, Cassee FR,[4] Per E Schwarze PE, Namork E.
Physicochemical characterisation of combustion particles from vehicle exhaust and residential wood smoke.
***Part Fibre Toxicol.* 2006**

Airborn combustion particle morphology and composition.

Vehicle exhaust and wood smoke

Table 2

Results from chemical bulk analysis. The mean values with standard deviations for mass percentages of TC and OC, and OC/TC ratio, as well as the Total PAH and Adjusted PAH (see text).

Sample	TC (%)	OC/TC (%)	OC (%)	Total PAH (ng/mg)	Adjusted PAH (ng/mg)
Tunnel St+	14.3 ± 0.1	65.1 ± 3.1	9.3 ± 0.4	73	510
Tunnel St-	51.0 ± 3.8	47.9 ± 0.3*	24.4 ± 2.0	381	747
Wood	82.6 ± 5.8*	42.7 ± 4.4*	35.4 ± 5.1	9745	11797
Diesel[x]	80.0 ± 5.1*	20.4 ± 1.1	16.3 ± 1.2	67	84

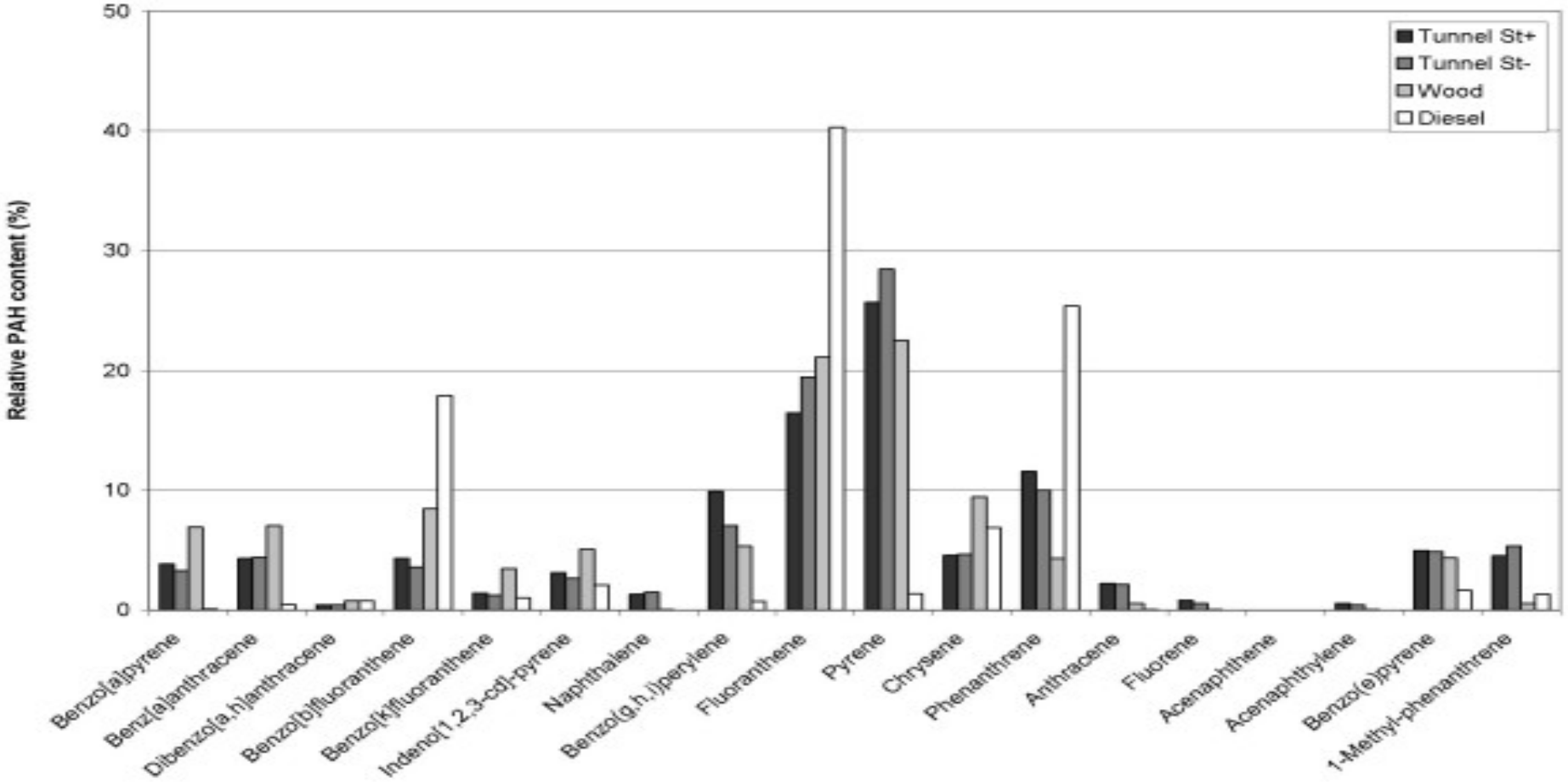
[x] The PAH sums for Diesel are based on data from the Certificate of Analysis (see text).

* Pairs of data where no significant differences were observed

Kocbach A, Li Y, Yttri KE, Cassee FR,[4] Per E Schwarze PE, Namork E.
Physicochemical characterisation of combustion particles from vehicle exhaust and residential wood smoke.
***Part Fibre Toxicol.* 2006**

Airborn combustion particle morphology and composition.

Veichle exhaust and wood smoke



PAH profiles. The histogram shows the levels of single PAHs divided by Total PAH for the four samples (Tunnel St+, Tunnel St-, Wood and Diesel).

Kocbach A, Li Y, Yttri KE, Cassee FR,[4] Per E Schwarze PE, Namork E.
Physicochemical characterisation of combustion particles from vehicle exhaust and residential wood smoke.
***Part Fibre Toxicol.* 2006**

Airborn combustion particle morphology and composition.

Veichle exhaust and wood smoke

The TEM analyses showed that:

- **combustion particles from vehicle exhaust and wood smoke differ in geometric primary particle diameter and turbostratic microstructure**
- **the bulk chemical analyses showed the PAH content was found to be much higher in wood smoke as compared to vehicle exhaust.**

Kocbach A, Li Y, Yttri KE, Cassee FR,[4] Per E Schwarze PE, Namork E.
Physicochemical characterisation of combustion particles from vehicle exhaust and residential wood smoke.
Part Fibre Toxicol. **2006**

Airborn combustion particle morphology and composition

Particle-bound PAHs in rural residential areas in Germany

- The target of this study was to investigate the particle-phase PAH composition of ambient samples in order to assess the influence of wood combustion on air quality in residential areas.
- **PM_{10} samples (particulate matter <10 µm) were collected during two winter seasons at two rural residential areas near Stuttgart in Germany**. Samples were extracted using toluene in an ultrasonic bath and subsequently analysed by gas chromatography–mass spectrometry.
- **Twenty-one PAH compounds were detected and quantified.** The PAH fingerprints of different wood combustion emissions were found in significant amounts in ambient samples and high correlations between total PAHs and other wood smoke tracers were found, indicating the dominant influence of wood combustion on air quality in residential areas.
- **Carcinogenic PAHs were detected in high concentrations and contributed 49% of the total PAHs in the ambient air.** To assess the health risk, we investigated the exposure profile of individual PAHs. The findings suggest that attention should be focused on using the best combustion technology available to reduce emissions from wood-fired heating during the winter in residential areas.

Aynul Bari M, Baumbach G, Kuch , Scheffknecht G.
Particle-phase concentrations of polycyclic aromatic hydrocarbons in ambient air of rural residential areas in southern Germany
***Air Qual Atmos Health*. 2010**

Airborn combustion particle morphology and composition

PAHs and trace metals in Athens' PM

The most commonly detected **trace metals in the TSP and PM fractions were Fe, Pb, Zn, Cu, Cr, V, Ni and Cd** and their concentrations were similar to levels observed in heavily polluted urban areas from local traffic and other anthropogenic emissions.

Analysis of 16 PAHs bound to PM showed that they are mostly traffic related. In general, the fine particulate PAHs concentrations were higher than coarse particles.

The most common PAHs in PM(10.2) and PM(2.1) were pyrene, phenanthrene, acenapthylene and fluoranthene, which are associated with diesel and gasoline exhaust particles.

Valavanidis A, Fiotakis K, Vlahogianni T, Bakeas EB, Triantafillaki S, Paraskevopoulou V, Dassenakis M.
Characterization of atmospheric particulates, particle-bound transition metals and polycyclic aromatic hydrocarbons of urban air in the centre of Athens (Greece).
***Chemosphere.* 2006**

Airborn combustion particle composition

What do they carry on?

Hormone transport: the case of trenbolone, a potent anabolic steroid, and its metabolites, with endocrine-modulating activity in all vertebrates (like other xenobiotics could influence obesity, sexual diseases, infertility, inflammations, endometric and prostate cancer

Talanta 85 (2011) 1317–1323

Contents lists available at ScienceDirect

Talanta

journal homepage: www.elsevier.com/locate/talanta

Liquid chromatography–tandem mass spectrometry analysis of 17α-trenbolone, 17β-trenbolone and trendione in airborne particulate matter

B.R. Blackwell*, Q. Cai, P.N. Smith, G.P. Cobb

The Institute of Environmental and Human Health, Department of Environmental Toxicology, Texas Tech University, PO Box 41163, Lubbock, TX 79416, United States

Airborn combustion particle composition

What do they carry on?

Reactive Oxygen Species were found to be present in PM, especially in the UFPs component.

Ntziachristos L, Froines JR, Cho AK, Sioutas C.
Relationship between redox activity and chemical speciation of size-fractionated particulate matter
***Part Fibre Toxicol.* 2007**

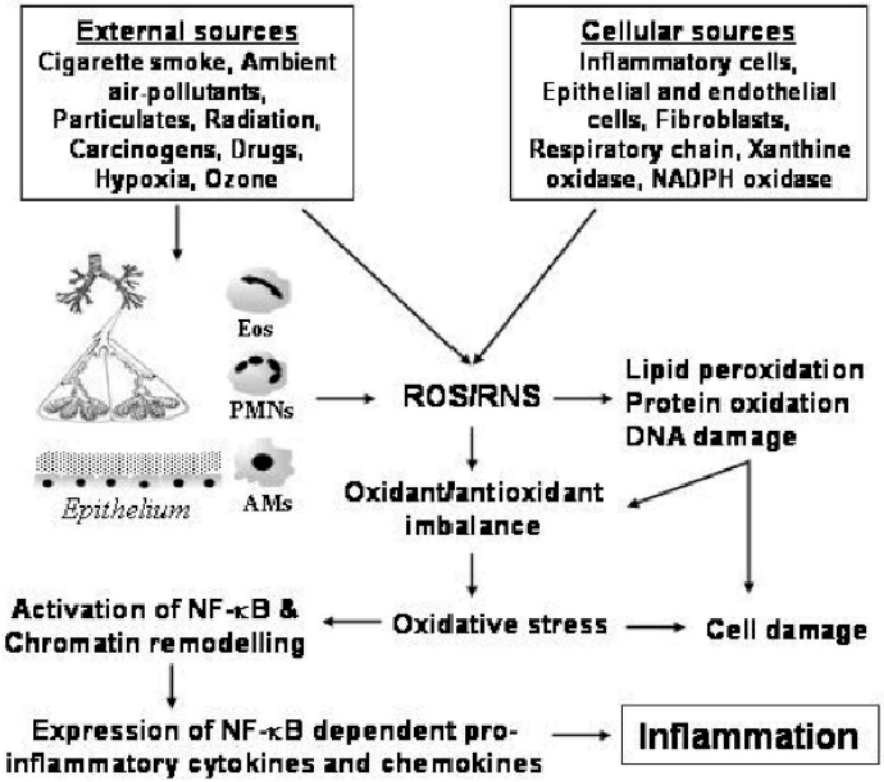
Venkatachari P, Hopke PK. Development and laboratory testing of an automated monitor for the measurement of atmospheric particle-bound reactive oxygen species (ROS) *Aerosol Science and Technology.* 2008;42(8):629–635.

Yungang Wang, Philip K. Hopke, Liping Sun, David C. Chalupa, Mark J. Utell J. Laboratory and Field Testing of an Automated Atmospheric Particle-Bound Reactive Oxygen Species Sampling-Analysis System
***J Toxicol.* 2011**

Biological effect of airborn particles

Biological effect of airborn particles

Genes, epigenetics and inflammation.



Rajendrasozhan S, Yang SR, Edirisinghe I, Yao H, Adenuga, D, Rahman I.
Deacetylases and NF-kappaB in redox regulation of cigarette smoke-induced lung inflammation: epigenetics in pathogenesis of COPD.

***Antioxid Redox Signal*, 2008.**

Biological effect of airborn particles

Ultrafine particles exert most of the oxidant properties of PM

To test this hypothesis, we compared the proatherogenic effects of ambient particles of <0.18 μm (ultrafine particles) with particles of <2.5 μm in genetically susceptible (apolipoprotein E–deficient) mice. These animals were exposed to concentrated **ultrafine particles, concentrated particles of <2.5 μm, or filtered air** in a mobile animal facility close to a Los Angeles freeway.

