What we know, where we are going, what the EU should do?

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Conflicts of Interest

European Academy Allergy Clinical Immunology

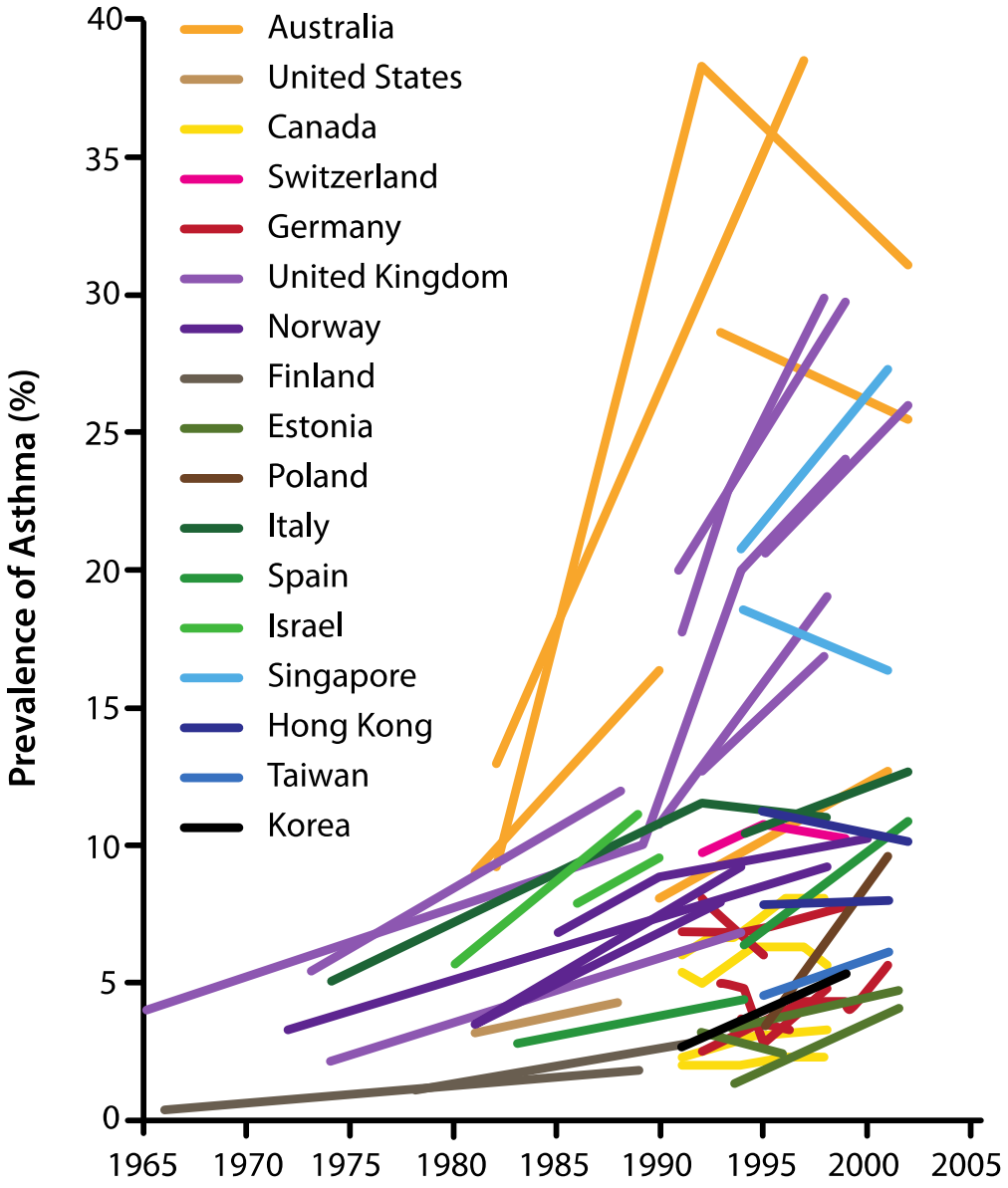
Bavarian Government

Technical University Münich

Kühne Foundation

BMW, parked motor vehicle **indoor air** quality

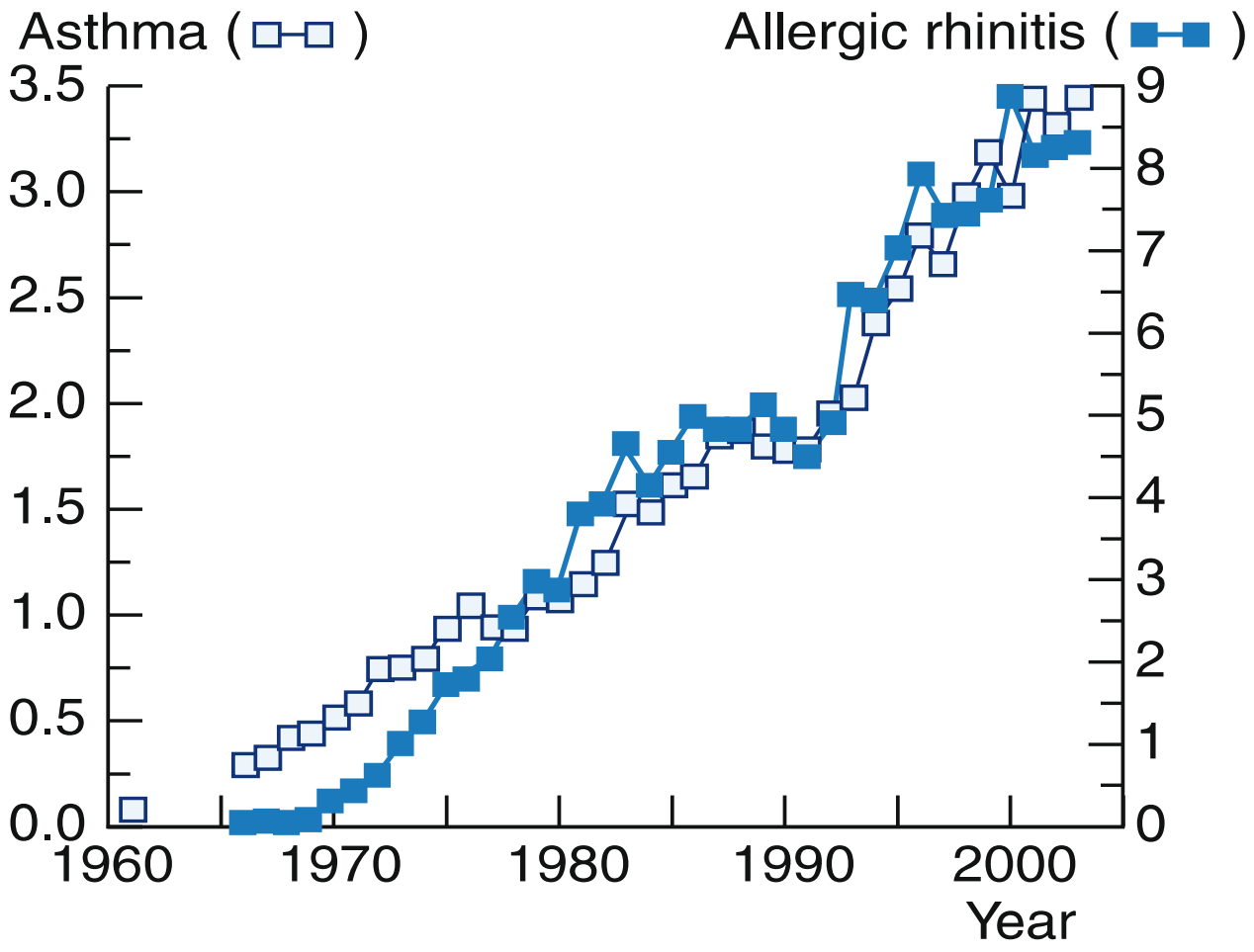
World-wide increase in IgE-mediated diseases



Eder et al., NEJM 2006

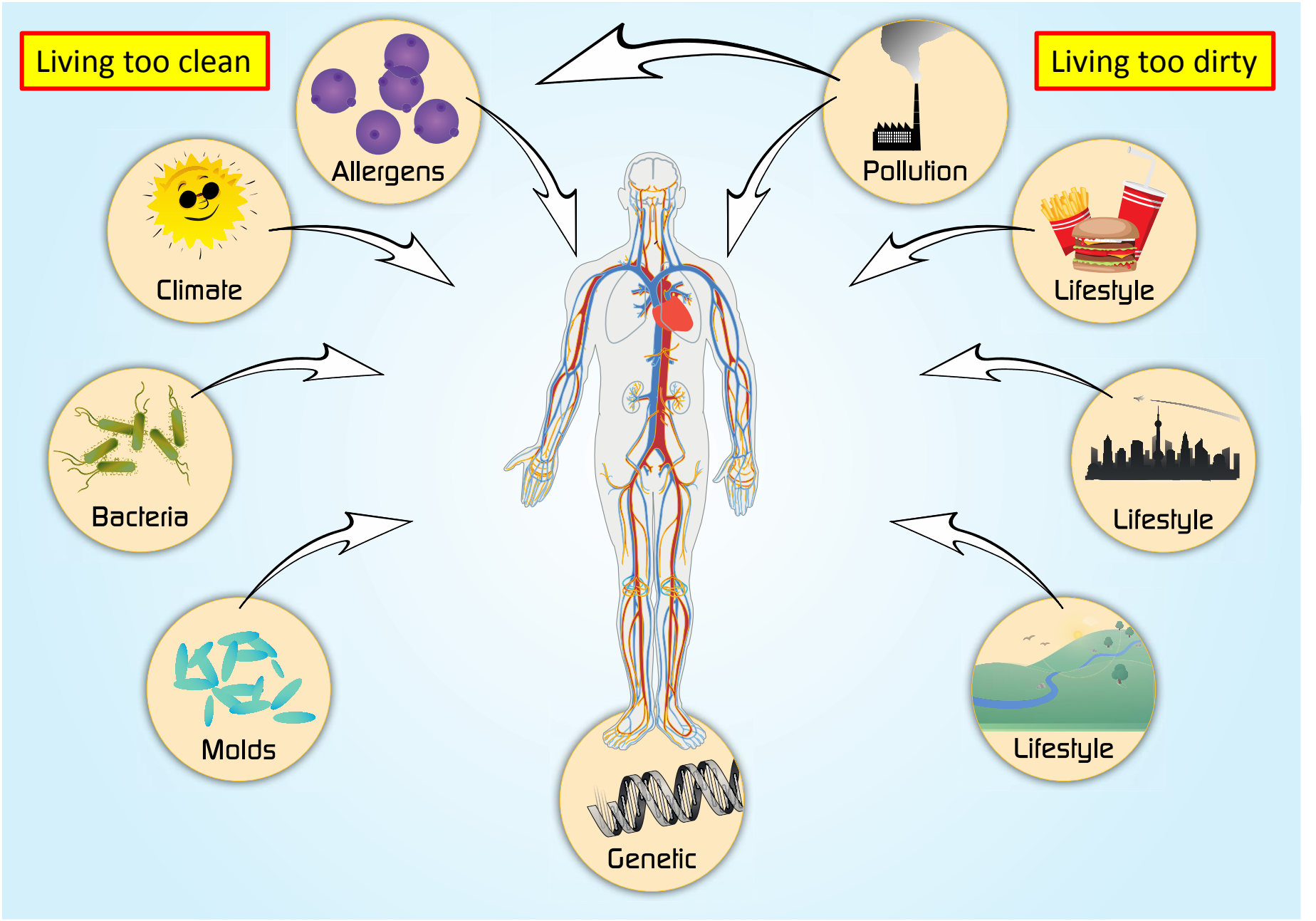
Increase in prevalence of allergic diseases

- allergic diseases in military recruits -



Haahtela et al., WAO 2013

Factors influencing allergic diseases



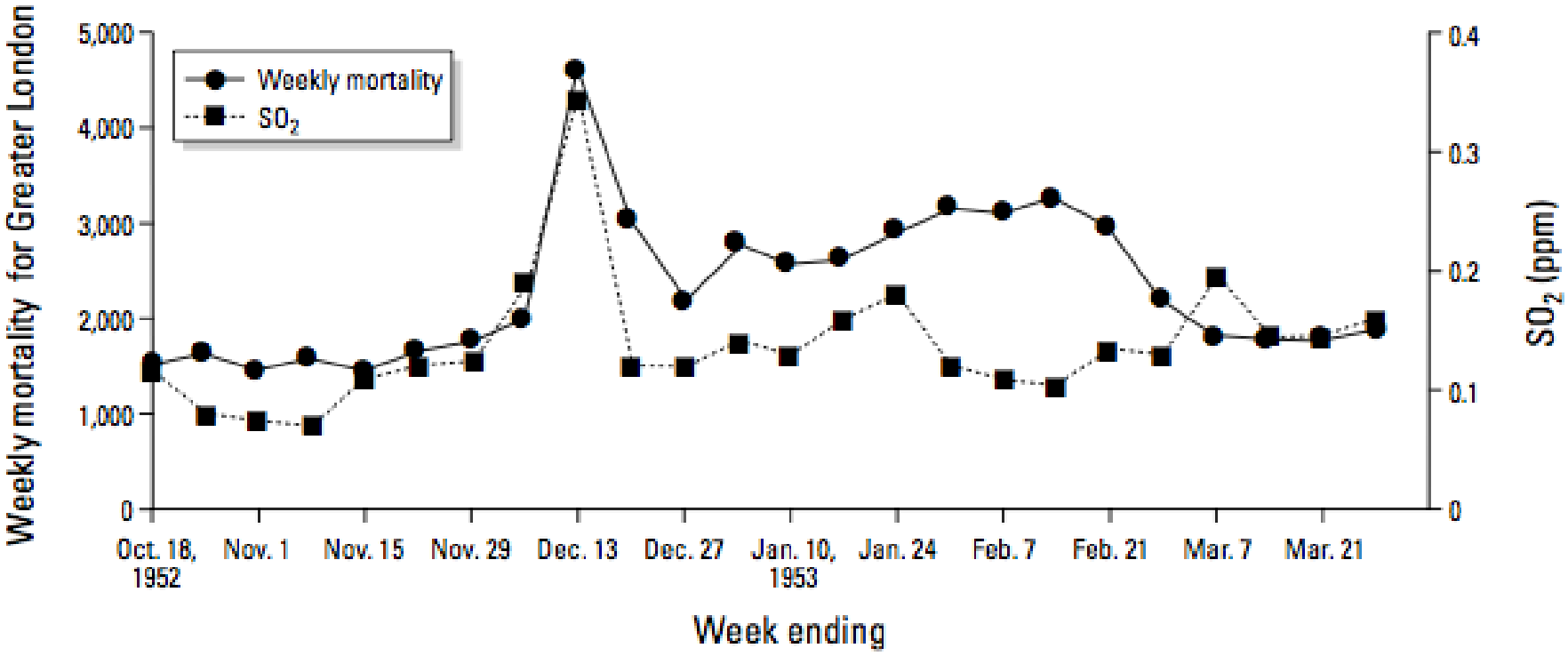
Pollution

Light pollution
Noise pollution

Air pollution:

- SO_2
- NH_3
- CO
- NOx
- O_3
- PM

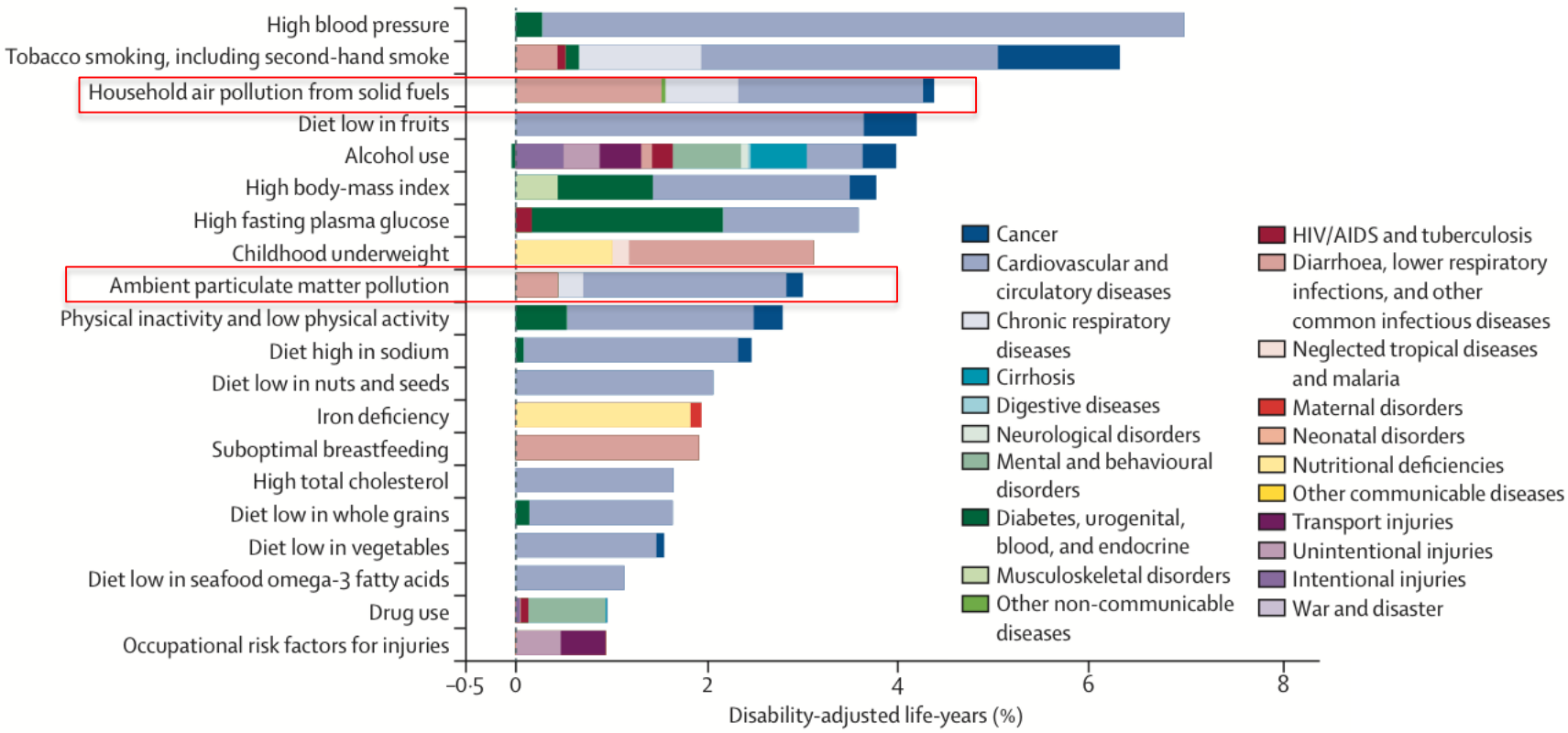
London smog: lethality



Bell and Davis, Env Health Persp. 2001

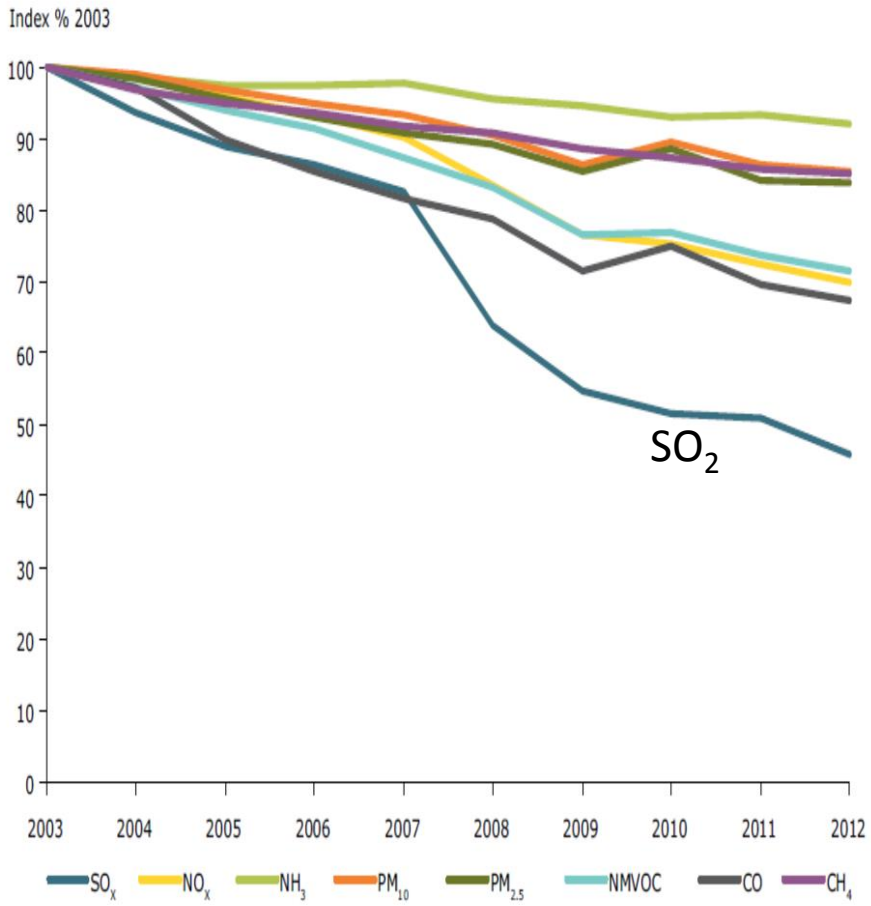
Burden of disease attributable to 20 leading risk factors in 2010

- expressed as a percentage of global disability-adjusted life-years, both sexes -