Ultrafine particle–exposed mice exhibited significantly larger early atherosclerotic lesions than mice exposed to $PM_{2.5}$ or filtered air.

Exposure to ultrafine particles also resulted in an inhibition of the antiinflammatory capacity of plasma high-density lipoprotein and greater systemic oxidative stress as evidenced by a significant increase in hepatic malondialdehyde levels and upregulation of Nrf2-regulated antioxidant genes.

We conclude that ultrafine particles concentrate the proatherogenic effects of ambient PM and may constitute a significant cardiovascular risk factor.

Jesus AAraujo, Berenice Barajas, Michael Kleinman, Xuping Wang, Brian J. Bennett, Ke Wei Gong, Mohamad Navab, Jack Harkema, Constantinos Sioutas, Aldons J. Lusis, Andre E. Nel

Ambient Particulate Pollutants in the Ultrafine Range Promote Early Atherosclerosis and Systemic Oxidative Stress

***Circ Res*.2011**

Biological effect of airborn particles

Oxidative stress

•Reactive oxygen species (ROS) include oxygen-containing compounds with strong oxidative capacity

•Molecules like

- **•H_2O_2**
- **•organic peroxides and nitrite peroxides**
- **•ions like hypochlorite ion (OCl^-) peroxide anion (O_2^-), and radicals like hydroxyl (OH) and superoxide radicals (O_2^-)**
- **•organic peroxyl (ROO)**

are all grouped as **"reactive oxygen species".**

Biological effect of airborn particles

Oxidative stress

- **ROS can be generated endogenously during the cell metabolism through reaction of the inhaled PM components such as metals (Fe, Cu, and Zn) and polycyclic aromatic hydrocarbon (PAH)**

- **The excess oxidative stress from the ROS leads to:**
  - **lipid peroxidation**
  - **DNA damage**
  - **Protein oxidation**

Biological effect of airborn particles

Oxidative stress

- Oxidative stress been implicated in the increased incidence of:
  - cardiopulmonary disease
  - asthma
  - chronic obstructive pulmonary disease

- Recently, ROS was found to be present in PM, especially in the UFPs component

- These particle-bound ROS are believed to induce effects on human health analogous to that of endogenous ROS

Ntziachristos L, Froines JR, Cho AK, Sioutas C.
Relationship between redox activity and chemical speciation of size-fractionated particulate matter
Part Fibre Toxicol. 2007

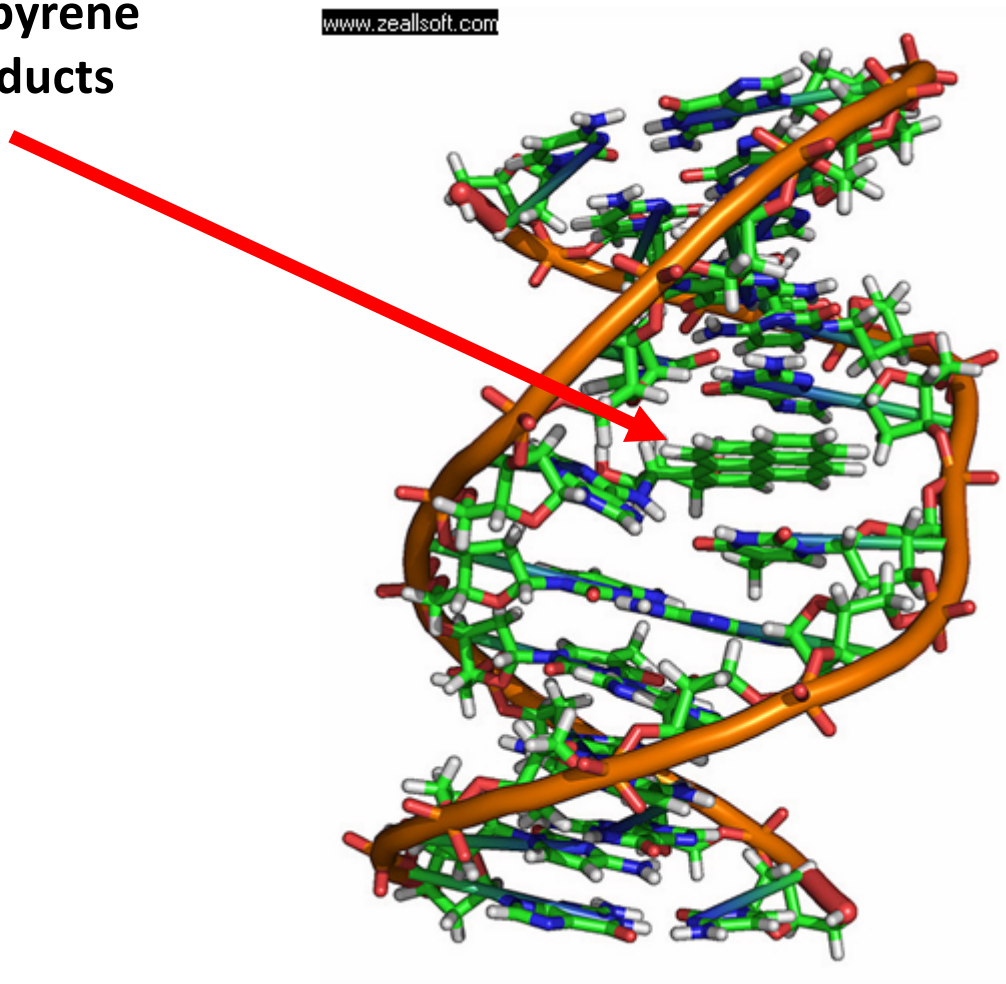
Venkatachari P, Hopke PK. Development and laboratory testing of an automated monitor for the measurement of atmospheric particle-bound reactive oxygen species (ROS) *Aerosol Science and Technology.* 2008;42(8):629–635.

Yungang Wang, Philip K. Hopke, Liping Sun, David C. Chalupa, Mark J. UtellJ Laboratory and Field Testing of an Automated Atmospheric Particle-Bound Reactive Oxygen Species Sampling-Analysis System
J Toxicol. 2011

Biological effect of airborn particles

Genotoxicity: DNA-adducts

Benzo(a)pyrene
DNA adducts



Biological effect of airborn particles

Genotoxycity: DNA-adducts

Personal exposure to PM2.5 correlates with the presence of **DNA-adducts 8-oxodG** in circulating lymphocytes, with an 11% increase for every 10 ug/m3 increase in personal PM2.5 exposure

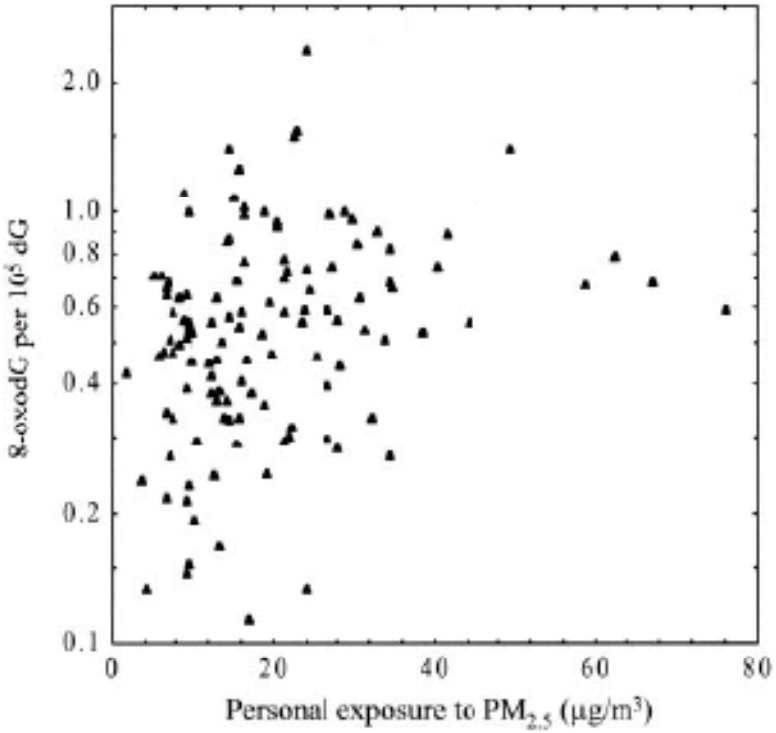


Fig. 1. Relationship between oxidative DNA damage assessed as 8-oxodG in lymphocyte DNA and personal exposure to $PM_{2.5}$ assessed over 48 h in 68 subjects with up to four samples each collected in each of the four seasons.

Mette Sørensen, Herman Autrup, Ole Hertel, Aåkan Wallin, Lisbeth E. Knudsen, and Steffen Loft2
Personal Exposure to PM2.5 and Biomarkers of DNA Damage
***Cancer Epidemiology, Biomarkers & Prevention* 2003**

Biological effect of airborn particles
Genotoxycity: DNA-adducts

After 3 hour exposure to secondhand smoke:

- **increase in blood PHAs concentration were found**

- **smoking-specific DNA adducts were found in circulating lymphocytes (co-migration with anti-DNA benzo(a)pyrene diol-epoxyde)**

Besaratinia A, Maas LM, Brouwer EMC, et al.
A molecular dosimetry approach to assess human exposure to environmental tobacco smoke in pubs.
***Carcinogenesis* 2002**

Biological effect of airborn particles
Genotoxycity: DNA fragmentation

DNA damage and repair capacity by comet assay in lymphocytes of white-collar active smokers and passive smokers (non- and ex-smokers) at workplace

Maria Enrica Fracasso [a,*], Denise Doria [a], Paola Franceschetti [a], Luigi Perbellini [b], Luciano Romeo [b]

[a] Department of Medicine and Public Health, Section of Pharmacology, University of Verona, Policlinico GB Rossi, P.le Scuro 10, 37134 Verona, Italy

[b] Department of Medicine and Public Health, Section of Occupational Health, University of Verona, Policlinico GB Rossi, P.le Scuro 10, 37134 Verona, Italy

Toxicology Letters, 2006

Biological effect of airborn particles
Genotoxycity: DNA fragmentation

Secondhand smoke exposure genotoxycity by *comet assay*
(% fragmented DNA on electrophoretic migration)

Table 4
Mean values ± S.D. of biomarkers of effects in lymphocytes of never smokers (controls), active smokers and passive smokers (non- and ex-smokers)

Group (no. subjects)	TM	%DNA	TL	Comets
Never smokers (47)	0.31 ± 0.03	2.62 ± 0.16	19.10 ± 1.24	8.35±0.85
Active smokers (41)	1.17 ± 0.22, $P = 0.0001$[a]	5.18 ± 0.66, $P = 0.0025$[a]	33.54 ± 1.88, $P = 0.0001$[a]	19.78±1.66, $P = 0.0001$[a]
Passive smokers				
Non-smokers (43)	0.48 ± 0.05, ns[a]	3.13 ± 0.25, ns[a]	22.44 ± 0.73, $P = 0.0166$[a]	13.02 ± 1.23, $P = 0.0285$[a]
Ex-smokers (24)	0.56 ± 0.06, $P = 0.0111$[a]	3.24 ± 0.26, ns[a]	26.20 ± 1.66, $P = 0.0021$[a]	13.33 ± 1.51, $P = 0.0052$[a]