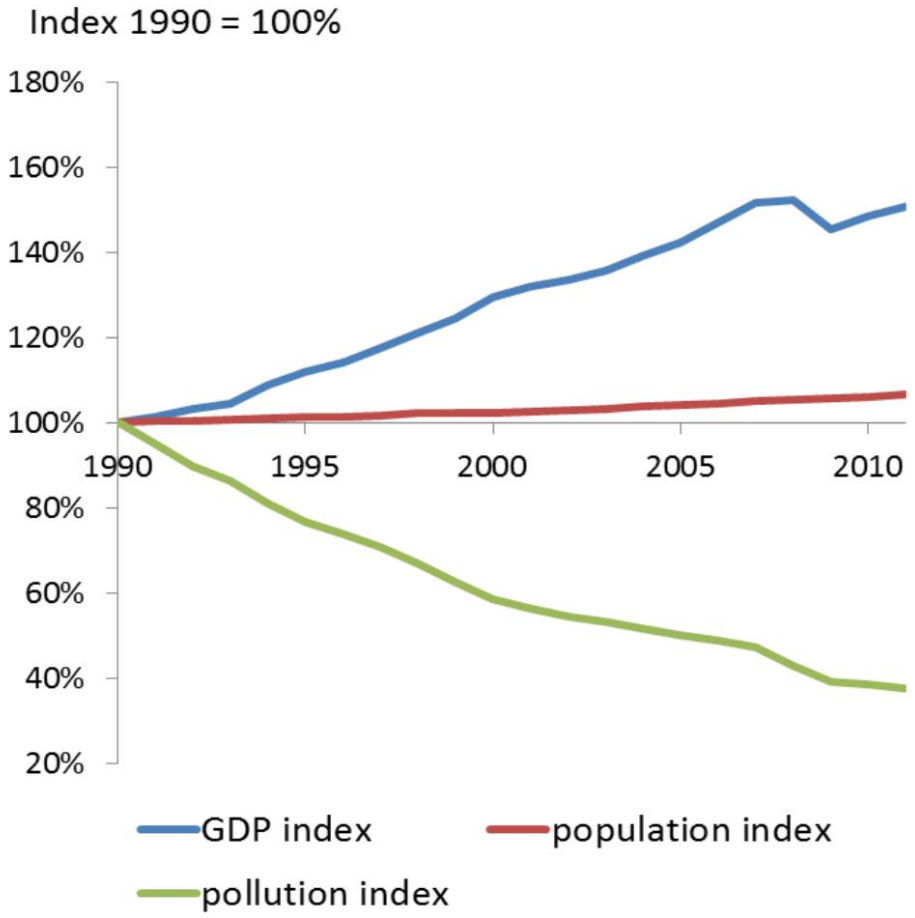


Lim et al., Lancet 2013

Time trends of Pollution in Europe

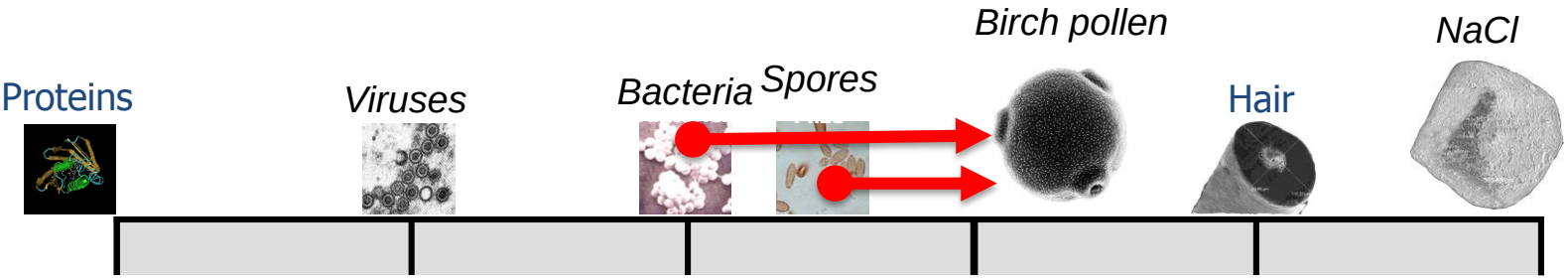


SO_2



Source:EEA

Nomenclature of Particles



0.01 µm | 0.1 µm | 1 µm | 10 µm | 100 µm | 1 mm

2.5 µm

TSP

Dust fall

PM_{10}

$PM_{2.5}$

PM_{1}

$PM_{0.1}$

nanoparticles

Coarse fraction

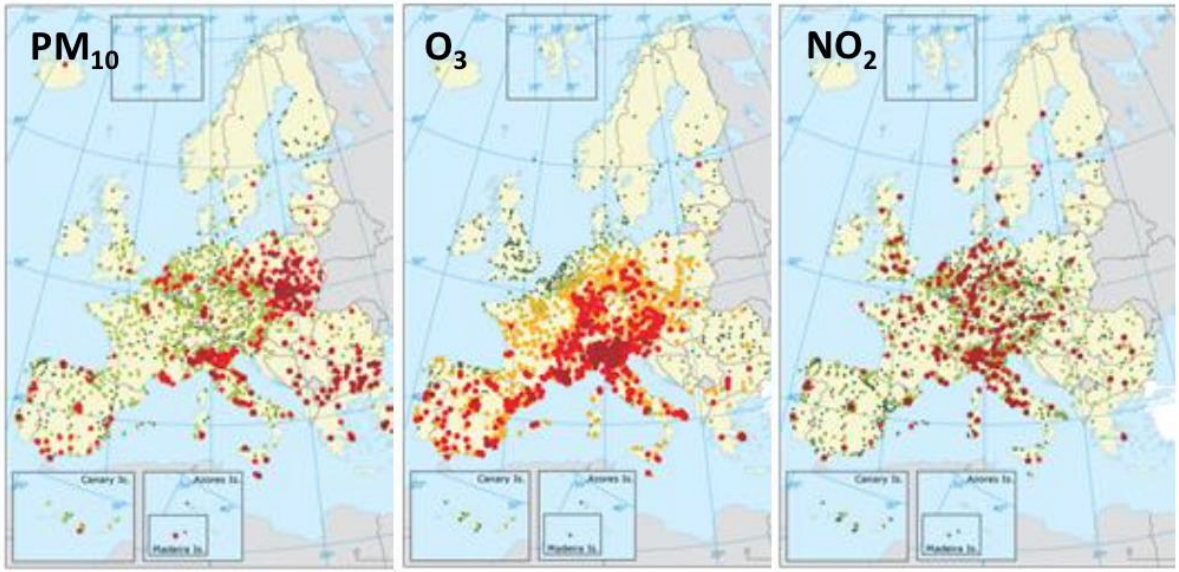
30 µm

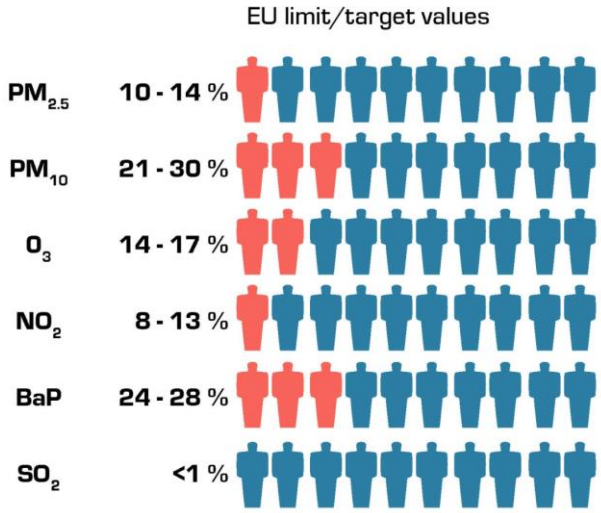
Fine fraction

Ultrafine

PM= particulate matter

Exceeding Current Air Pollution Standards





Source:EEA

Sources of PM 2.5

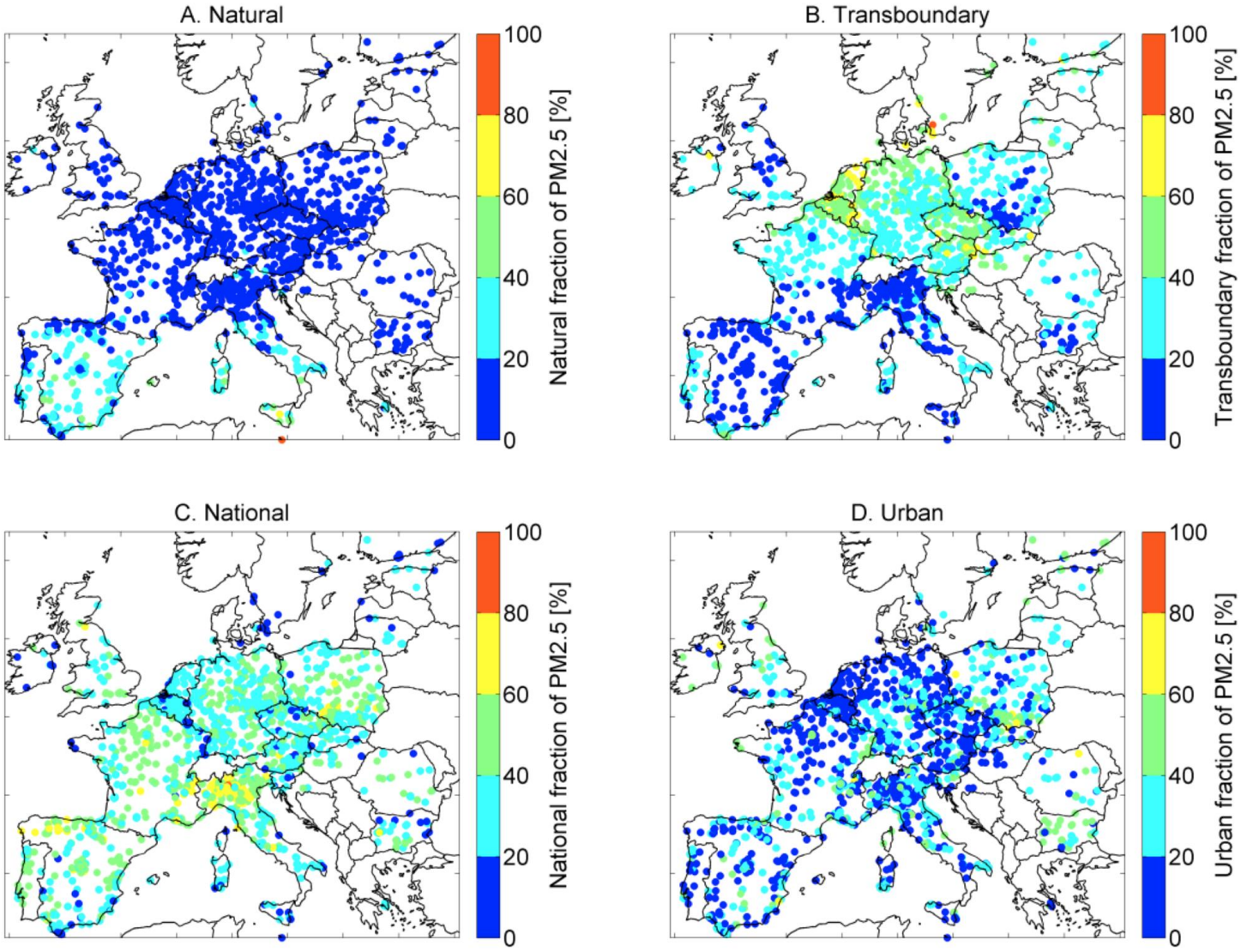
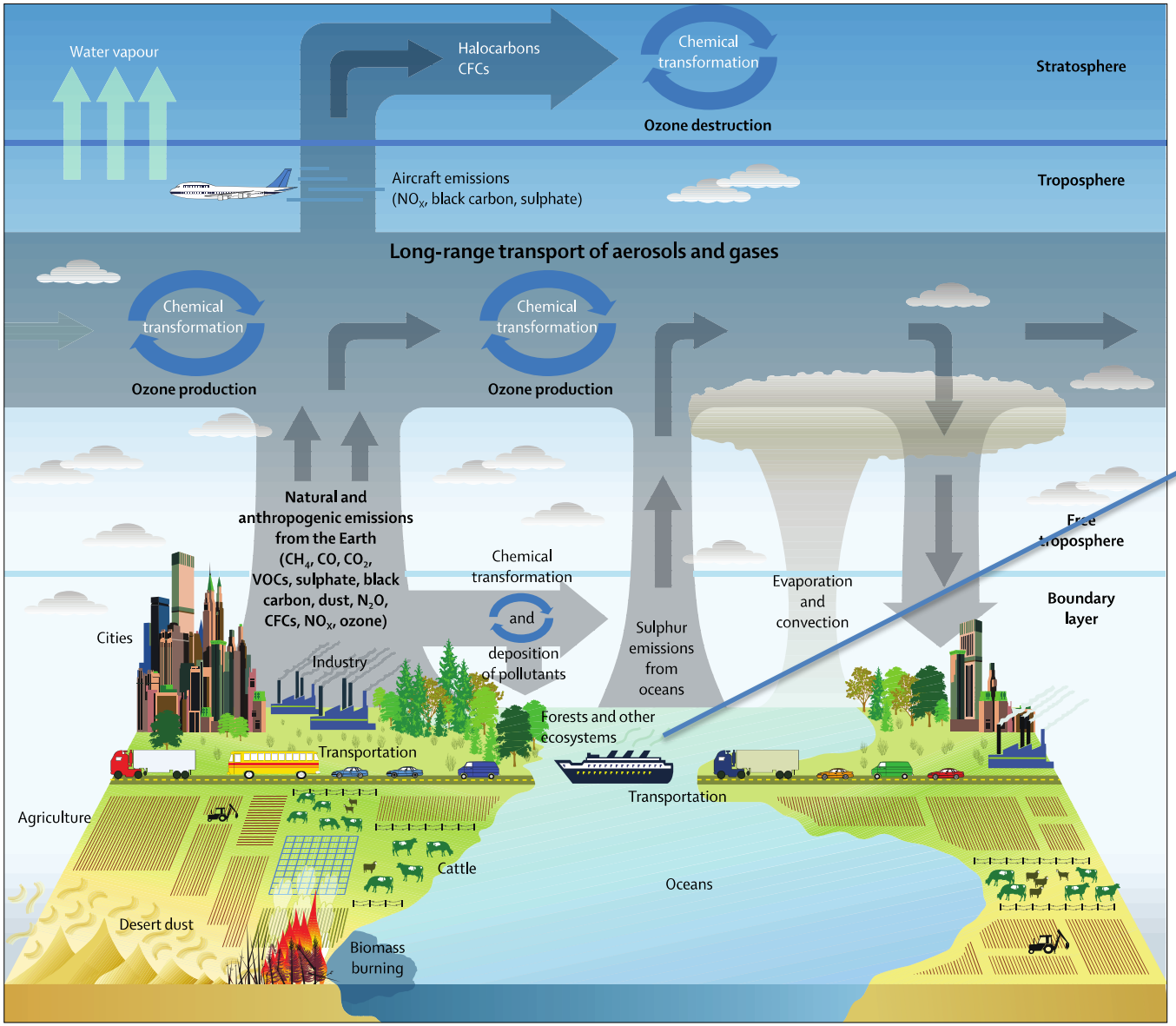


Figure 2.1. Spatial origins of PM2.5 at background monitoring stations covered by GAINS, shown as relative fractions of total modelled PM2.5 at each station in 2009.

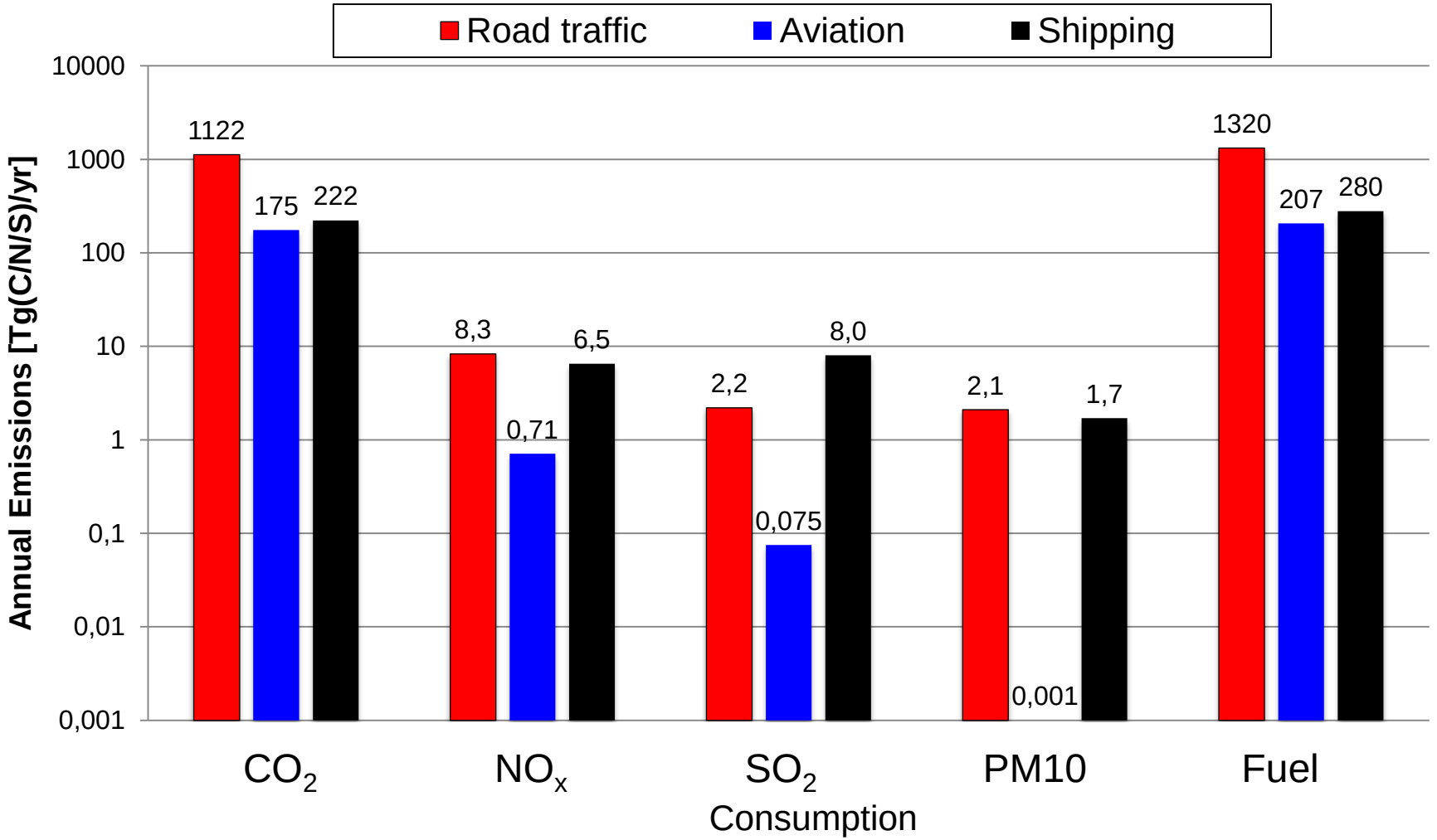
Atmospheric pollutants



and
Off-road
engines

Guarnieri & Balmes, Lancet, 2014

Sources of pollution



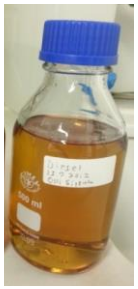
Eyring, J Geophys Ter, 2005

Sulphur in ship emissions generates clouds

A satellite image from 4 March 2009 showing ship tracks — the bright streaks of clouds that form around the particles in ship exhaust — over the northeast Pacific Ocean. The ship tracks are brighter than the natural marine clouds around them because they contain lots of small cloud droplets, which you can see in this zoomed-in image. NASA image by the LANCE/EOSDIS MODIS Rapid Response Team.

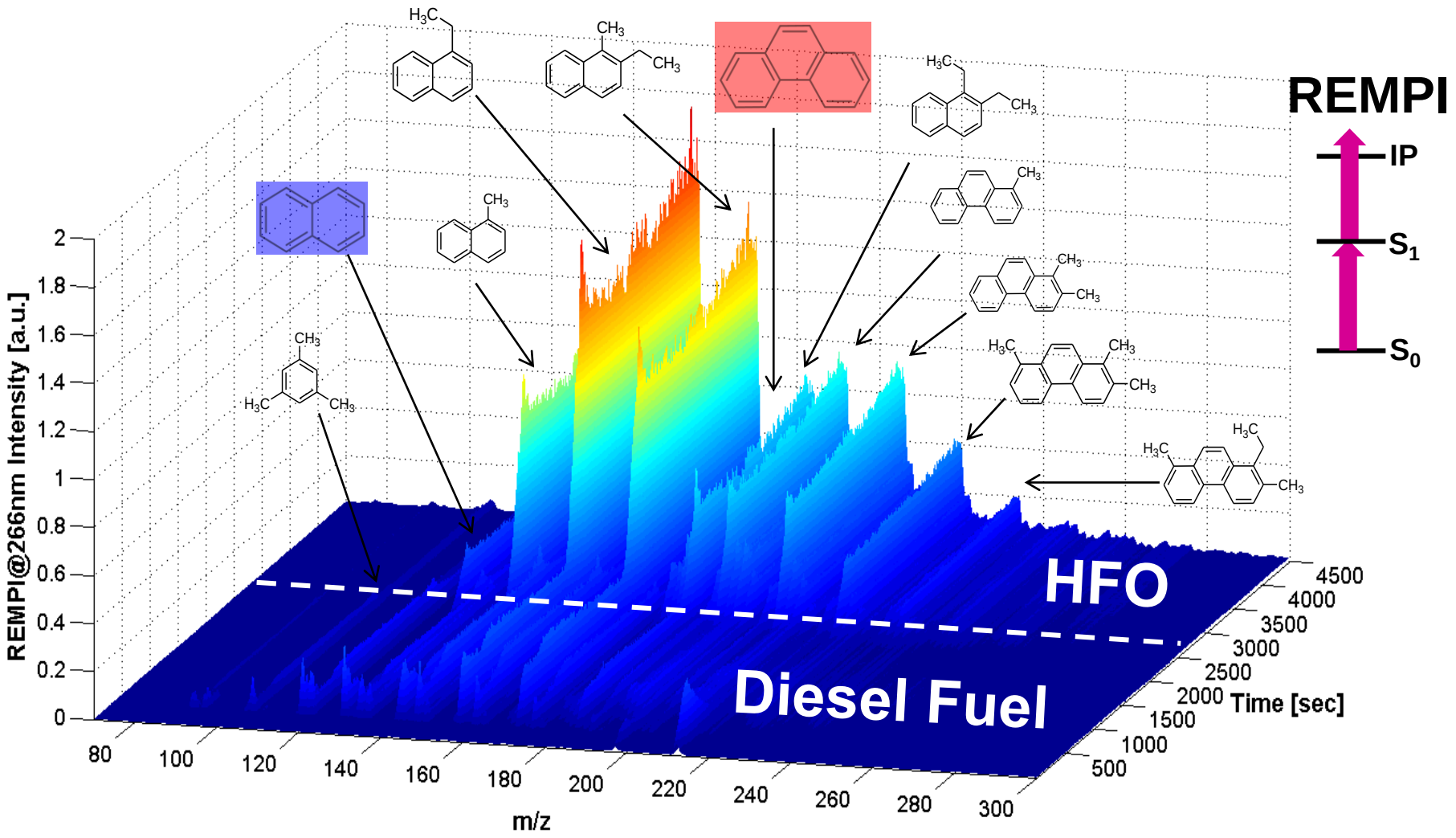
http://www.isgtw.org/feature/clearing-cloudy-view-cloud-formation

Heavy Fuel Oil

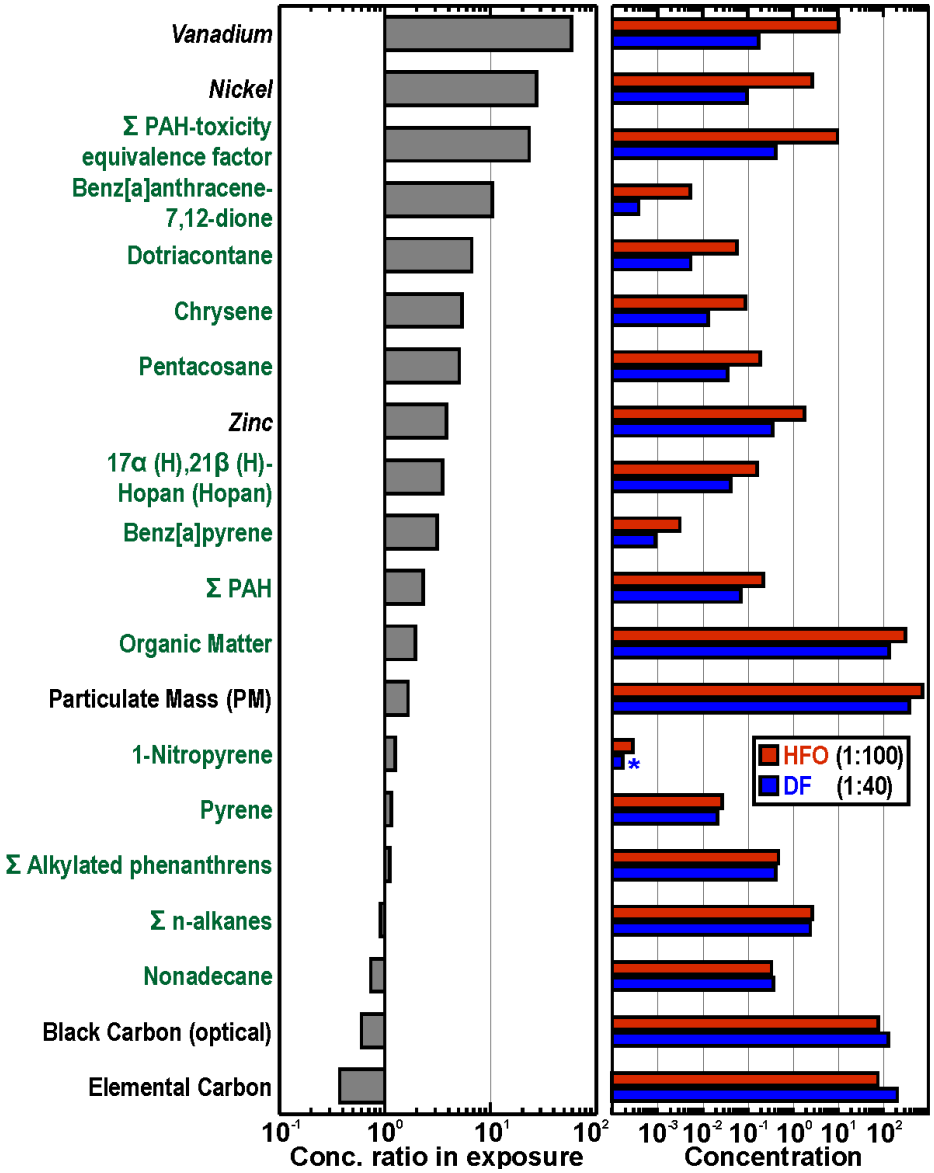


Diesel Fuel

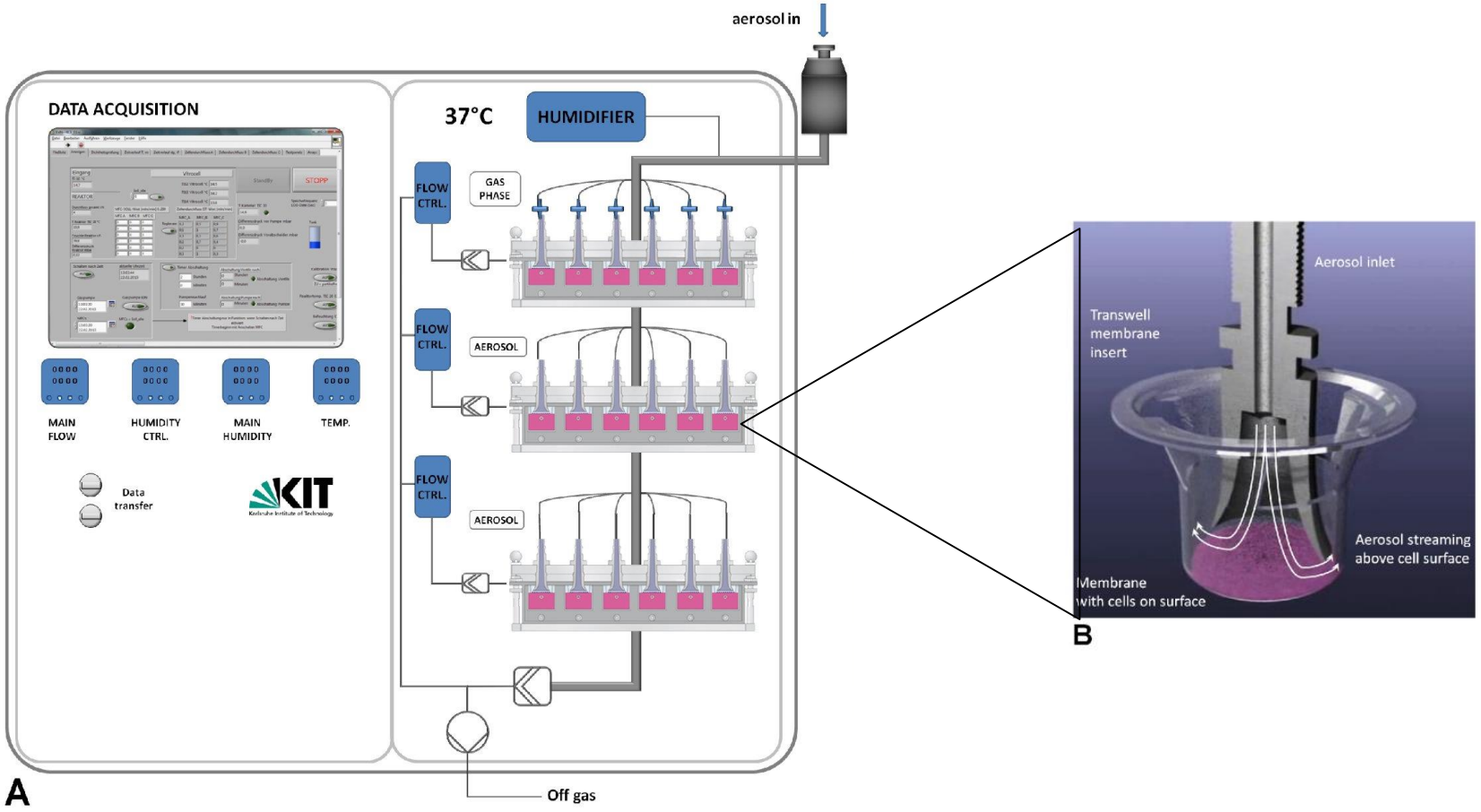
Switching from light fuel oil (DF) to heavy fuel oil (HFO) ➔
Increase of Polycyclic Aromatic Hydrocarbons (PAH) in exhaust gas