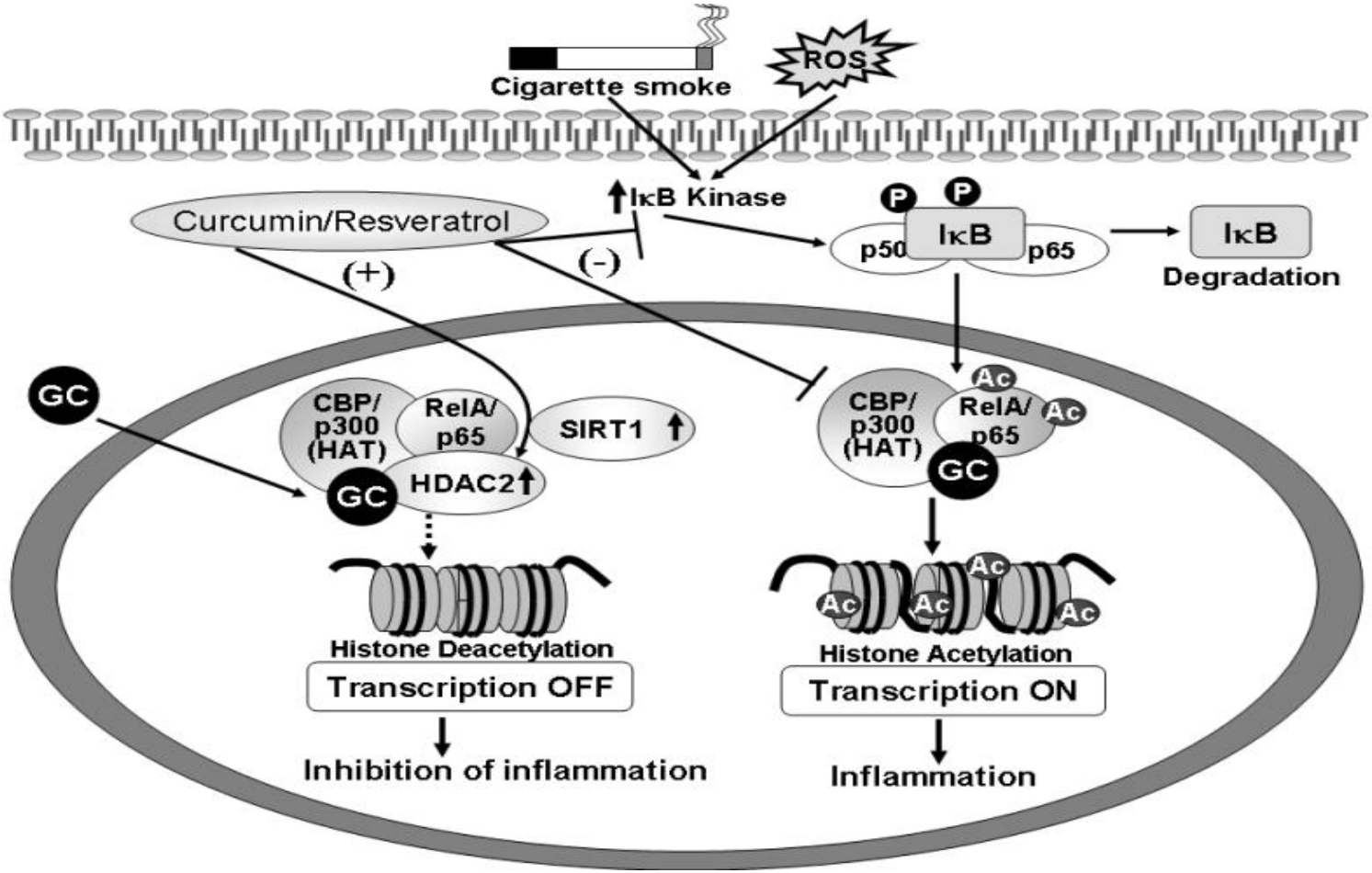
ns: Not significant.
[a] Active and passive smokers compared to never smokers ($P < 0.05$) by Mann–Whitney U-test.

Fracasso ME, et al., *Toxicology Letters*, 2006

Biological effect of airborn particles

Epigenetics: alteration in transcription rates.

Up- and down-regulation of inflammation genes by means of cytoplasmic alterations (methylation / de-methylation)



Rahman I.

Dietary polyphenols mediated regulation of oxidative stress and chromatin remodeling in inflammation.
Nutr Rev. **2008**

Biological effect of airborn particles

Kendall M, Ding P, Kendall K.

Particle and nanoparticle interactions with fibrinogen: the importance of aggregation in nanotoxicology.

Abstract

Ingested, inhaled or injected particles come into contact with biological fluids containing polymers, such as the protein fibrinogen. We studied interactions between well-characterized submicron particles or nanoparticles (NPs) and human fibrinogen. In vitro aggregation and zeta potential measurements of different sized and functionalized polystyrene, carbon black and silica NPs suspended in fibrinogen solutions were made. Particle size, surface charge and aggregation behaviour significantly changed in the presence of fibrinogen. Polymer (protein) bridging and bridge flocculation was observed. We concluded: (1) NP aggregation rate in a fibrinogen solution depended on particle surface type; (2) amine-functionalized particles aggregated more slowly in fibrinogen; and (3) particle morphology strongly influenced biologically available surface for protein attachment, but this did not correlate well with particle surface area for complex particles (calculated or measured). Interaction of particles and NPs with pro-coagulant polymers may therefore dictate the NP surface dose presentation to cells/organs and subsequent cellular effects, in and ex vivo.

Nanotoxicology **2011**

Biological effect of airborn particles

Oxidative stress

• Size-fractionated (i.e. < 0.15; < 2.5 and 2.5 – 10 μm in diameter) ambient PM samples were collected from four different locations in the period from June 2003 to July 2005, and were chemically analyzed for elemental and organic carbon, ions, elements and trace metals and polycyclic aromatic hydrocarbons

•The redox activity of the samples was evaluated by means of the dithiothreitol activity assay and was related to their chemical speciation by means of correlation analysis

•Our analysis indicated

- **•a higher redox activity on a per PM mass basis for ultrafine (< 0.15 μm) particles compared to those of larger sizes.**
- **•A high correlation of the PM redox activity with the organic carbon (OC) content of PM as well as the mass fractions of species such as polycyclic aromatic hydrocarbons (PAH), and selected metals**

Ntziachristos L, Froines JR, Cho AK, Sioutas C.
Relationship between redox activity and chemical speciation of size-fractionated particulate matter
***Part Fibre Toxicol.* 2007**

Biological effect of airborn particles

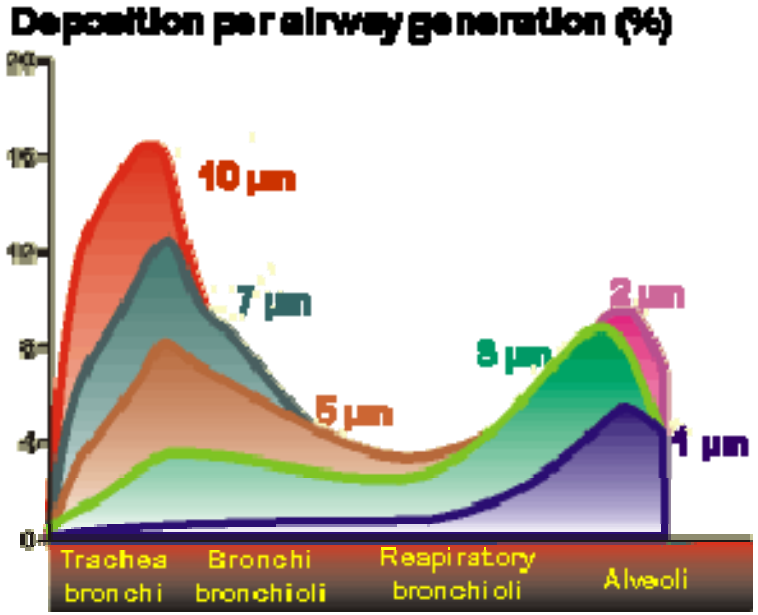
Smoking, COPD (Chronic Osbtructive Pulmonary Disease), and genes

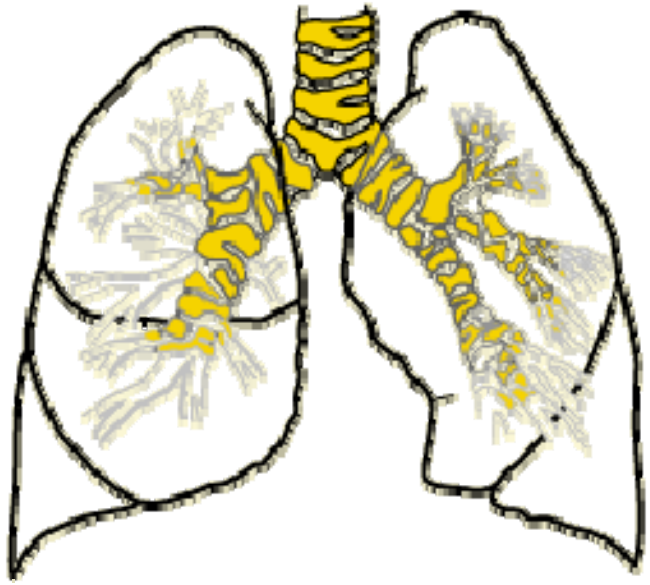
- Smoking-induced changes include the up-regulation of inflammatory genes (IL-1b, IL-6, IL-8, CCL2, and CCL8) and the decreased expression of growth factor/receptor genes (BMPR2, CTGF, FGF1, KDR and TEK) and genes coding for vessel maintenance factors (EDNRB). All these genes exhibited a similar profile in moderate COPD patients. The up-regulation of MMP1 and MMP9 was the main change associated with COPD.
- Inflammatory genes as well as the endothelial selectin gene (SELE) were down-regulated in patients with more severe COPD. Clustering analysis revealed a closer relationship between moderate COPD and smokers than between both subsets of COPD patients for this selected set of genes.
- The study reveals striking similarities between smokers and COPD patients with moderate disease emphasizing the crucial role of cigarette smoking in the genesis of these changes, and provides additional evidence of the involvement of the matrix metalloproteinase's in the remodeling process of the lung in COPD

Laia Llinàs, et al.
Similar gene expression profiles in smokers and patients with moderate COPD.
Pulmonary Pharmacology & Therapeutics 2011

Particle distribution in the human body

Airways



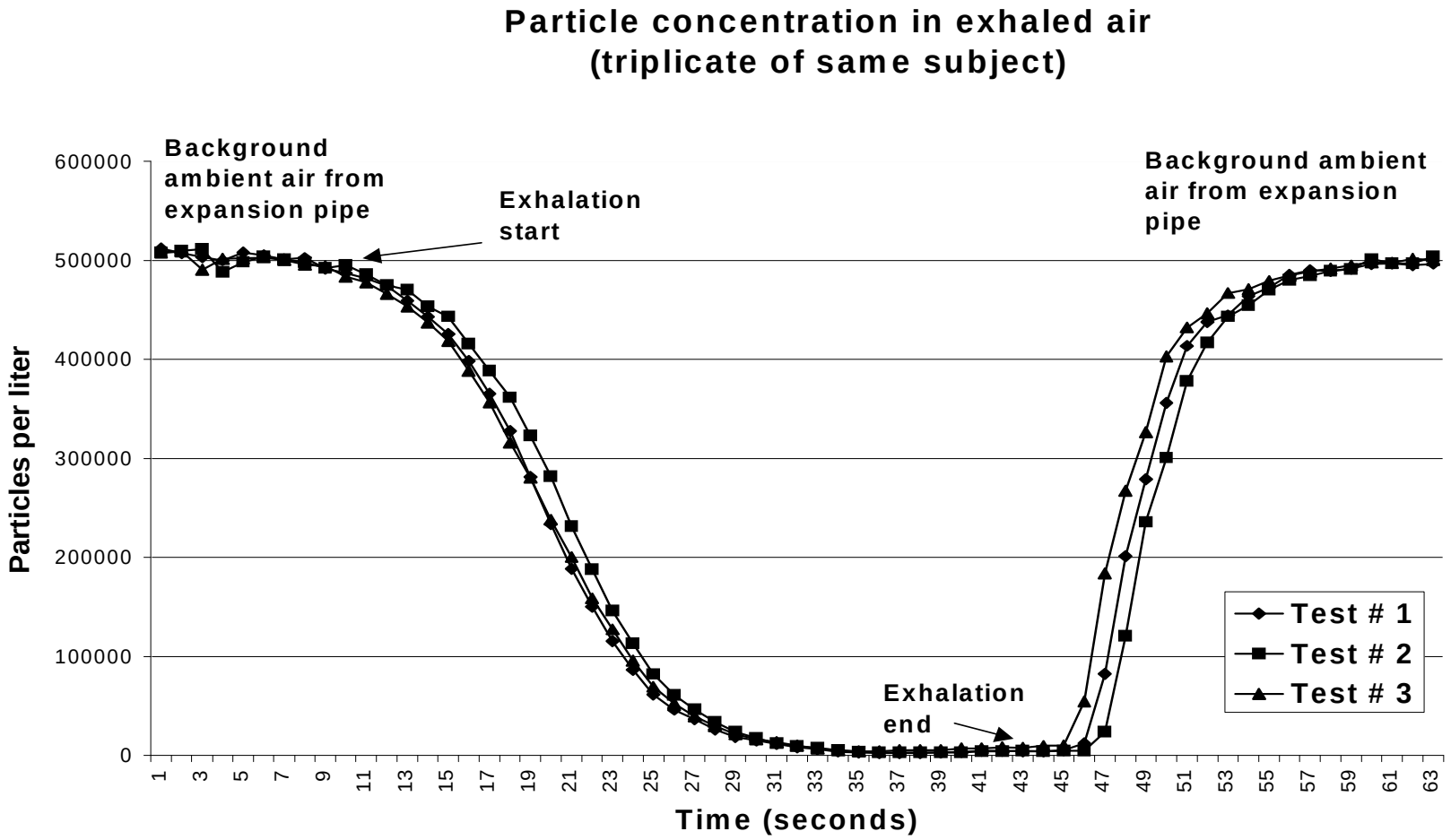


Particle distribution in the human body

Airways

Particle distribution in the human body

Airways



Invernizzi G, Ruprecht A, et al
***Biomarkers*, 2006.**

Particle distribution in the human body

Pulmonary translocation: direct or macrophage-mediated alveolar crossing

Translocation of inhaled ultrafine particles from the lungs into the blood may impair cardiovascular function. We administered ultrafine (20-nm) and fine (200-nm) gold colloid or fluorescein-labeled polystyrene particles to mice intratracheally and examined their localization in the lung and extrapulmonary organs.

After administration of 20- or 200-nm fluorescent particles, free particles were detected infrequently in blood vessels, on the endocardial surface, and in the kidney and liver only in the mice that received 20-nm particles, whereas phagocytes containing 20- or 200-nm particles were found in the extrapulmonary tissues.

Fluorescent particle-laden alveolar macrophages administered intratracheally translocated from alveoli to extrapulmonary organs via the blood circulation.

Thus, small amounts of ultrafine particles are transported across the alveolar wall into the blood circulation via endocytotic pathways, but particle-laden alveolar macrophages translocate both ultrafine and fine particles from the lungs to the extrapulmonary organs.

Furuyama A, Kanno S, Kobayashi T, Hirano S.
Extrapulmonary translocation of intratracheally instilled fine and ultrafine particles via direct and alveolar macrophage-associated routes.

Arch Toxicol. **2009**

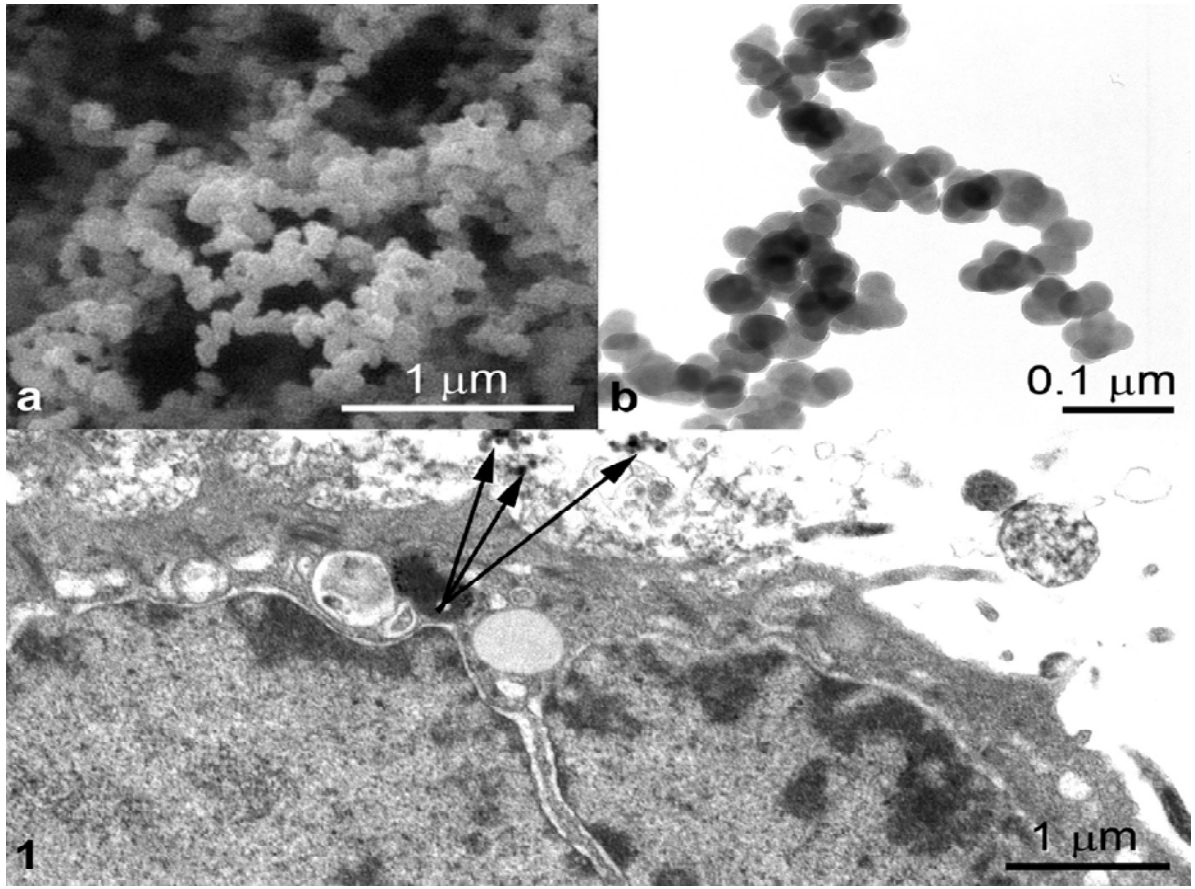
Particle distribution in the human body

How do PAHs enter the cell?

Figure 1.
(A) An SEM image illustrating the lacy openwork character typical of the BDS aggregates; individual, solid, spherical particles, 50–70 nm in diameter, are the fundamental structural units of the aggregates.

(B) A TEM image of BDS showing individual spheres, 30–50 nm in diameter, arranged in branching clusters. The difference in diameter of the spheres in the SEM versus TEM images results from the 10–20 nm gold/palladium conductive coating that was applied to the SEM samples.

(C) A TEM image of a portion of the surface of a BEAS-2B cell with individual spherical particles, 30–50 nm in diameter, and small aggregates (arrows) immediately adjacent to the cell membrane.
Cells were photographed after 42 hr exposure.



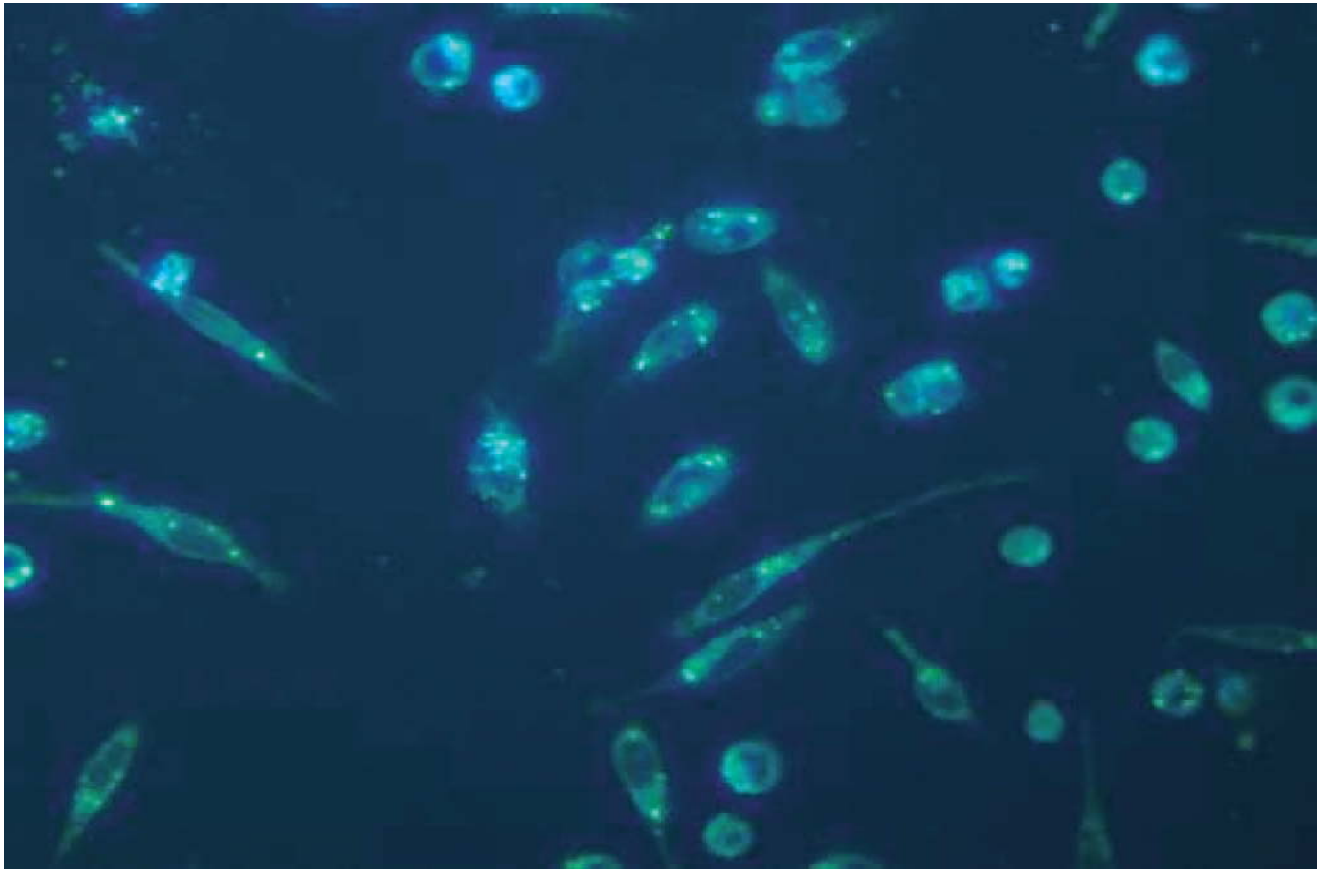
Penn A, Murphy G, Barker S,Henk W,Penn L
Combustion-Derived Ultrafine Particles Transport Organic Toxicants to Target Respiratory Cells.
Environ Health Perspect 2005

Particle distribution in the human body

How do PAHs enter the cell? The case of butadiene particles

Figure 2. Fluorescence localized in punctate cytoplasmic vesicles of BEAS-2B cells. Cells were photographed 4 hr after BDS, without carrier, was sprinkled onto the surface of the BEGM overlying the cells.

Excitation/emission wavelengths = 360/420 nm. Magnification, 400·.



Penn A, Murphy G, Barker S,Henk W,Penn L
Combustion-Derived Ultrafine Particles Transport Organic Toxicants to Target Respiratory Cells.
Environ Health Perspect 2005

Spatial variability

Spatial variability of PM and epidemiology

Schools

Paired indoor and outdoor concentrations of fine and coarse particulate matter (PM), PM2.5, reflectance black carbon (BC), and nitrogen dioxide (NO(2)) were determined for sixteen weeks in 2008 at four elementary schools (two in high and two in low traffic density zones) in a U.S.-Mexico border community to aid a binational health effects study.

- **Strong spatial heterogeneity was observed for all outdoor pollutant concentrations.**
- **Concentrations of all pollutants, except coarse PM, were higher in high traffic zones than in the respective low traffic zones.**
- **Black carbon and NO (2) appear to be better traffic indicators than fine PM.**
- **Indoor air pollution was found to be well associated with outdoor air pollution, although differences existed due to uncontrollable factors involving student activities and building/ventilation configurations.**
- **Results of this study indicate substantial spatial variability of pollutants in the region, suggesting that children's exposures to these pollutants vary based on the location of their school.**

Raysoni AU, Sarnat JA, Sarnat SE, Garcia JH, Holguin F, Luèvano SF, Li WW.

Binational school-based monitoring of traffic-related air pollutants in El Paso, Texas (USA) and Ciudad Juárez, Chihuahua (México).
***Environ Pollut.* 2011**

Spatial variability of PM and epidemiology

Metropolitan cities: New York, USA.

Peltier RE, Lippmann M.

Spatial and seasonal distribution of aerosol chemical components in New York City: (1) Incineration, coal combustion, and biomass burning.

J Expo Sci Environ Epidemiol.2011

We describe spatial and temporal patterns of fine particulate matter (PM(2.5)) and of 12 of its constituent chemical elements commonly observed in measurements at residential locations in New York City (NYC).

- **These elements, that is, Ni, V, As, Se, S, Cl, Na, K, Pb, Cu, Zn, and Mn, had significant spatial and temporal variability at 10 PM (2.5) sampling locations during our winter and summer sampling campaigns.**
- By grouping the elements into traditional source apportionment categories, we show that specific chemical components of PM (2.5) considered to have a common source category, such as As and Se for coal combustion, do not always follow the same temporal or spatial pattern.
- PM (2.5) mass had only limited spatial variability and a slight summertime concentration enhancement. Measurements at residential locations were, on average, consistent with EPA sampling network measurements, although we found that during times of low regional concentration, EPA measurements underestimated the PM(2.5) concentration at residential locations.

These results have implications for improved understanding of exposures to specific sources of PM (2.5), and raise some concerns about source profiles used in source-receptor modeling tracer input selection.

Spatial variability of PM and epidemiology

Metropolitan cities: Quito, Ecuador.

We measured PAH continuously for one year at two residential sites in Quito, and PAH and traffic patterns for one week near a busy roadway.

At the near-roadway site, PAH concentrations were 3–6-fold higher than at the residential sites. Cars and buses accounted for >95% of PAH at the near-roadway site.

Brachtl MV, Durant JL, Perez CP, Oviedo J, Sempertegui F, Naumova EN, Griffiths JK

Spatial and temporal variations and mobile source emissions of polycyclic aromatic hydrocarbons in Quito, Ecuador
***Environ Pollut.* 2009**

Spatial variability of PM and epidemiology

Metropolitan cities: Milano, Italy.