Organic composition of the exhaust particles

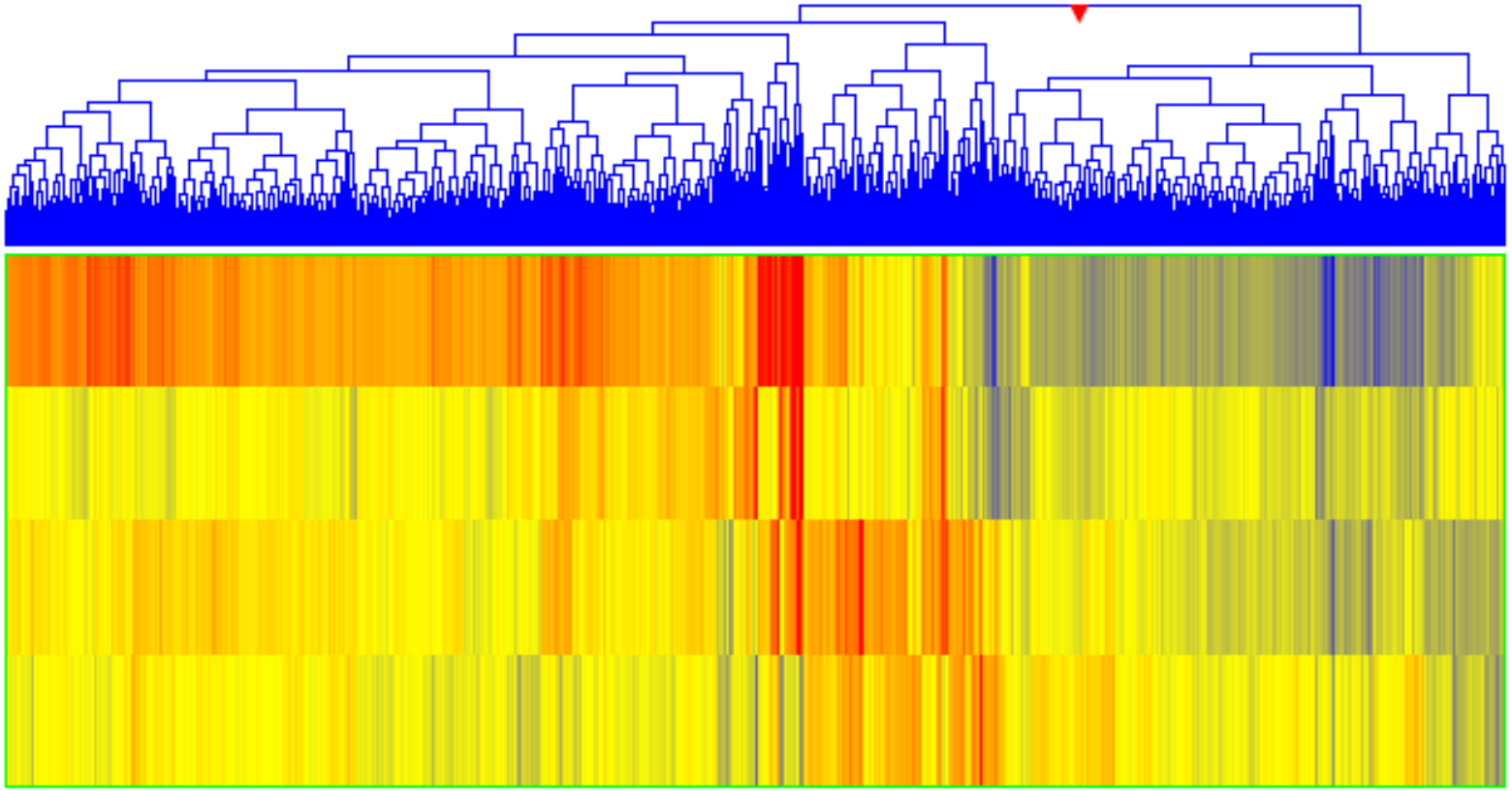


Exposing human cells at the air-liquid interface



Genome wide RNA target analysis

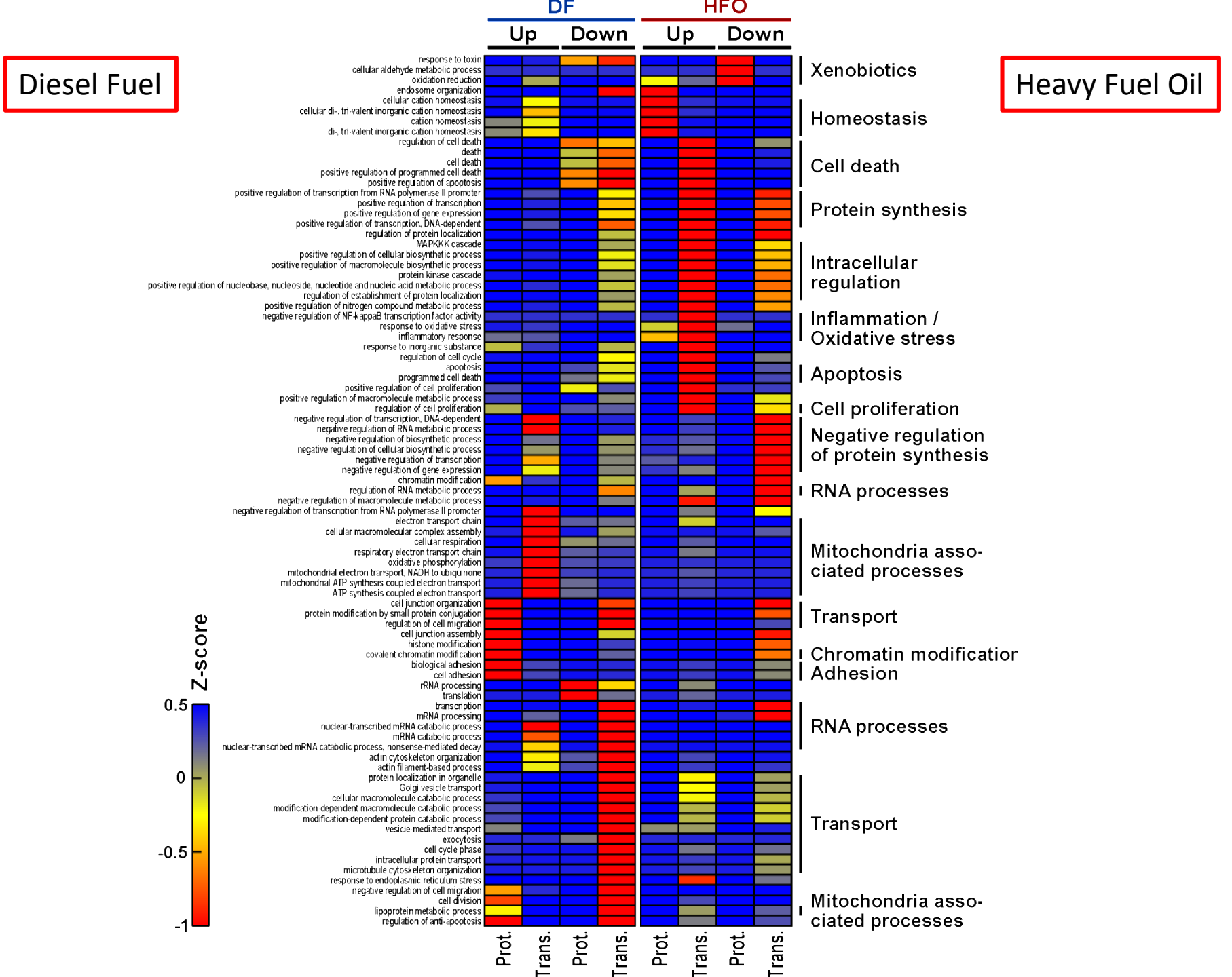
- Referenced against clean air - *



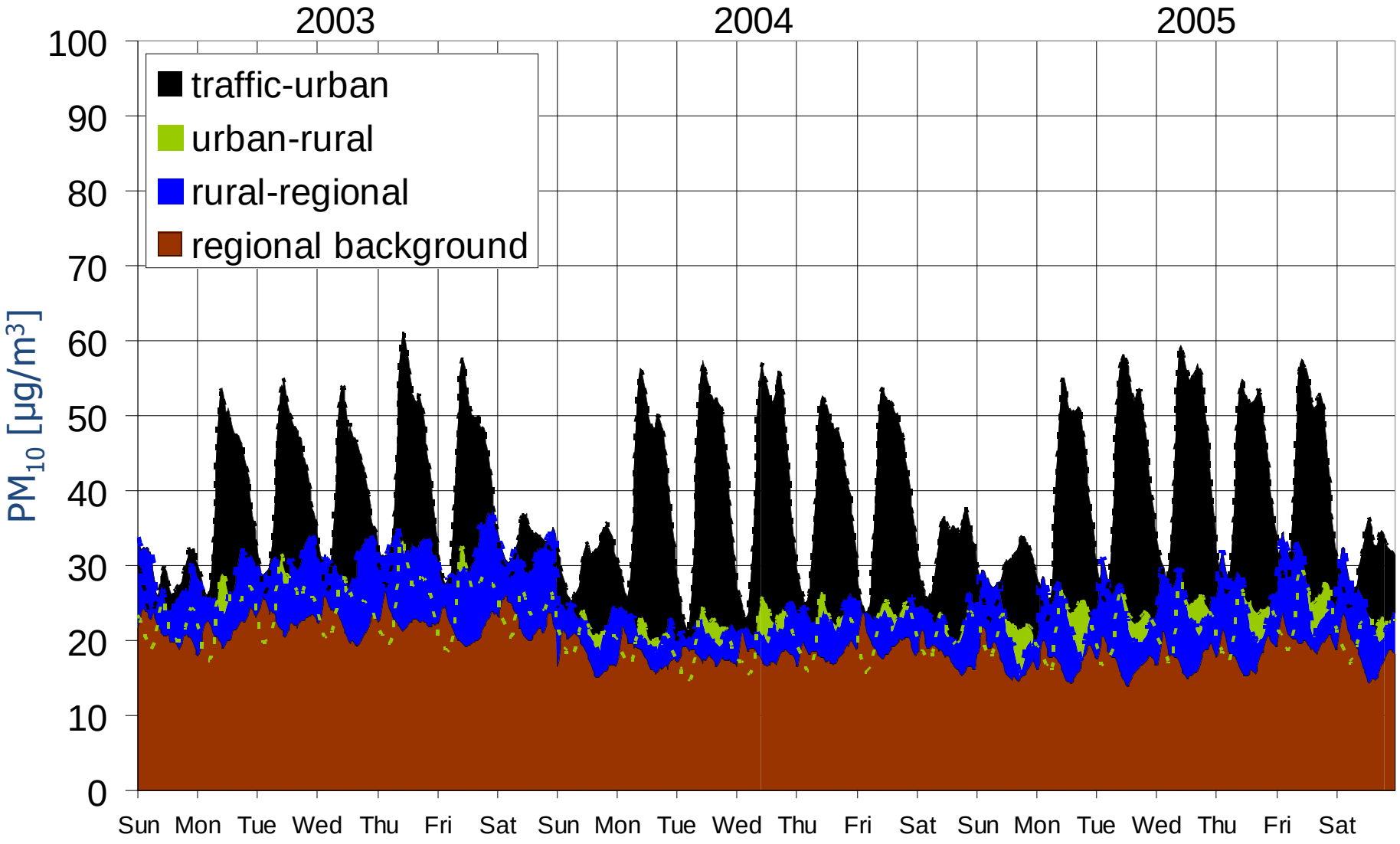
>1.5-fold Up-regulated genes

>1.5-fold Down-regulated genes

- about 42,000 genes, against clean air


Diesel Fuel
Heavy Fuel Oil
DF
HFO
Up
Down
Up
Down
response to toxin
cellular aldehyde metabolic process
oxidation reduction
endosome organization
cellular cation homeostasis
cellular di-, tri-valent inorganic cation homeostasis
cation homeostasis
di-, tri-valent inorganic cation homeostasis
regulation of cell death
death
cell death
positive regulation of programmed cell death
positive regulation of apoptosis
positive regulation of transcription from RNA polymerase II promoter
positive regulation of transcription
positive regulation of gene expression
positive regulation of transcription, DNA-dependent
regulation of protein localization
MAPKKK cascade
positive regulation of cellular biosynthetic process
positive regulation of macromolecule biosynthetic process
protein kinase cascade
positive regulation of nucleobase, nucleoside, nucleotide and nucleic acid metabolic process
regulation of establishment of protein localization
positive regulation of nitrogen compound metabolic process
negative regulation of NF-kappaB transcription factor activity
response to oxidative stress
inflammatory response
response to inorganic substance
regulation of cell cycle
apoptosis
programmed cell death
positive regulation of cell proliferation
positive regulation of macromolecule metabolic process
regulation of cell proliferation
negative regulation of transcription, DNA-dependent
negative regulation of RNA metabolic process
negative regulation of biosynthetic process
negative regulation of cellular biosynthetic process
negative regulation of transcription
negative regulation of gene expression
chromatin modification
regulation of RNA metabolic process
negative regulation of macromolecule metabolic process
negative regulation of transcription from RNA polymerase II promoter
electron transport chain
cellular macromolecular complex assembly
cellular respiration
respiratory electron transport chain
oxidative phosphorylation
mitochondrial electron transport, NADH to ubiquinone
mitochondrial ATP synthesis coupled electron transport
ATP synthesis coupled electron transport
cell junction organization
protein modification by small protein conjugation
regulation of cell migration
cell junction assembly
histone modification
covalent chromatin modification
biological adhesion
cell adhesion
rRNA processing
translation
transcription
mRNA processing
nuclear-transcribed mRNA catabolic process
mRNA catabolic process
nuclear-transcribed mRNA catabolic process, nonsense-mediated decay
actin cytoskeleton organization
actin filament-based process
protein localization in organelle
Golgi vesicle transport
cellular macromolecule catabolic process
modification-dependent macromolecule catabolic process
modification-dependent protein catabolic process
vesicle-mediated transport
exocytosis
cell cycle phase
intracellular protein transport
microtubule cytoskeleton organization
response to endoplasmic reticulum stress
negative regulation of cell migration
cell division
lipoprotein metabolic process
regulation of anti-apoptosis
Z-score
0.5
0
-0.5
-1
Prot.
Trans.
Prot.
Trans.
Prot.
Trans.
Prot.
Trans.
Xenobiotics
Homeostasis
Cell death
Protein synthesis
Intracellular regulation
Inflammation / Oxidative stress
Apoptosis
Cell proliferation
Negative regulation of protein synthesis
RNA processes
Mitochondria asso-ciated processes
Transport
Chromatin modification
Adhesion
RNA processes
Transport
Mitochondria asso-ciated processes

Diurnal Variation: Bremen (traffic site)