ARTICLE IN PRESS AEA10365_proof ■ 18 April 2011 ■ 1/6

Atmospheric Environment xxx (2011) 1–6

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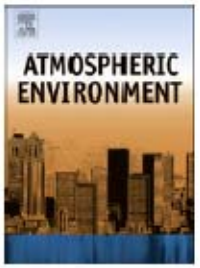
journal homepage: www.elsevier.com/locate/atmosenv



Measurement of black carbon concentration as an indicator of air quality benefits of traffic restriction policies within the ecopass zone in Milan, Italy

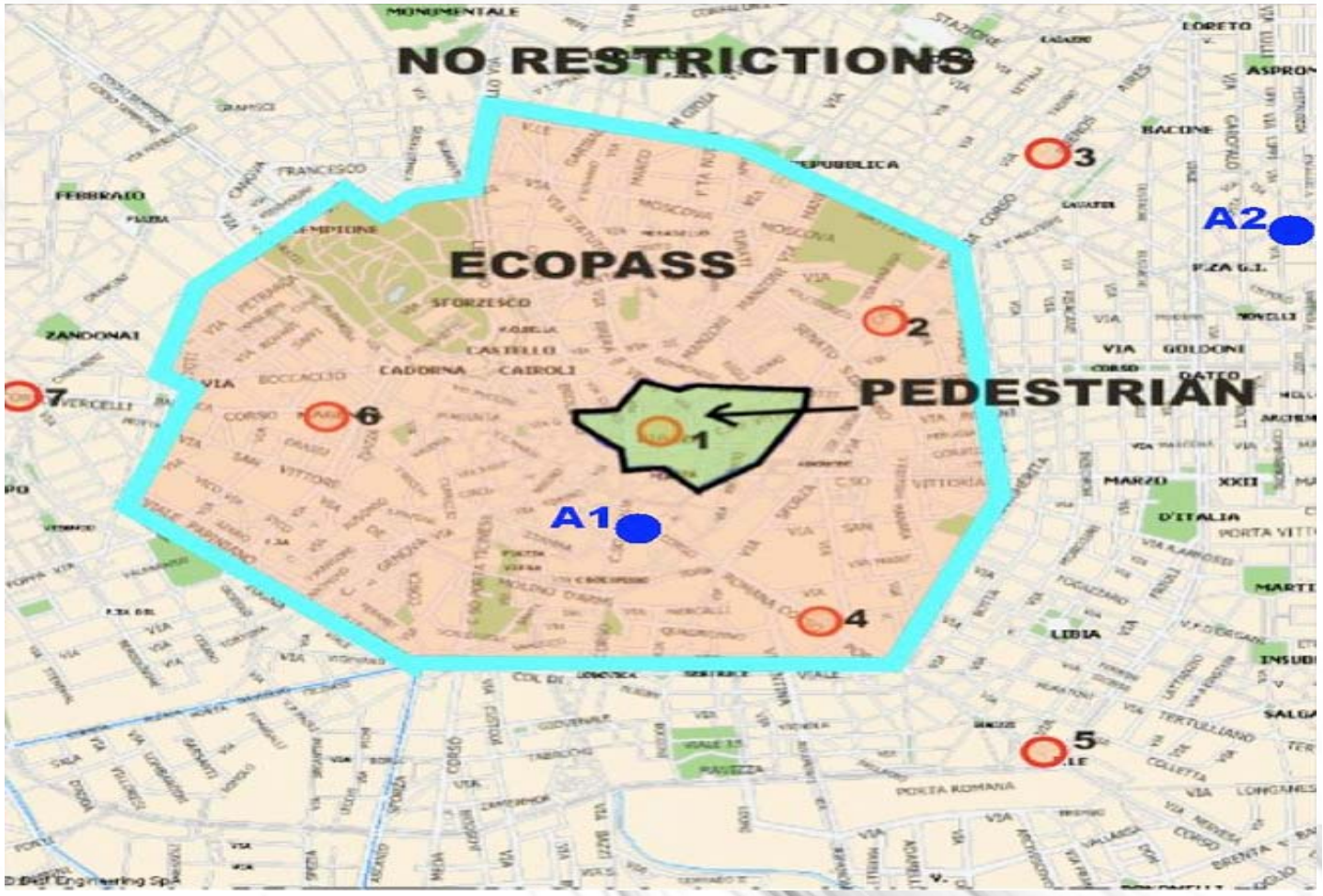
Giovanni Invernizzi [a,*], Ario Ruprecht [a], Roberto Mazza [b], Cinzia De Marco [b], Griša Močnik [c], Costantinos Sioutas [d], Dane Westerdahl [e]

[a] LARS, Environmental Research Laboratory SIMG-Italian College GPs, ISDE-International Doctors for the Environment, Milan, Italy
[b] Istituto Nazionale dei Tumori, Milan, Italy
[c] Aerosol d.o.o., Ljubljana, Slovenia
[d] University of Southern California, Los Angeles, CA, USA
[e] Cornell University, Ithaca, NY, USA

PM and PM components spatial variability

Metropolitan cities: Milano, Italy.

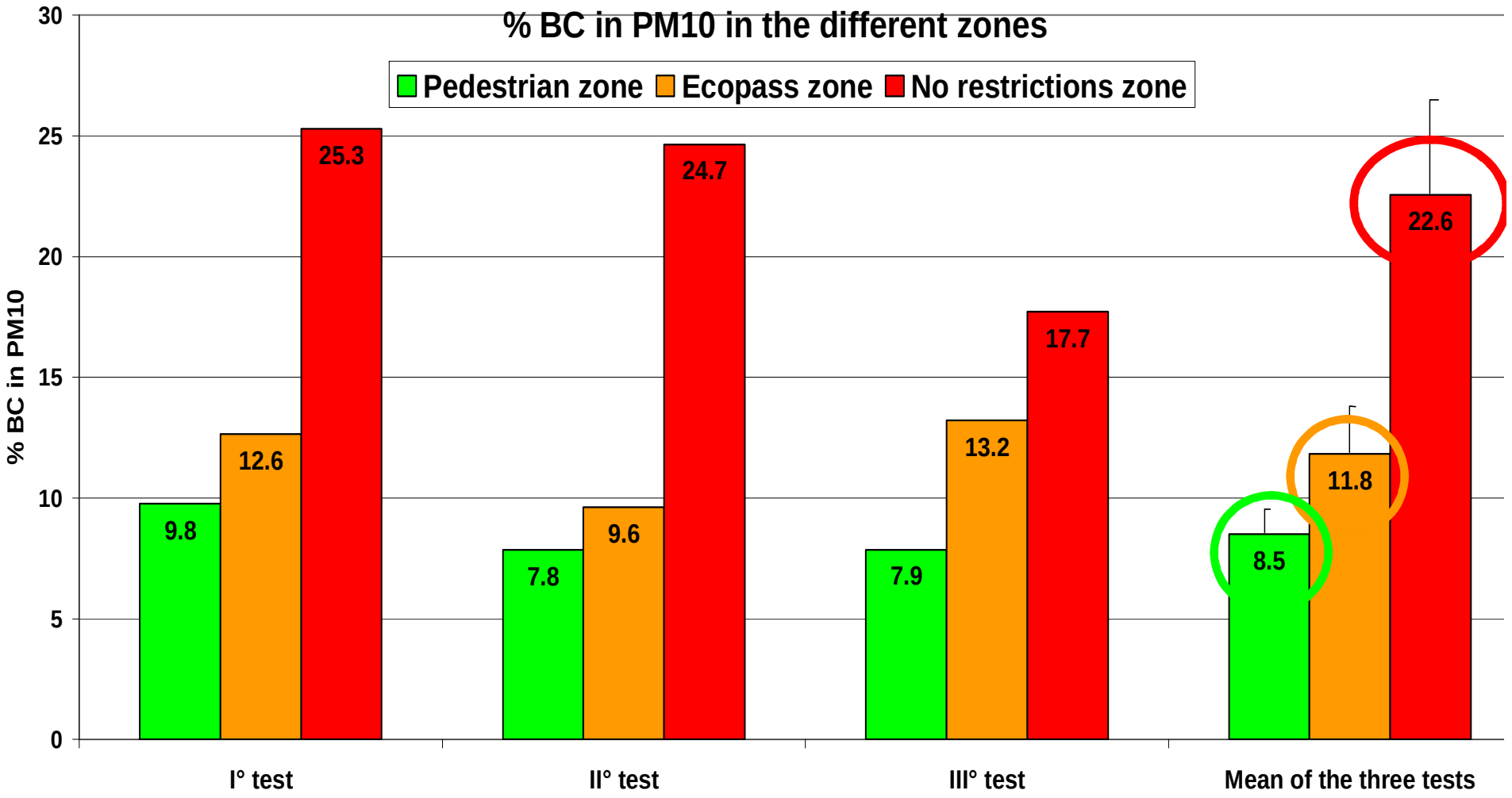
Black carbon concentration gradients in 1 km range



PM and PM components spatial variability

Metropolitan cities: Milano, Italy.

Black carbon concentration gradients in 1 km range



BC / PM_{10} ratios in the zones with different traffic intensity

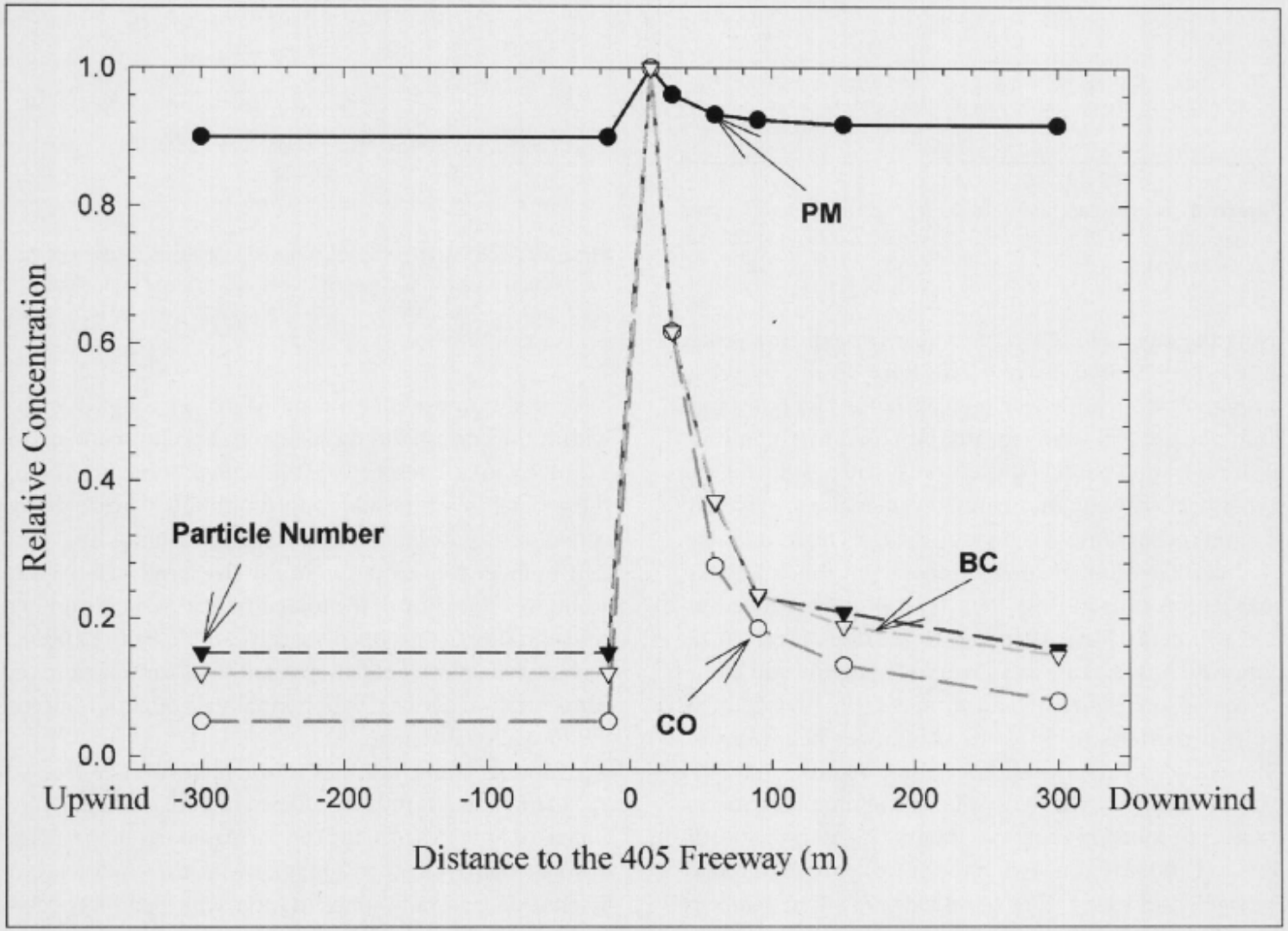


Figure 8. Relative mass, number, BC, and CO concentrations vs. downwind distance.

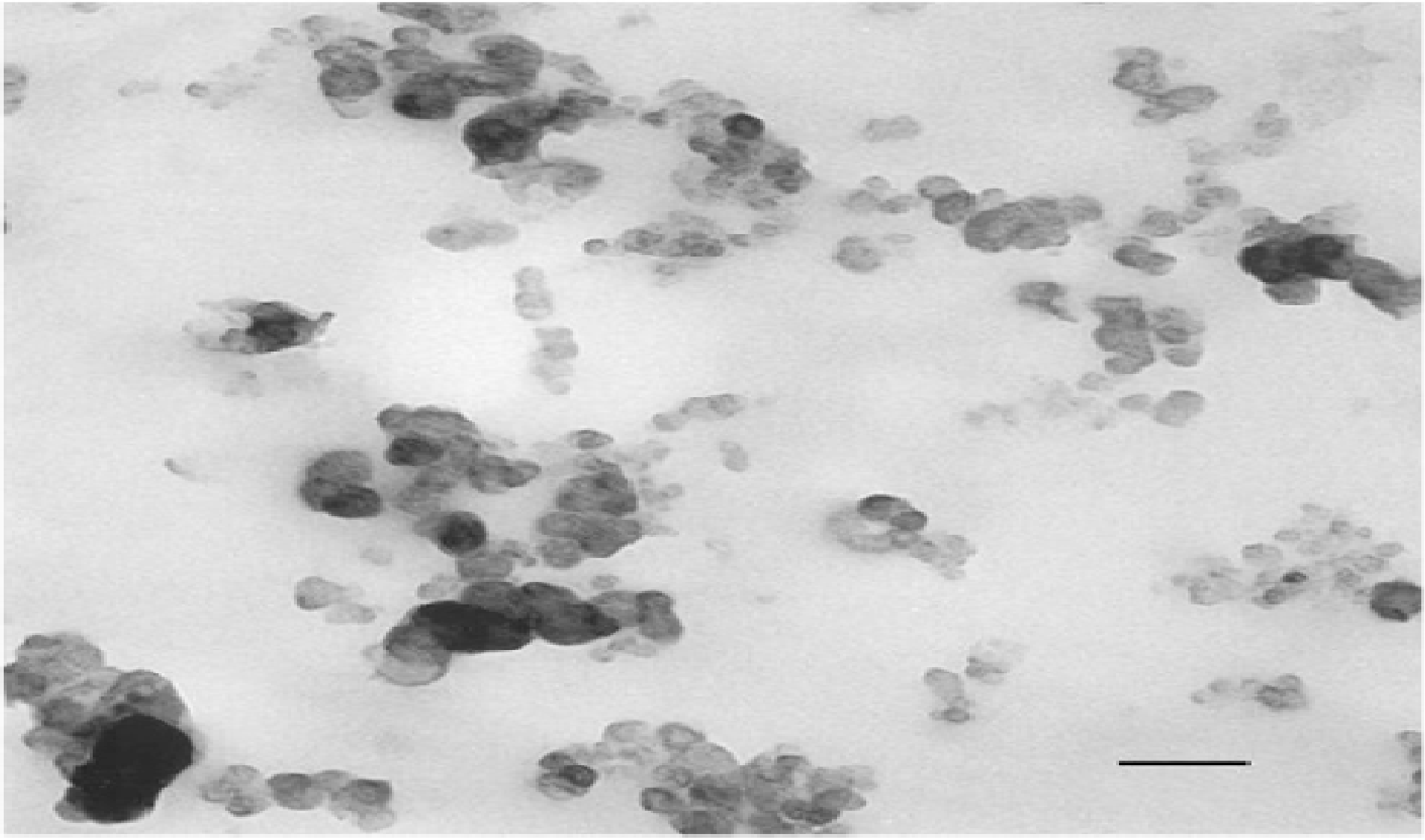


Figure 1. Ambient particulate matter (PM) sampled from a British city and imaged using electron microscopy. Inhalable PM (< 10 μm in aerodynamic diameter) consists of aggregates of very small carbon spherules. *Scale bar* = 100 nm. PM from biomass smoke consists of similar aggregates of carbon spherules. Reprinted by permission from Reference 58.

Grigg J, Proc Am Thorac Soc Vol 6. pp 564-569, 2009

PM and PM components spatial variability

Epidemiological evidence

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Respiratory Effects of Exposure to Diesel Traffic in Persons with Asthma

James McCreanor, M.R.C.P., [illegible], Mark J. Nieuwenhuijsen, Ph.D.,
James Stewart-Evans, M.Sc., Eleni Malliarou, M.Sc., Lars Jarup, Ph.D.,
Robert Harrington, M.S., Magnus Svartengren, M.D., In-Kyu Han, M.P.H.,
Pamela Ohman-Strickland, Ph.D., Kian Fan Chung, M.D.,
and Junfeng Zhang, Ph.D.

N Engl J Med 2007;357:2348-58.

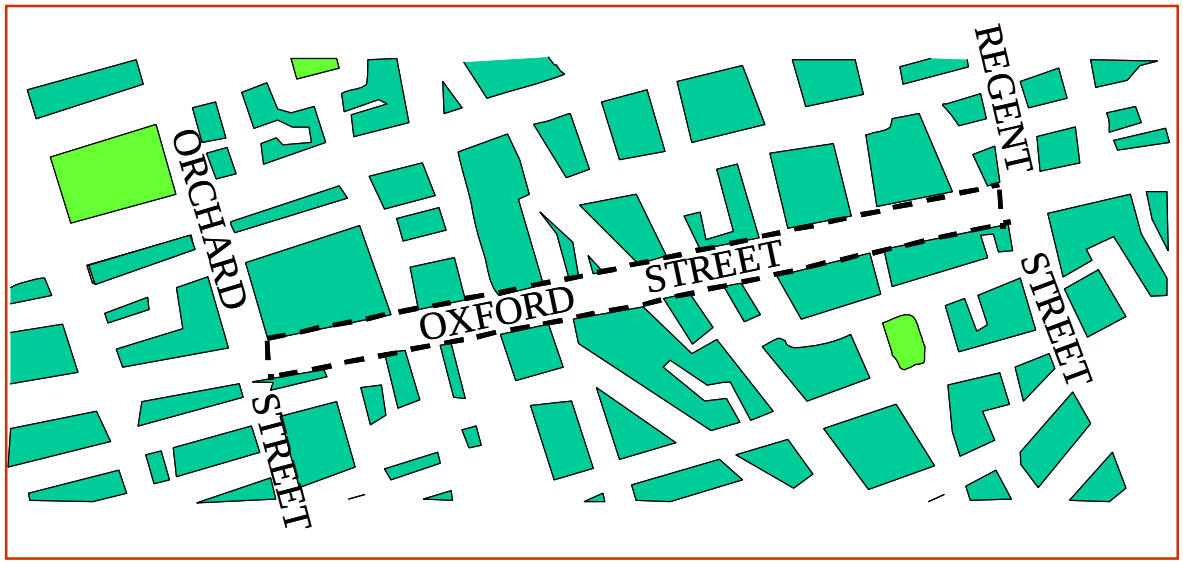
PM and PM components spatial variability

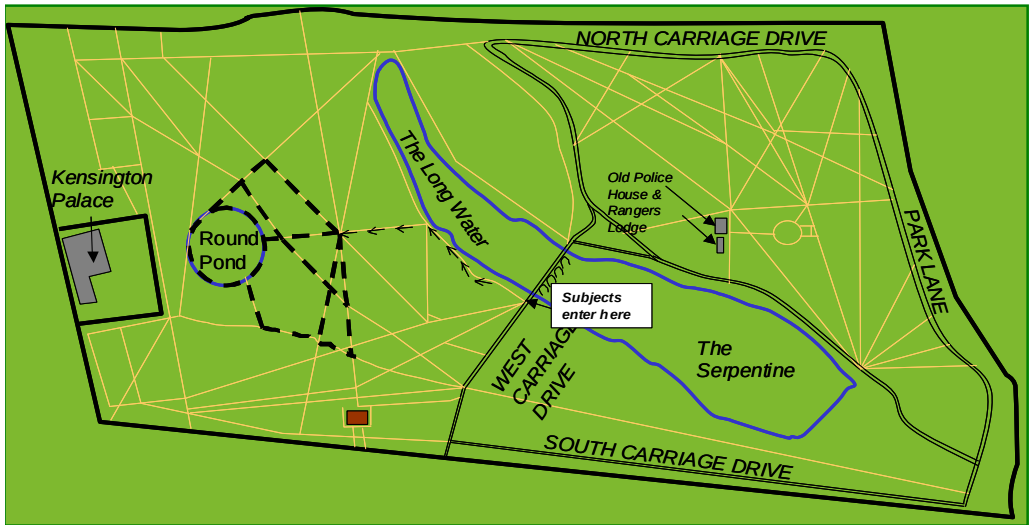
Epidemiological evidence

Respiratory Effects of Exposure to Diesel Traffic in Persons with Asthma (in London city)
McCreanor et al, *New England J Medicine* 2007; 357:2348

Diesel bus route

Oxford street





Hyde Park

No traffic

PM and PM components spatial variability

Epidemiological evidence

Table 1. Baseline Characteristics of the Study Participants.*

Characteristic	All Participants (N=60)	Participants with Mild Asthma (N=31)	Participants with Moderate Asthma (N=29)	P Value
Female sex — no. (%)	29 (48)	14 (45)	15 (52)	0.61
Age — yr				0.13
Mean	32	31	34	
Range	19–55	20–49	19–55	
Height — cm	172±8.8	172±8.4	171±9.3	0.67
Body-mass index†	23.2±3.7	23.2±3.6	23.2±3.9	0.98
White race — no. (%)‡	47 (78)	26 (84)	21 (72)	0.28
FEV_1 — % of predicted value	88.9±10.8	93.4±6.9	84.1±12.3	<0.001
Atopy — no. (%)§	42 (84)	24 (89)	18 (78)	0.31
Methacholine PC_{20} — mg/ml¶	2.82±2.47	2.73±2.43	2.92±2.56	0.78
Treatment with inhaled corticosteroids — no. (%)	37 (62)	12 (39)	25 (86)	<0.001
Unlimited exercise tolerance — no. (%)	51 (85)	28 (90)	23 (79)	0.23
Asthma affected by exercise — no. (%)				0.27
Yes	44 (73)	20 (65)	24 (83)	
Not sure	4 (7)	3 (10)	1 (3)	
Asthma affected by traffic fumes — no. (%)				0.19
Yes	17 (28)	7 (23)	10 (34)	
Not sure	30 (50)	19 (61)	11 (38)	

* Plus–minus values are means ±SD. P values are for comparisons according to the severity of asthma. FEV_1 denotes forced expiratory volume in 1 second.
† The body-mass index is the weight in kilograms divided by the square of the height in meters.
‡ Race was self-reported.
§ Ten participants (six with moderate asthma) did not have skin-prick tests.
¶ Methacholine PC_{20} denotes the concentration of methacholine required to provoke a 20% decrease in the FEV_1.

Table 2. Exposure Measurements for Oxford Street and Hyde Park and Lung Function before Exposure.*

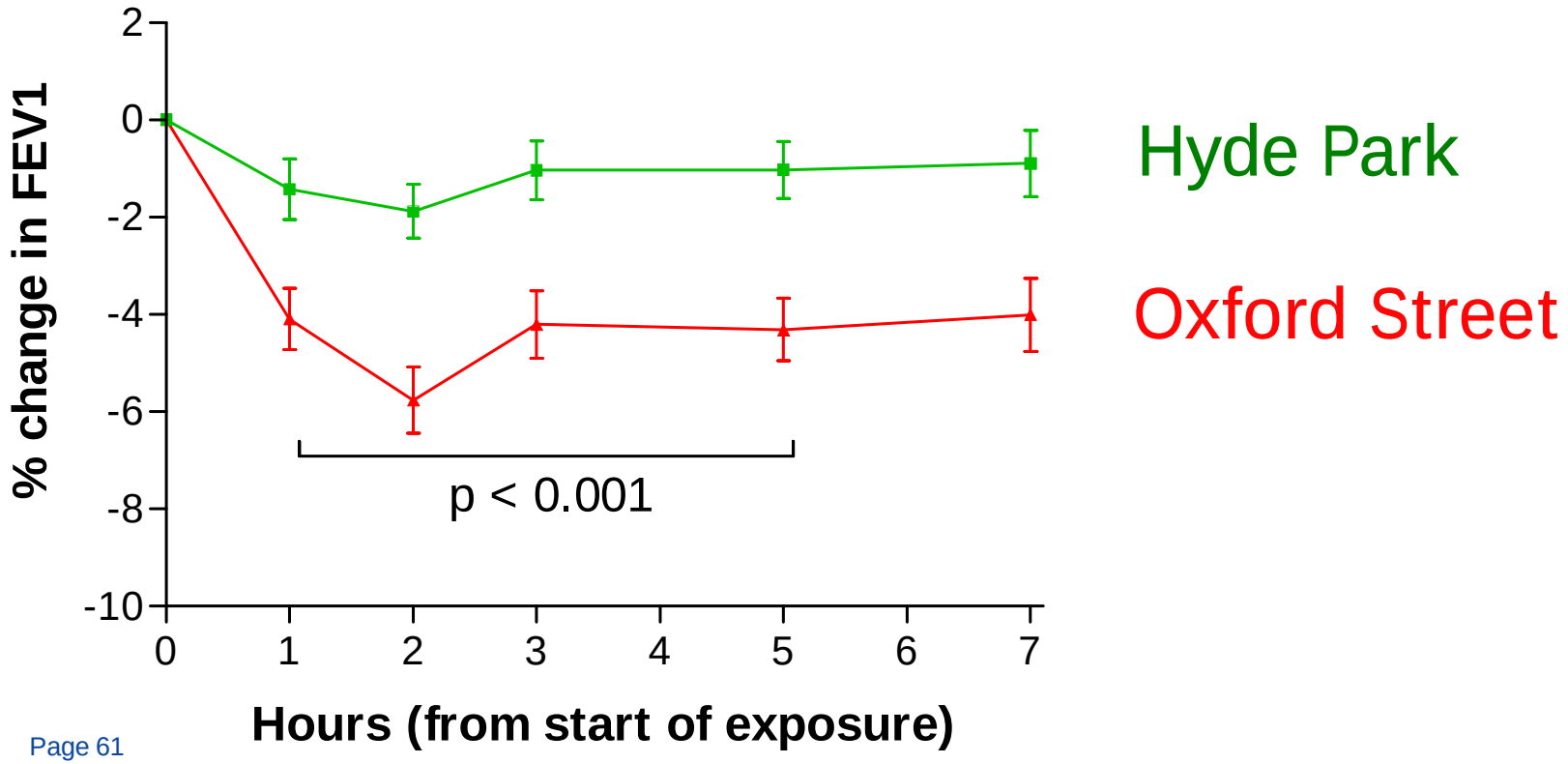
Variable	Oxford Street	Hyde Park	P Value
Exposure			
Nitrogen dioxide in previous week ($\mu g/m^3$)			0.90
Median	23.5	22.3	
Range	1.46–135	0.49–61.6	
Temperature (°C)			0.04
Median	10.8	9.1	
Range	4–17.1	2.5–17.2	
Relative humidity (%)			0.03
Median	66	76	
Range	41.9–93.2	43.2–93.3	
$PM_{2.5}$ ($\mu g/m^3$)			<0.001
Median	28.3	11.9	
Range	13.9–76.1	3–55.9	
Ultrafine particles (thousands/cm^3)			<0.001
Median	63.7	18.3	
Range	39.5–92.4	10.3–37.1	
Elemental carbon ($\mu g/m^3$)			<0.001
Median	7.5	1.3	
Range	3.9–16	0.4–6.7	
Nitrogen dioxide ($\mu g/m^3$)			<0.001
Median	142	21.7	
Range	10.7–289	2.4–146	
PM_{10} ($\mu g/m^3$)†			0.03
Median	125	72	
Range	62–161	60–100	