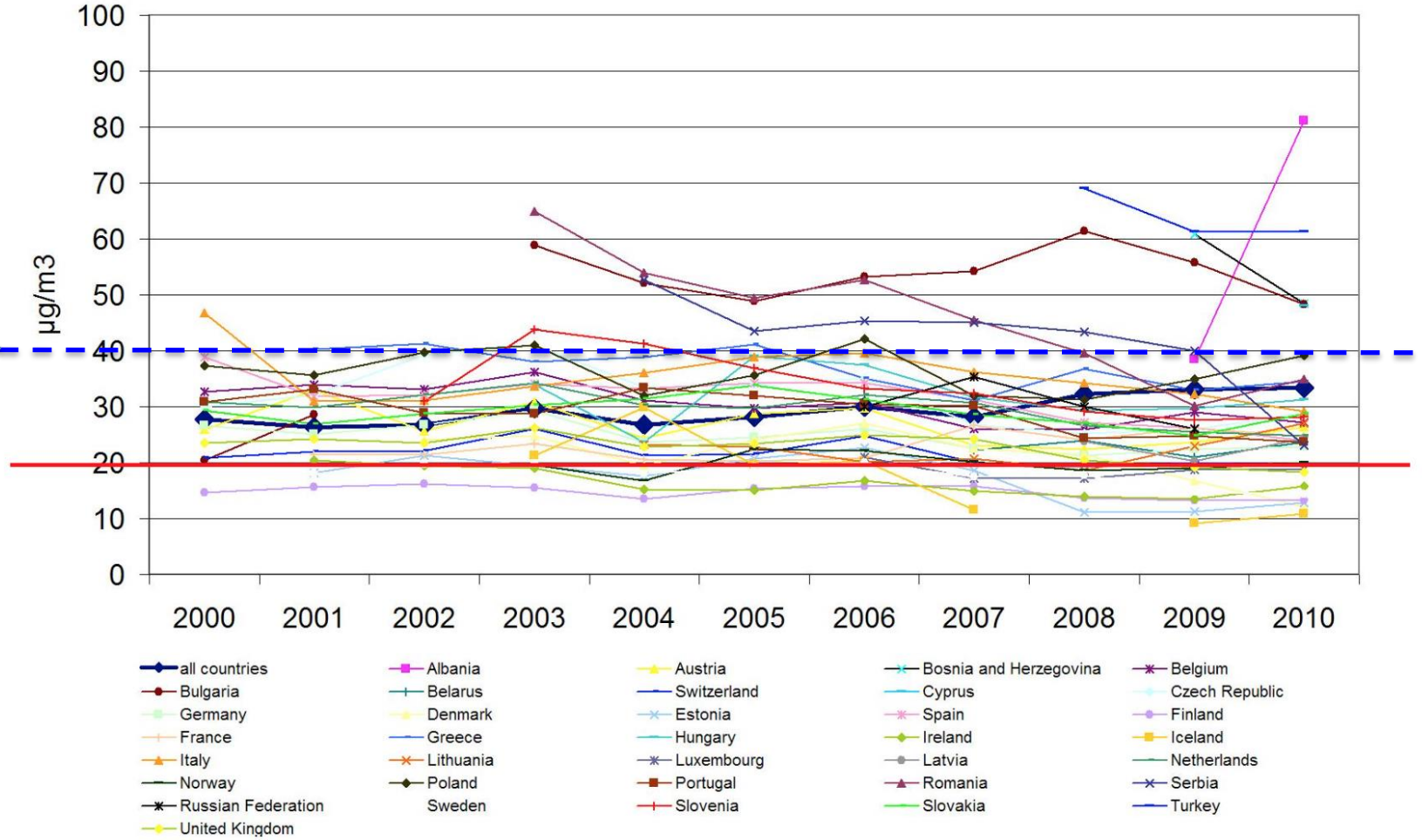


Quass et al., EAC Salzburg, 2007

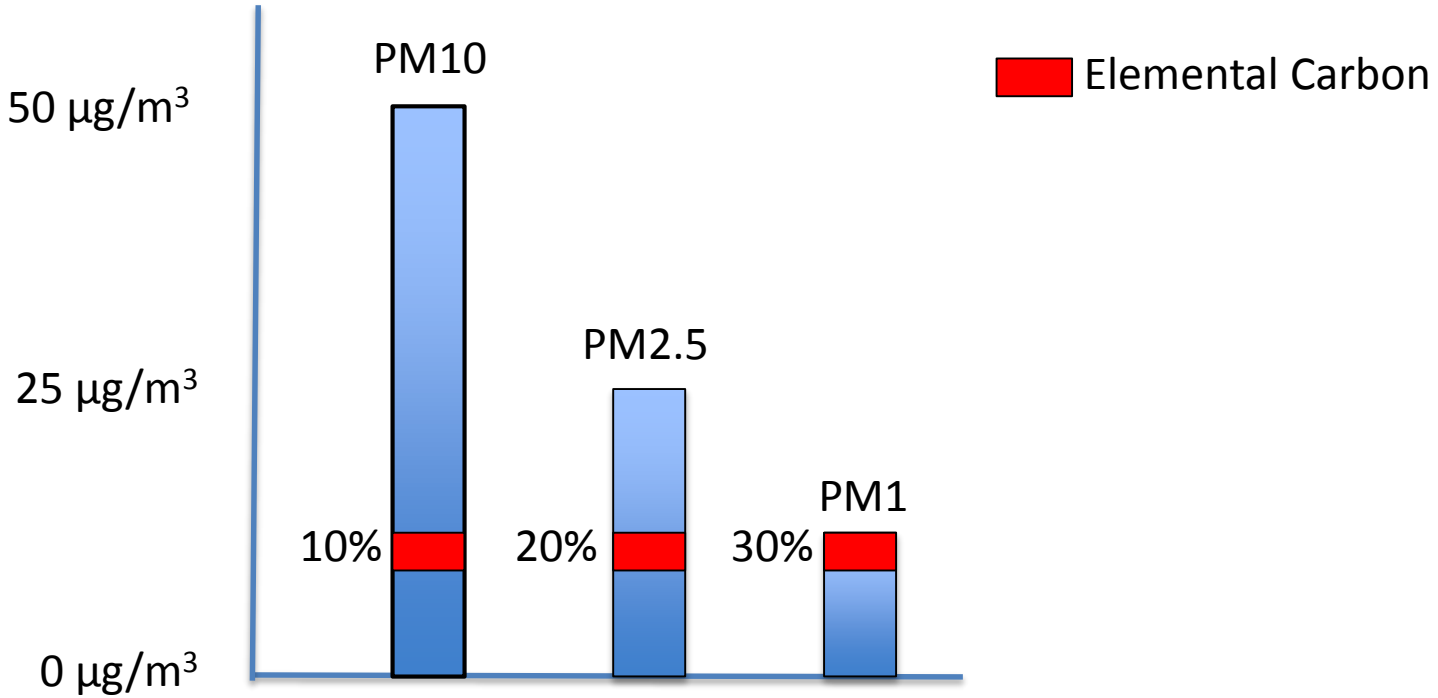
EU-wide Yearly Values of PM10

EU Guideline = 40µg/m³

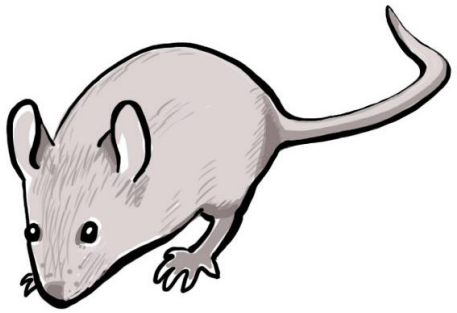
WHO Guideline = 20 µg/m³



Which Measure to Monitor in Ambient Air

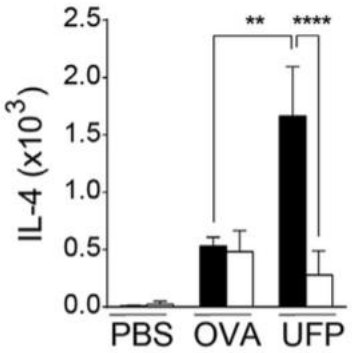


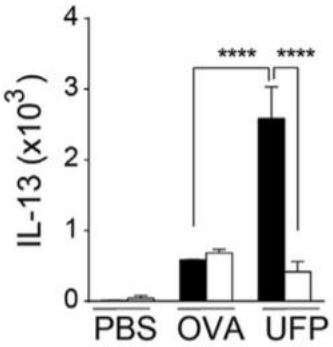
Animal Experimental Data on Allergy and PM2.5

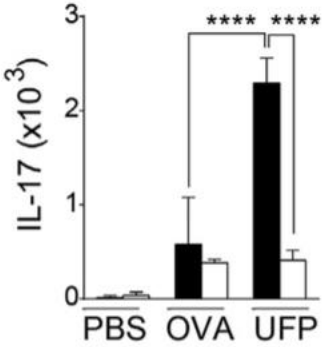


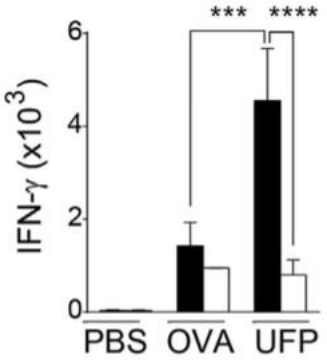
WT
CD11c-AhR -/-

Allegry









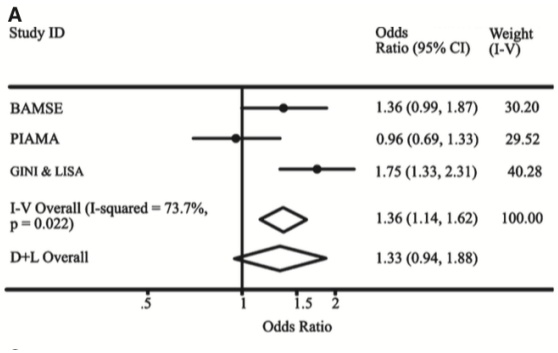
<PM2.5

Effects of Air Pollution on Childhood Allergic Sensitization

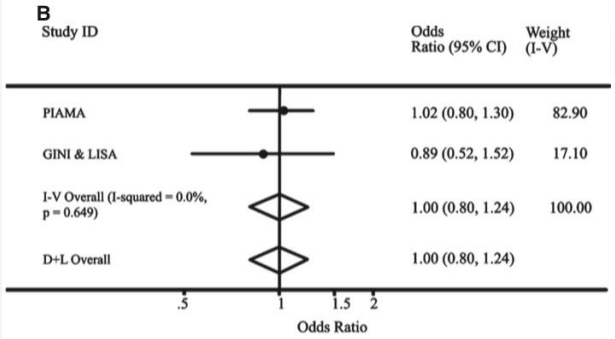
PM 2.5

(effects of 2 µg/m^3 increase)

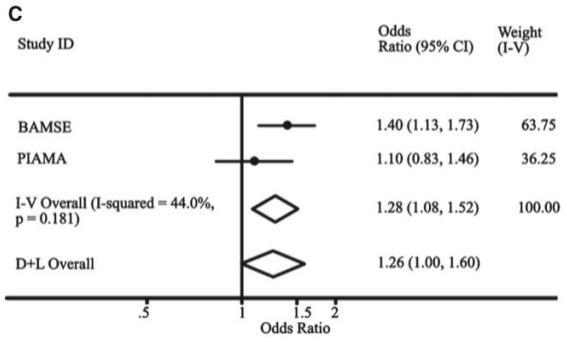
Outdoor allergens



Indoor allergens

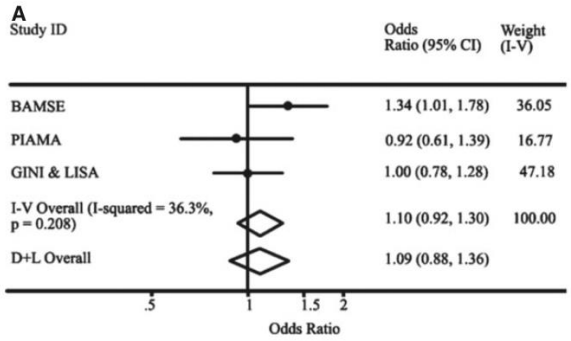


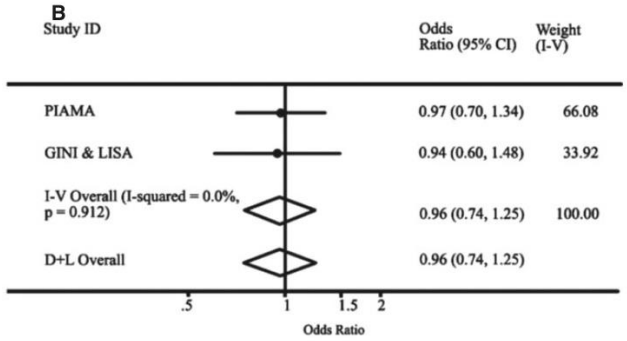
Food allergens

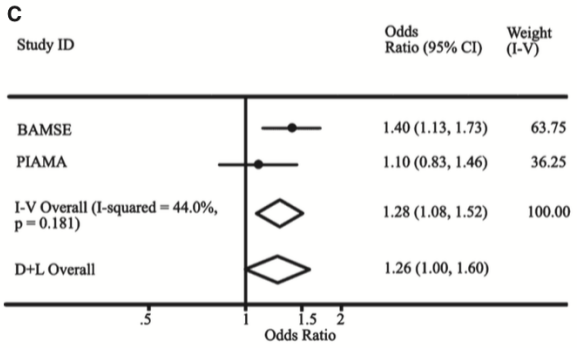


NO_2

(effects of 10 µg/m^3 increase)



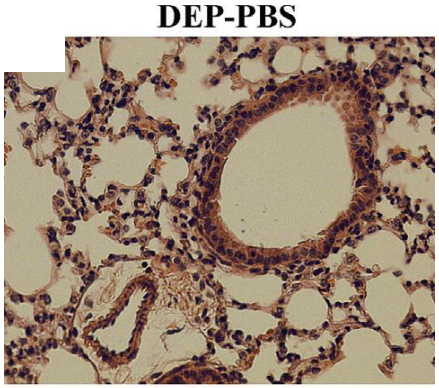


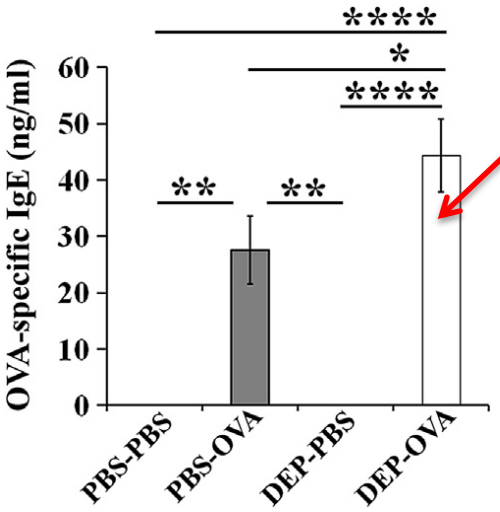


Bowatte et al., Allergy 2015

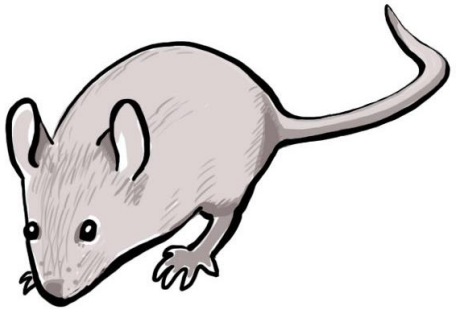
Diesel exhaust particles (DEP) and sensitization

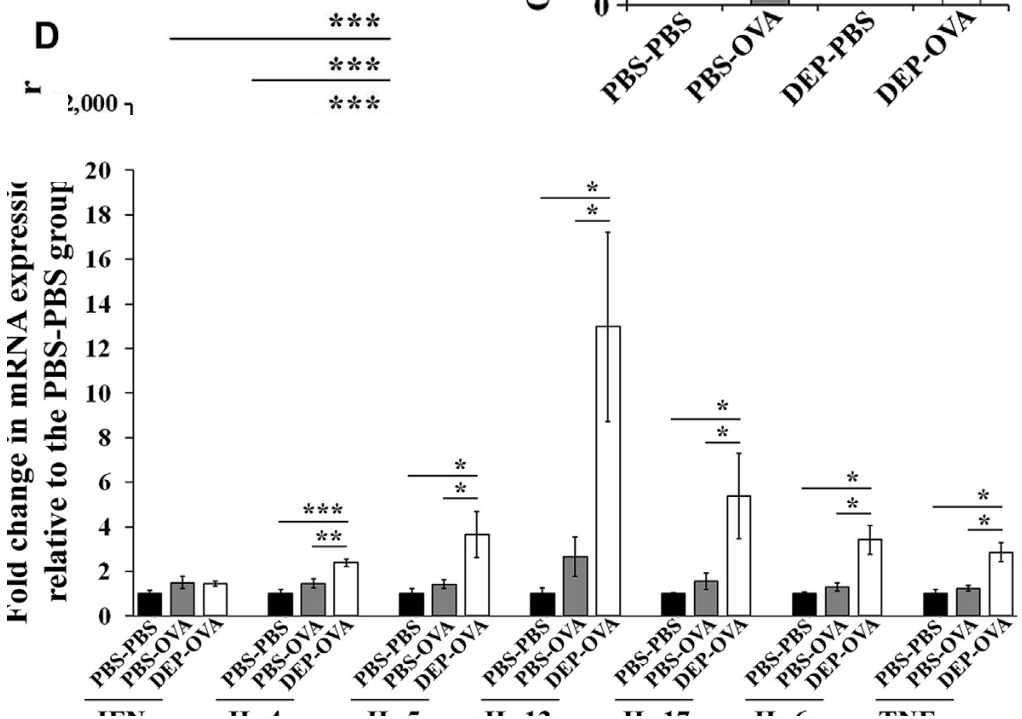
Allergy Parameter





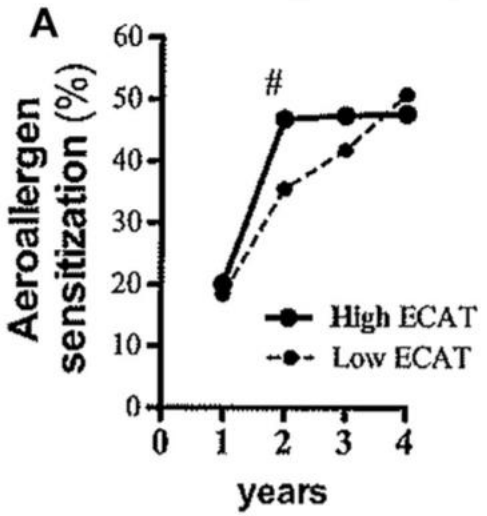
White bars = with Diesel Particles

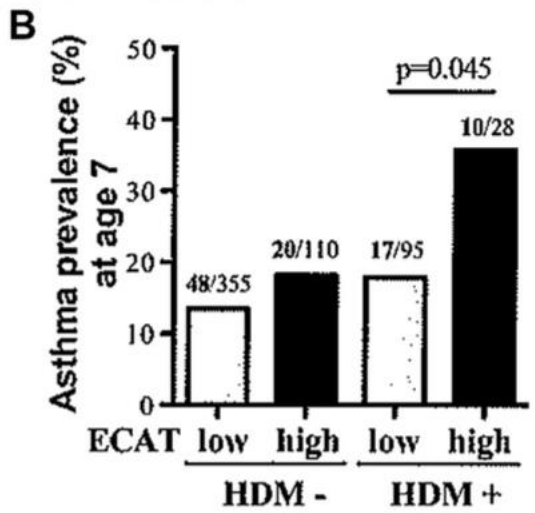


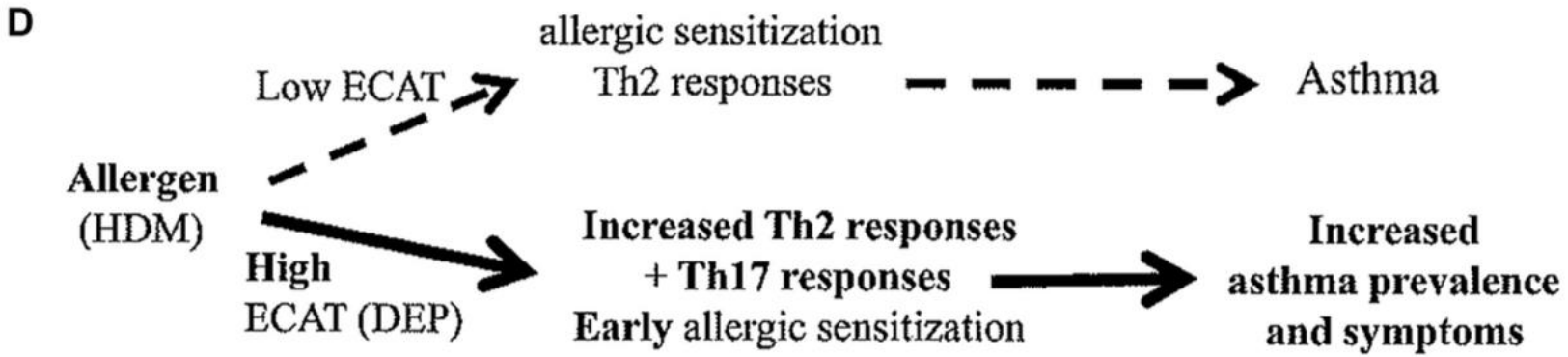


Manners *et al.*, JACI, 2014

Effect of Diesel Particles on allergic asthma







ECAT= elemental carbon attributed to traffic (≈ diesel particles)