PM and PM components spatial variability

Epidemiological evidence

Lung function (FEV1) of asthmatics decreased significantly while walking along the diesel bus route (Oxford street)

McCreanor et al, NEJM 2007



Spatial variability and misclassification: implications for epidemiological studies

Community-level spatial heterogeneity of chemical constituent levels of fine particulates and implications for epidemiological research

Bell ML, Ebis Ku, Peng RD

***J Exposure Science Environmental Epidemiology* 2011**

- **Studies of the health impacts of airborne particulates' chemical constituents typically assume spatial homogeneity and estimate exposure from ambient monitors.**
- **However, factors such as local sources may cause spatially heterogeneous pollution levels.**

Community-level spatial heterogeneity of chemical constituent levels of fine particulates and implications for epidemiological research

Bell ML, Ebis Ku, Peng RD

***J Exposure Science Environmental Epidemiology* 2011**

Spatial variability and misclassification: implications for epidemiological studies

- This work examines the degree to which constituent levels vary within communities and whether exposure misclassification is introduced by spatial homogeneity assumptions
- Analysis considered PM2.5, elemental carbon (EC), organic carbon matter, ammonium, sulfate, nitrate, silicon, and sodium ion (Na) for the United States, 1999–2007.

Community-level spatial heterogeneity of chemical constituent levels of fine particulates and implications for epidemiological research

Bell ML, Ebis Ku, Peng RD

***J Exposure Science Environmental Epidemiology* 2011**

Spatial variability and misclassification: implications for epidemiological studies

- Spatial heterogeneity was present for all constituents, yet lower for ammonium, sulfate, and nitrate. Lower correlations were associated with higher distance between monitors, especially for nitrate and sulfate, and with lower long-termlevels, especially for sulfate and Na. Analysis of colocated monitors revealed measurement error for all constituents, especially EC and Na.
- Exposure misclassification may be introduced into epidemiological studies of PM2.5 constituents due to spatial variability, and is affected by constituent type and level.
- When assessing health effects of PM constituents, new methods are needed for estimating exposure and accounting for exposure error induced by spatial variability.

Community-level spatial heterogeneity of chemical constituent levels of fine particulates and implications for epidemiological research

Bell ML, Ebis Ku, Peng RD

***J Exposure Science Environmental Epidemiology* 2011**

PM and PM components spatial variability

Epidemiological evidence

Black carbon burden in the induced sputum of healthy children is inversely related with lung function

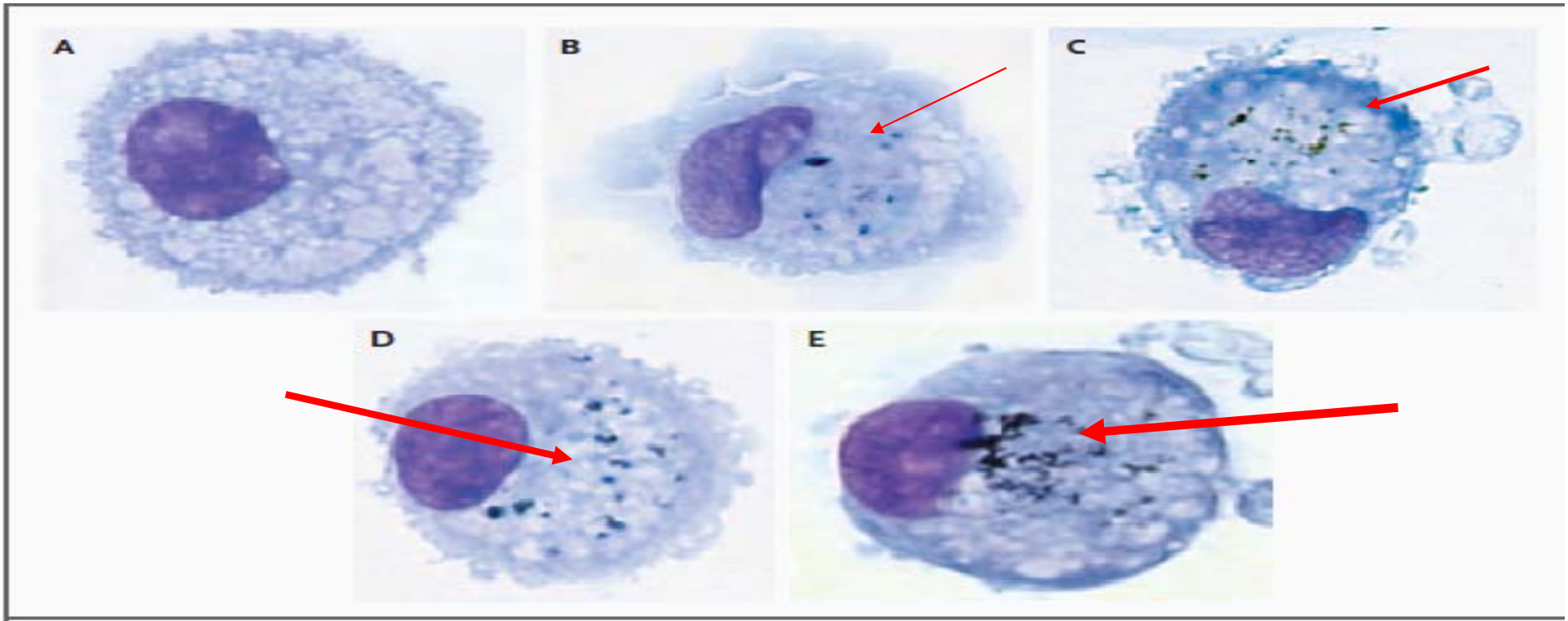


Figure 1. Representative Images of Carbon in Airway Macrophages from Healthy Children.

Panel A shows a macrophage with no carbon. Increasing levels of carbon are shown in Panels B through E. Airway macrophages were obtained from sputum, stained with Diff-Quik, and viewed with an oil-immersion lens. For each child, the area occupied by carbon in 100 randomly selected airway macrophages was determined by means of image analysis, and the median area (in square microns) per cell was calculated.

Kulkarni N, et al. NEJM 2006; 355:21-30.

PM and PM components spatial variability

Epidemiological evidence

Inverse correlation between black carbon burden in induced sputum and pulmonary function in children

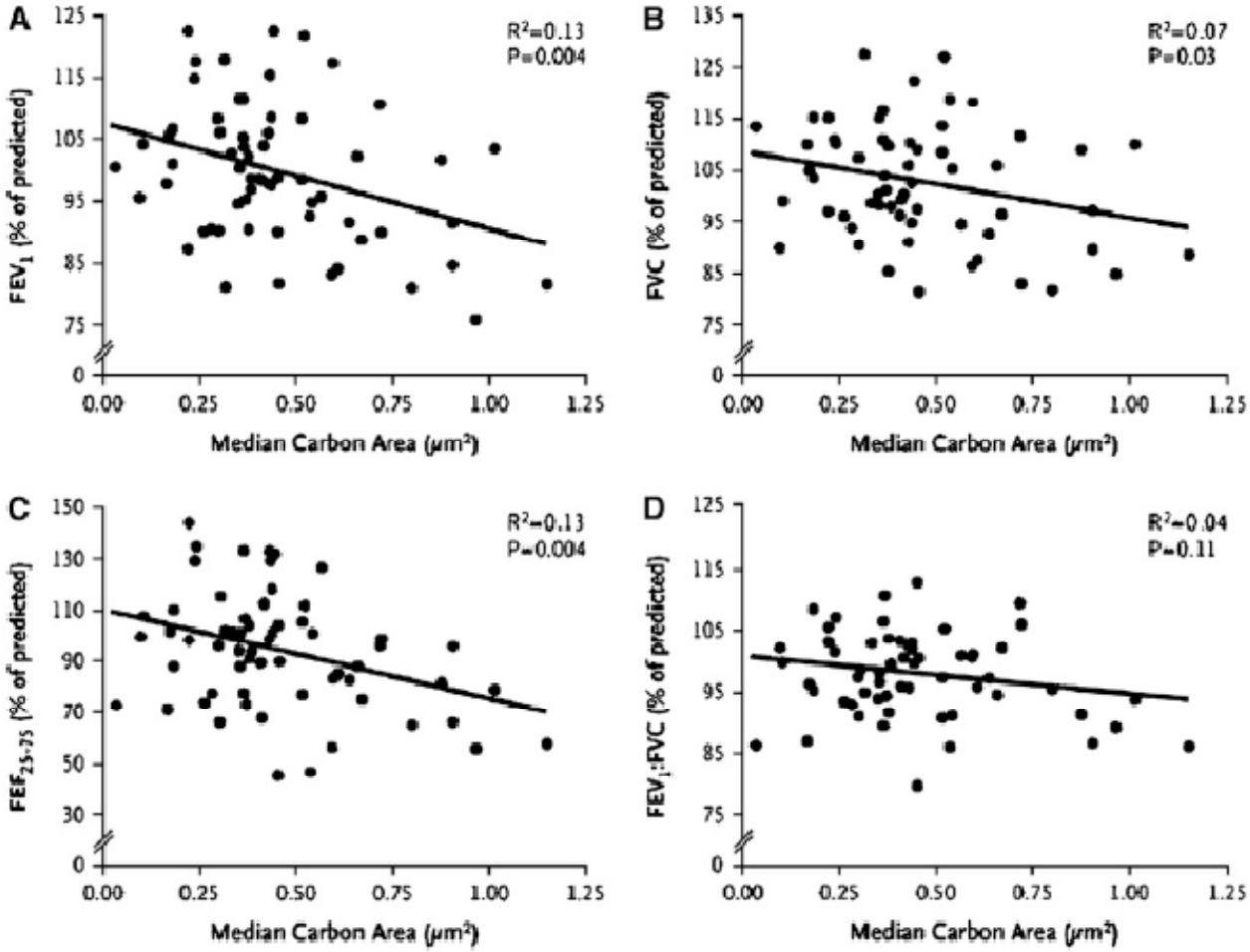


Figure 3. Association between the area of carbon (area of black material) in airway macrophages and (*A*) forced respiratory volume in 1 second (FEV_1), (*B*) forced vital capacity (FVC), (*C*) mid-expiratory flow between 25% and 75% of the forced vital capacity (FEF_{25-75}), and (*D*) FEV_1/FVC ratio. Data are from healthy school-age children of nonsmoking parents. The median area of carbon was calculated from 100 airway macrophages per child. There is a significant inverse association for all values, except for the FEV_1/FVC ratio. Reprinted by permission from Reference 23.

Kulkarni N, et al. NEJM 2006; 355:21-30.

PM and PM components spatial variability

Epidemiological evidence

HEI

SPECIAL REPORT 17

January 2010

Traffic-Related Air Pollution: A Critical Review of the Literature on Emissions, Exposure, and Health Effects

A Special Report of the HEI Panel on the Health Effects of Traffic-Related Air Pollution

EXECUTIVE SUMMARY

PM and PM components spatial variability
Epidemiological evidence
Traffic-related effects – HEI Report 2010

1. The Panel concluded that the evidence is "sufficient" to infer a causal association between traffic exposure and exacerbations of asthma.
Evidence A.