Brandt et al., JACI 2015

$NO - NO_2$ equilibrium

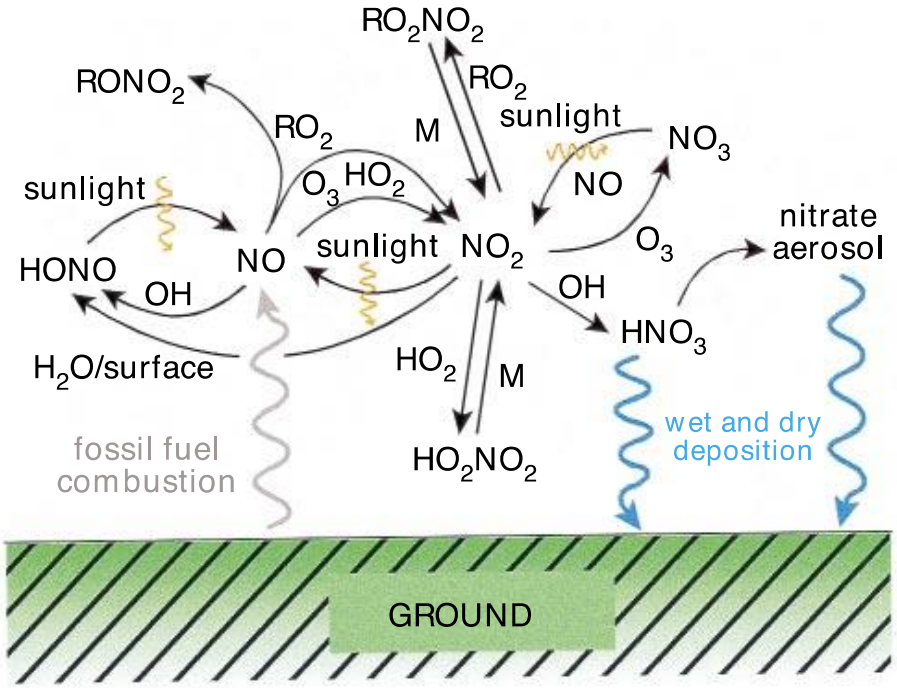
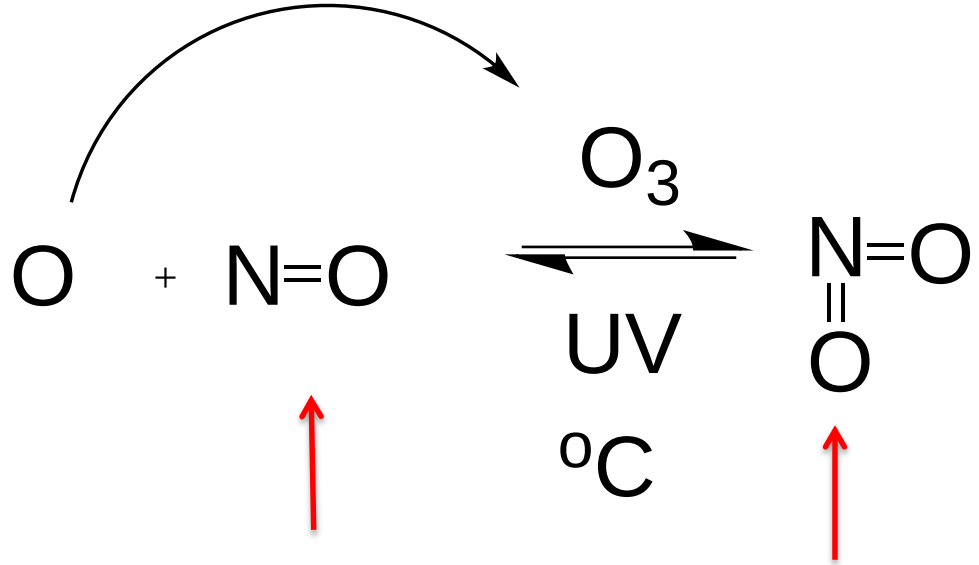


Figure 5. Daytime atmospheric chemistry of nitrogen oxides in the boundary layer (from PORG (1997)).

Fowler *et al.*, New Phytol. (1998), 139, 11–23

Equilibrium of Nitrogen Oxides (NOx) and Ozone



Diesel car exhaust	16.3 ppm	0.4 ppm
Atmosphere city	50 µg/m^3	70 µg/m^3
village	8 µg/m^3	18 µg/m^3
NIOHS life-time limit:	25 ppm	1 ppm

Fowler et al., New Phytol. (1998), 139, 11–23

NO_2 and Allergy

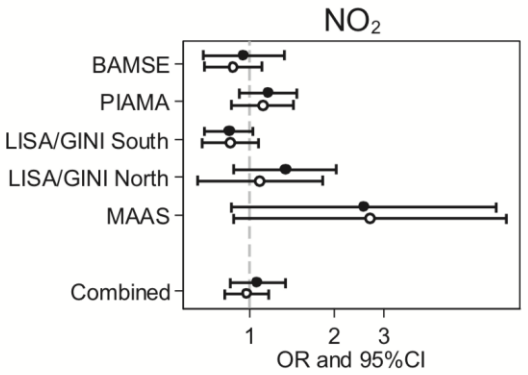
TABLE 4. Association between Allergy-Related Symptom Adjusted* Odds Ratios (OR) with 95% Confidence Intervals

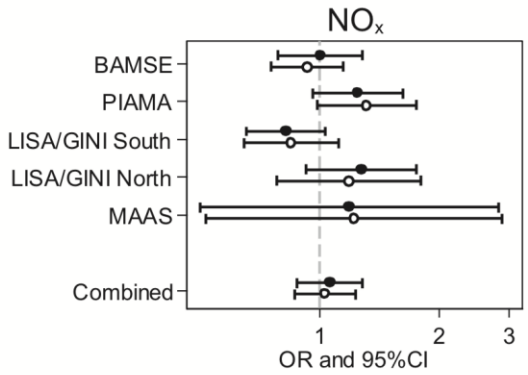
	Urbar	
	NO_2 Outdoors	
	OR	95% CI
Hay fever ever	4.24	1.01–17.84
Bronchial asthma ever	1.82	0.36–9.36
Eczema on day of investigation†	0.54	0.13–2.29
Rhinitis and itchy and reddened eyes	9.08	2.06–40.11
Wheezing	14.95	2.59–86.35
Itchy skin	1.97	0.65–6.03
Sensitization against		
Pollen	4.96	1.56–15.74
House dust mite or cat	3.51	1.03–11.96
Milk or egg	4.20	1.12–15.72

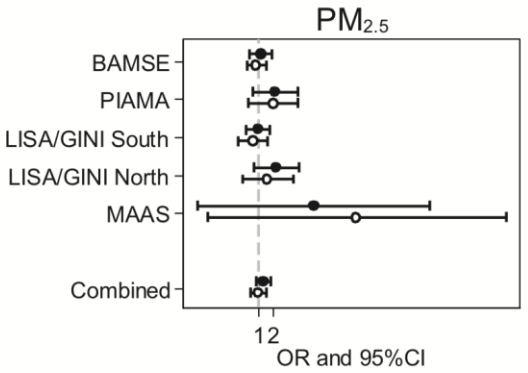
* Adjusted for older siblings, gender, and education of parents.
† Additionally adjusted for physician who investigated the skin.

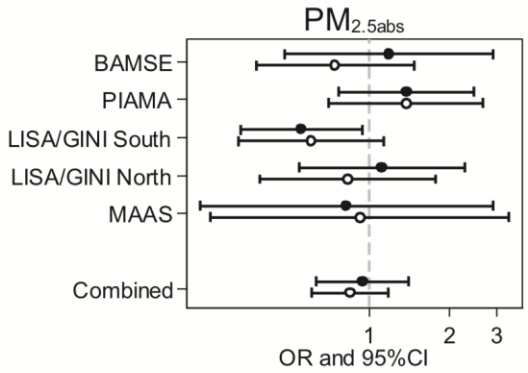
Krämer et al., Epidemiology, 2000

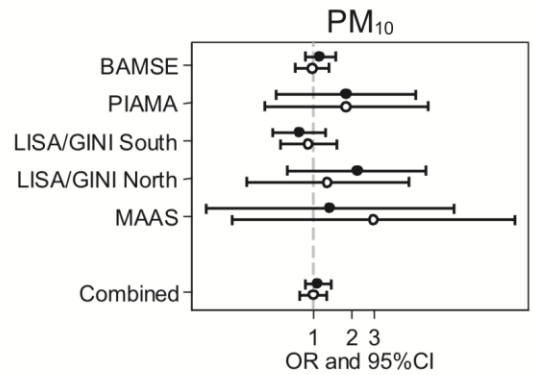
Effect of Air Polltion on Allergic disease

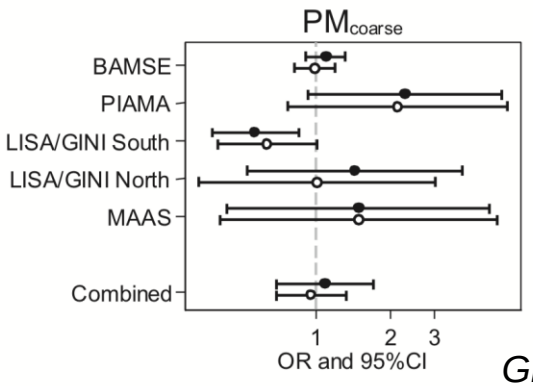












- Birth address
- Current address

Gruzieva, JACI 2014

Distance to a road and allergic sensitization

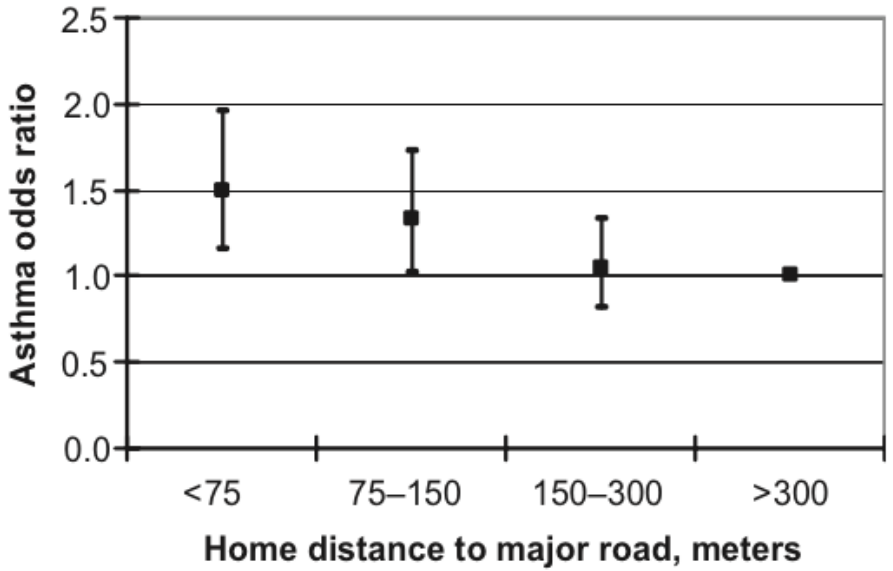


FIGURE 2
Traffic proximity and risk of asthma in the CHS.[6] (Reproduced with permission from McConnell R, Berhane K, Yao L, et al. *Environ Health Perspect*. 2006;114(5):769).

McConnel et al., Env. Health Persp. 2006

Conclusions on Air Pollution and Health

1. The most dangerous air pollutant is Particulate Matter (PM) probably from combustion

2. The next pollutant to target is NOx

3. The easiest way to quickly limit air pollution is to change fuels:
   Go for Methane (CNG or LNG) or Ethanol combustion

4. To monitor pollution effectively, go for smaller PM (like PM2.5 or PM1) that monitor elemental carbon (EC) from combustion

5. Pollen should be included in air quality monitoring

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Renate Effner
Christine Weil
Danijel Kupresanin
Elke Bartusel