Executive Summary Table 1. Criteria for Assessing the Presence or Absence of Causal Associations in Studies of the Health Effects of Traffic-Related Air Pollution[a,b]

A. *Sufficient Evidence to Infer the Presence of a Causal Association*

The evidence was deemed sufficient to conclude that an association observed between a metric of traffic exposure and a disease (or biomarker of disease) risk was causal in studies where chance, bias, and confounding could be ruled out with reasonable confidence, and the effect estimates were consistent in magnitude and direction.

Traffic-specific criterion. Classification A was applied:

When all studies were of the appropriate quality, at least one study measured traffic density or modeled traffic exposure[c], measures of socioeconomic status were taken into account in distance-only studies, and the studies' results were consistent.

PM and PM components spatial variability
Epidemiological evidence
Traffic-related effects – HEI Report 2010

2. The Panel reviewed 17 studies on respiratory symptoms, of which all but one relied on proximity to roads or traffic-density measures, and concluded that the evidence for a causal association is "suggestive but not sufficient." Evidence B.

B. *Suggestive but Not Sufficient Evidence to Infer the Presence of a Causal Association*
The evidence was deemed suggestive but not sufficient to conclude that an association between a metric of traffic exposure and a specific disease (or biomarker of disease) risk was causal in studies where chance, bias, and confounding could not be ruled out with reasonable confidence.
Traffic-specific criterion. Classification B was applied:
When all the criteria for Classification A were met except that only studies that used distance-based metrics were available
OR
When all the criteria for Classification A were met except that not all the studies that used distance-only metrics took into account measures of socioeconomic status or the studies took into account measures of socioeconomic status but the results were not consistent.

PM and PM components spatial variability

Epidemiological evidence

Traffic-related effects - HEI Report 2010

3. Very few studies of <u>all-cause mortality or cardiovascular mortality</u> and long-term exposure met the criteria for inclusion in the report. Mostly because of the small number of studies, the evidence for an association of all-cause mortality with longterm exposure was classified as "suggestive but not sufficient" to infer a causal association. Evidence B.

B. *Suggestive but Not Sufficient Evidence to Infer the Presence of a Causal Association*

The evidence was deemed suggestive but not sufficient to conclude that an association between a metric of traffic exposure and a specific disease (or biomarker of disease) risk was causal in studies where chance, bias, and confounding could not be ruled out with reasonable confidence.

Traffic-specific criterion. Classification B was applied:

When all the criteria for Classification A were met except that only studies that used distance-based metrics were available

OR

When all the criteria for Classification A were met except that not all the studies that used distance-only metrics took into account measures of socioeconomic status or the studies took into account measures of socioeconomic status but the results were not consistent.

PM and PM components spatial variability

Epidemiological evidence

Traffic-related effects - HEI Report 2010

4. The studies reviewed were heterogeneous in their design, approach to exposure assessment, and lung-function measures. Given their limited comparability, the Panel concluded that the evidence is "suggestive but not sufficient" to infer a causal association between short- and long-term exposure to traffic-related pollution and decrements in lung function.

Evidence B.

B. *Suggestive but Not Sufficient Evidence to Infer the Presence of a Causal Association*

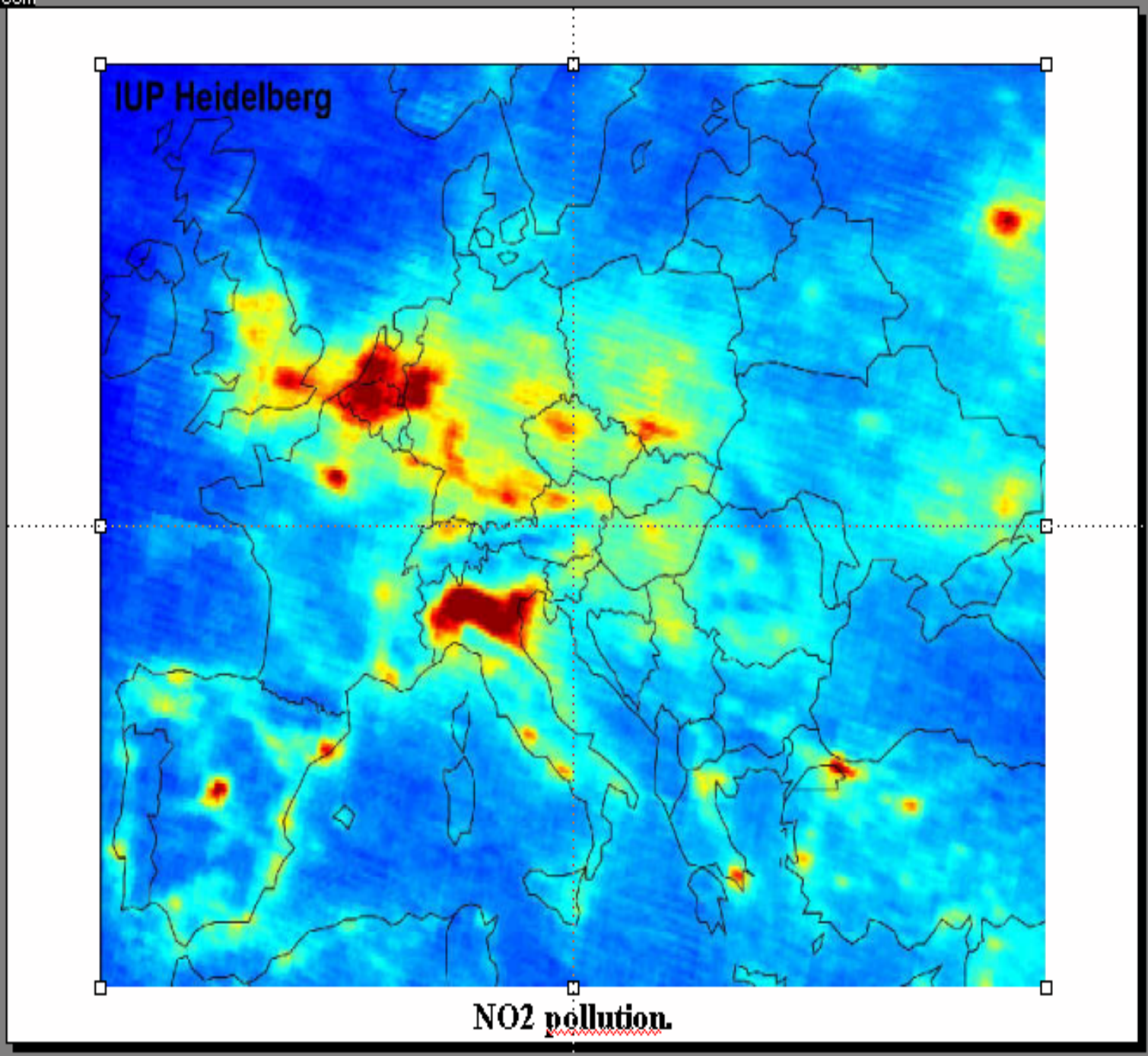
The evidence was deemed suggestive but not sufficient to conclude that an association between a metric of traffic exposure and a specific disease (or biomarker of disease) risk was causal in studies where chance, bias, and confounding could not be ruled out with reasonable confidence.

Traffic-specific criterion. Classification B was applied:

When all the criteria for Classification A were met except that only studies that used distance-based metrics were available

OR

When all the criteria for Classification A were met except that not all the studies that used distance-only metrics took into account measures of socioeconomic status or the studies took into account measures of socioeconomic status but the results were not consistent.



NO2 pollution.

We would like to remember that according to UNESCO 2010 was the year of biodiversity, while **2011 is the year of sustainability.**

In the present context of scientific community here hosted at ICTP, we as **International Society Doctors for the environment and Italian Society of General Medicine**) with our presence we want to underline:

1) the important role of **aerosol studies** and definitions of pollutant sources, helpful **for the protection of the environment where humankind lives** and other different forms of life;

2) that with this workshop a **big effort has been done**, that is necessary and keep a high etical tension (moral – collective of all scientific communities) **for making overcome the concept of respect of life, of person, and of families.**

We know what a premature/anticipated death, caused i.e. by pollution, mean for a family.

Animals and plants that in this contingency of climatic changes are already exposed to particular selective pressure.

Now and immediately, in this moment of climatic changes (dry period / aridity) and in this context of **climatic changes, induced also by an unbalanced economic development model, based on exaggerated consumptions for a part of population, and scarcity and poverty, illness and war for another.**

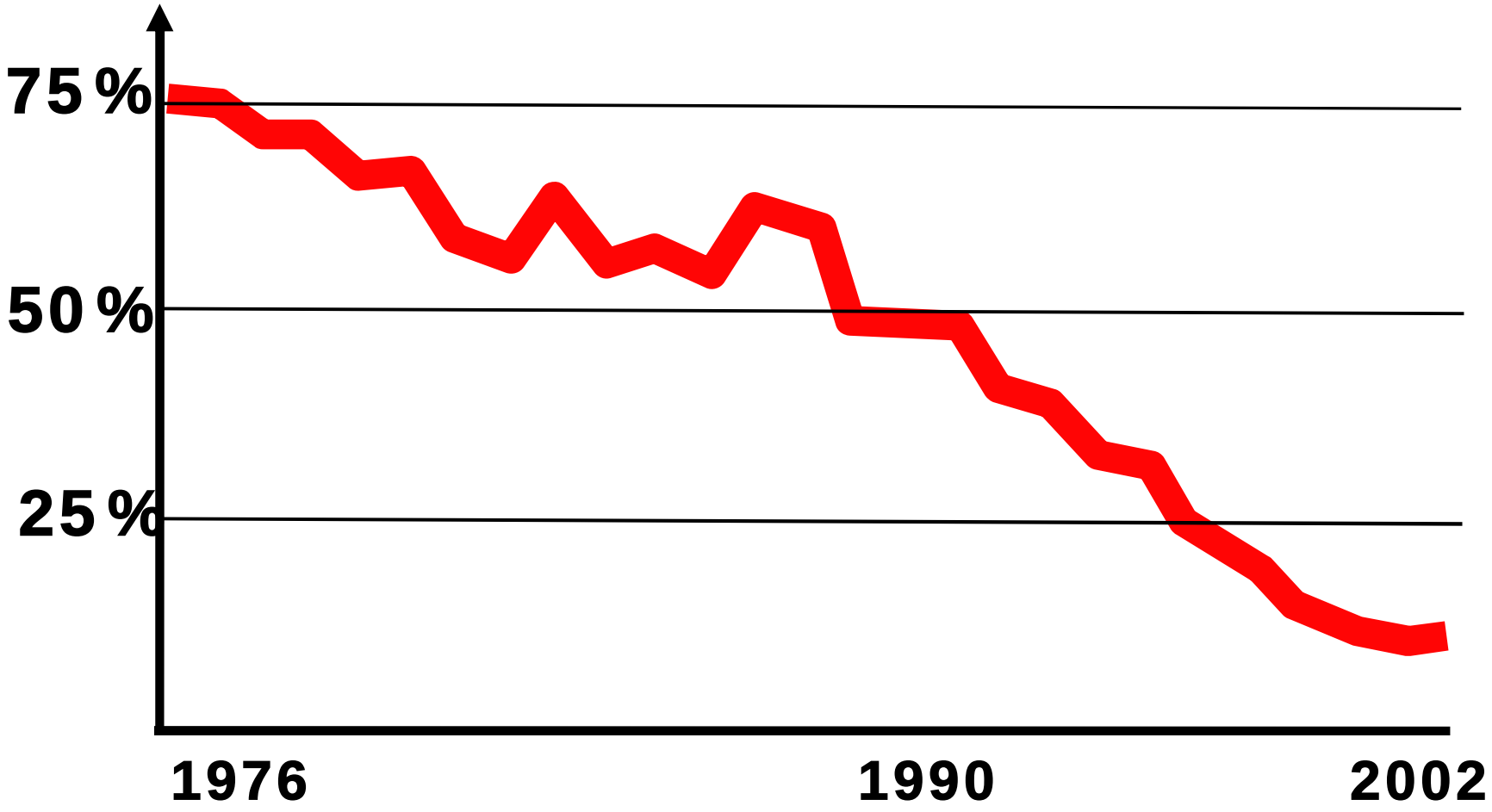
Choices and decisions are needed, **that are originated from significant multidisciplinary studies and analyses,** aimed at not worsening lifestyle of population of different regions and places, and prenting avoidable/ unnecessary deaths/casualties, expecially among children.

The purpose of ethical-minded scientists is expecially the **defence of the part of population that is more weak and in need,** with respect of which the Market push to obtain how much is possible, investing minimal resources.

The **moving of the industrial production towards develping countries**, just as the relatively rapid climate changes , **modify traditional development models**, that maintained in equilibrium for long whole populations in the planet, **with negative effects on community life**, as well on the surival of individual and families.

Is it possible to reduce pollution exposure? Yes!

% of days exceeding current air quality standards in Los Angeles - 1976 to 2002



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Thank you very much for your attention!

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