Dr. G. Reese, Germany
Dr. W. Weber, Germany

Meteo Swiss
Dr. Regula Gehrig
Dr. Bernard Clot

Increasing proportion of NO_2

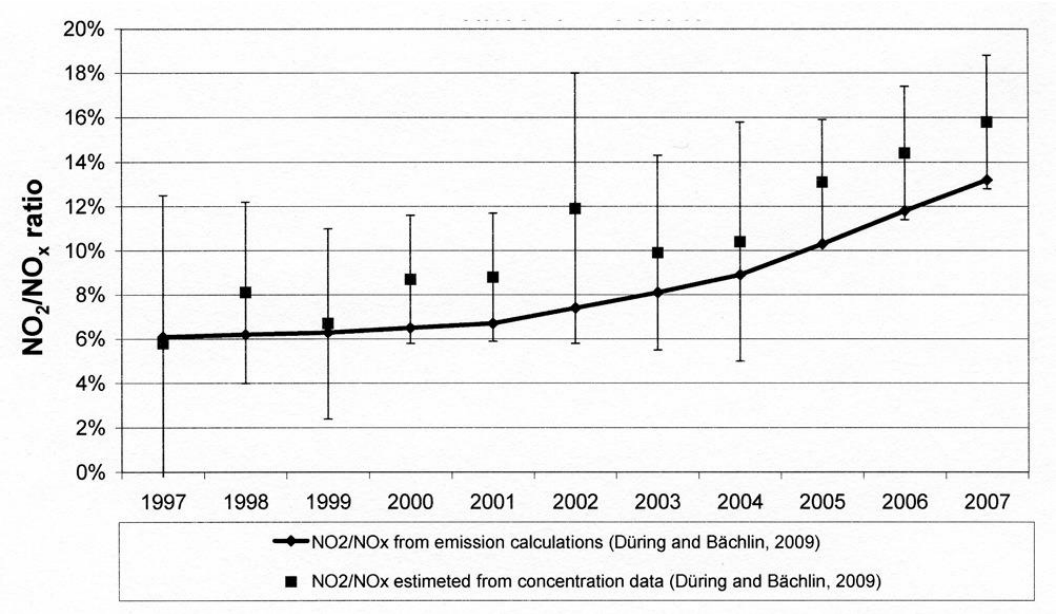
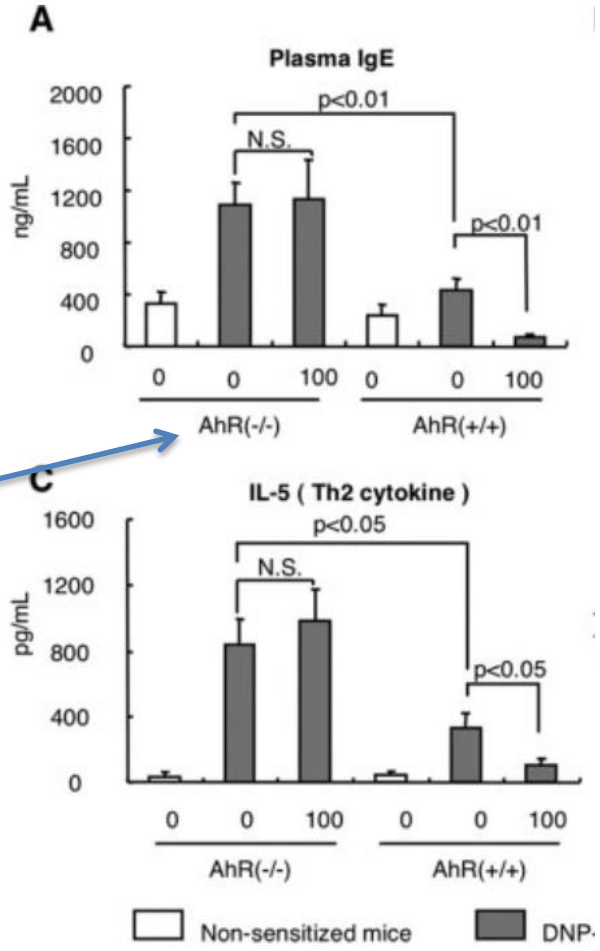


Figure 6: Comparison of annual mean NO_x-concentrations, calculated with OSPM, with observed data from the measurement site Corneliusstraße in Duesseldorf for the years 1997–2006. NO_x_b = NO_x background concentration.

Düring *et al. Meteorol. Z.,* ***20****, 2011*

Effect of Aryl Hydrocarbon Receptor (AhR) on Allergic Sensitization



Aryl Hydrocarbon knockout Mice

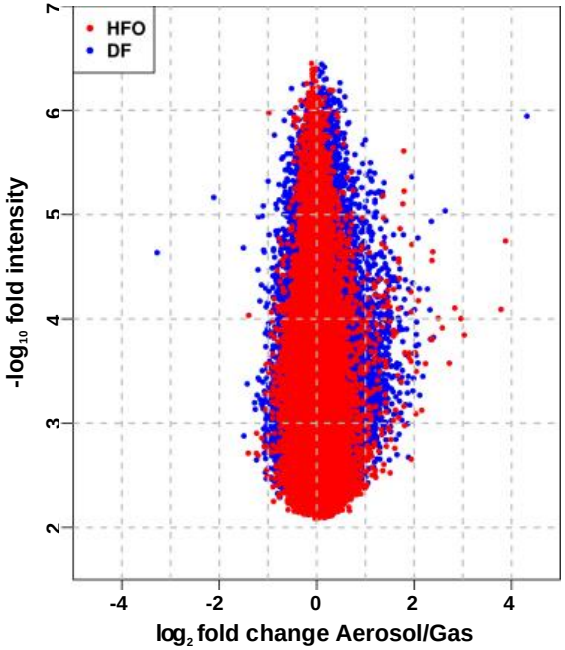
In this figure:
AhR is NOT Airway Hyperreactivity

DNP= nitrated Ascaris protein

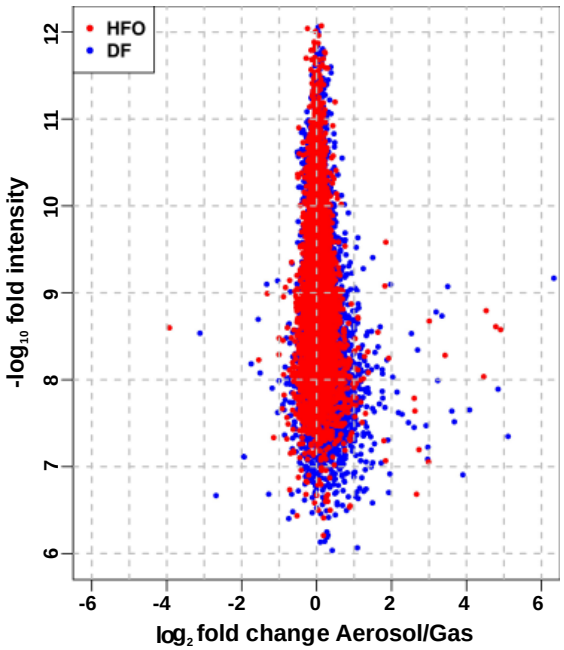
Negishi et al., J Immunol 2005

Toxicologic evaluation of particles: More reponses with DF

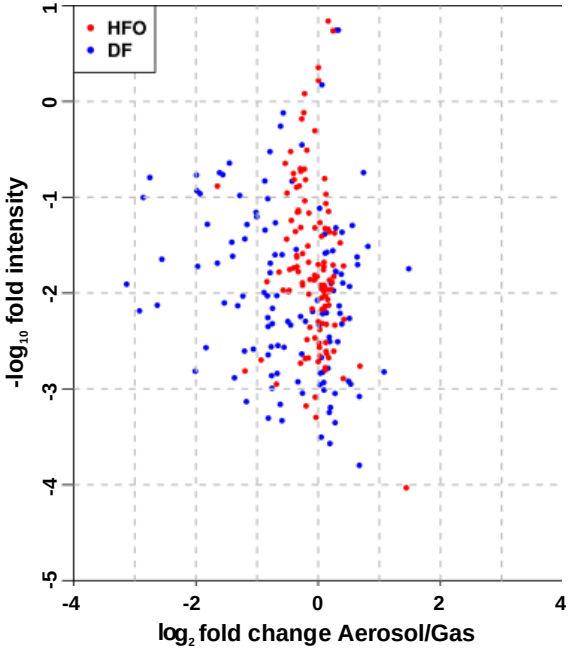
Transcriptome



Proteome

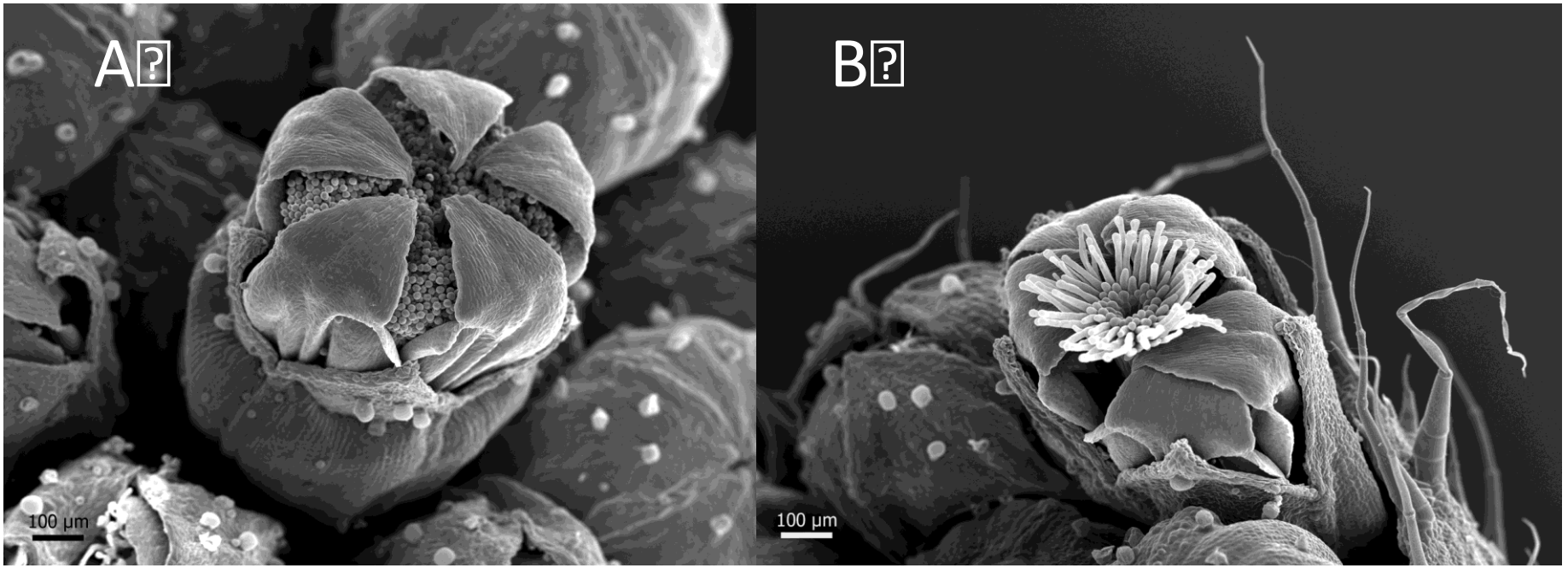


Metabolome



HFO
DF

Effect of Air Pollution on Pollen

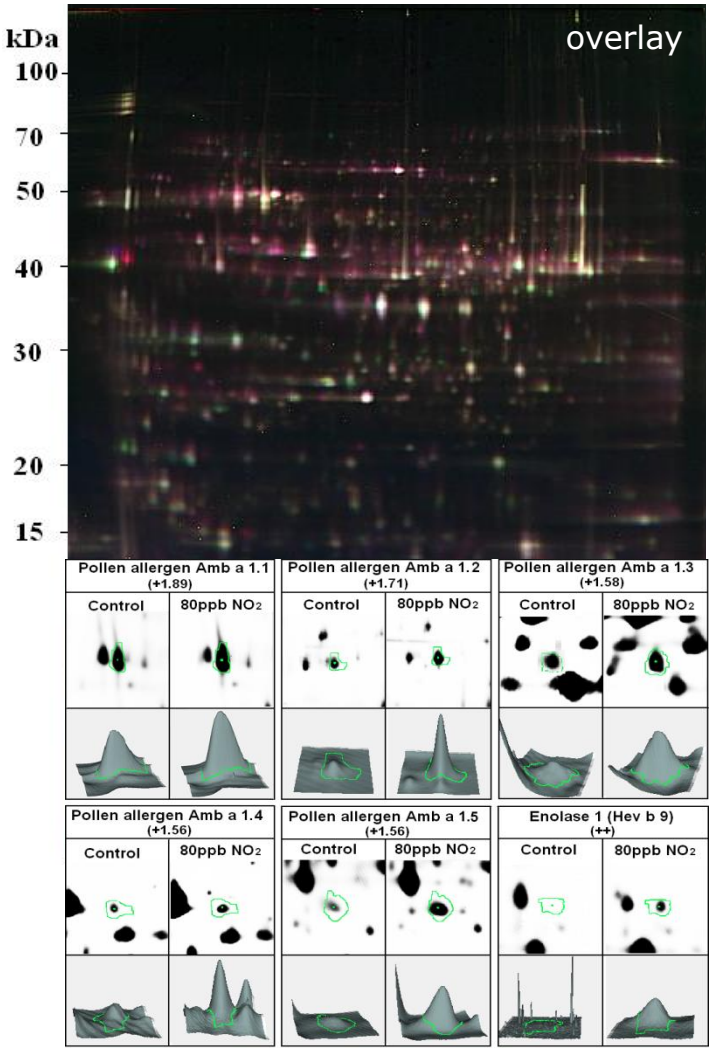


Source: Buters et al, Allergo J 2015

Beck et al., PLOSone 2013

NO_2 treatment of Ambrosia plants

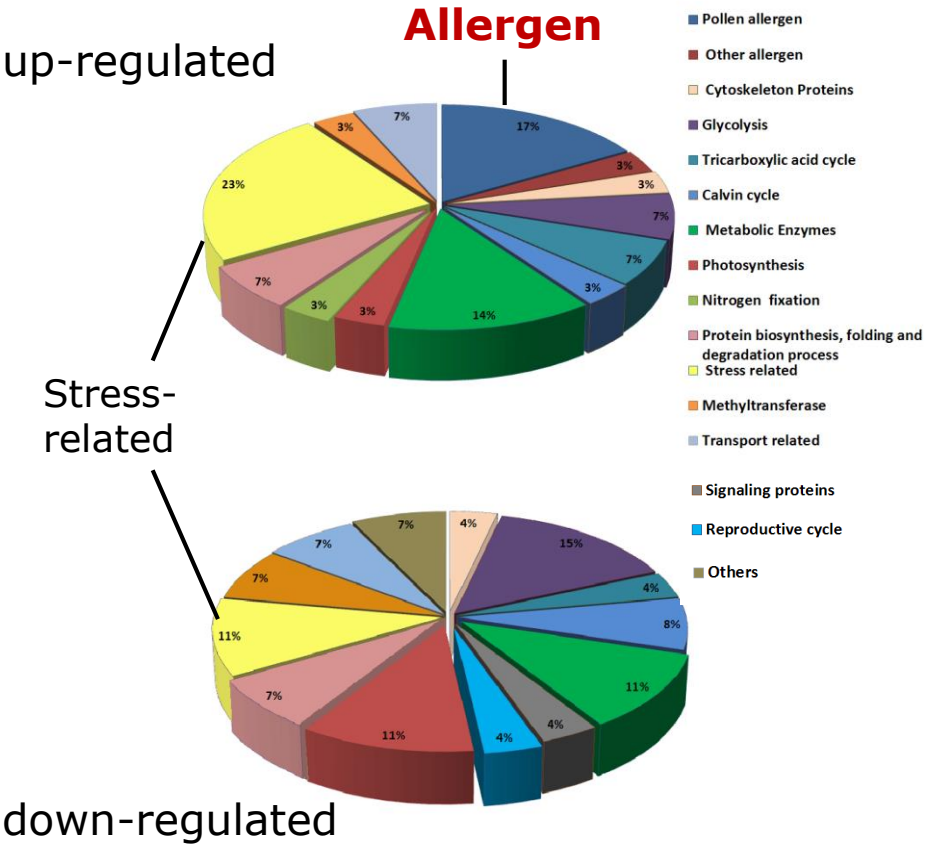
40ppb NO_2 vs. 80ppb NO_2



up-regulated

Stress-related

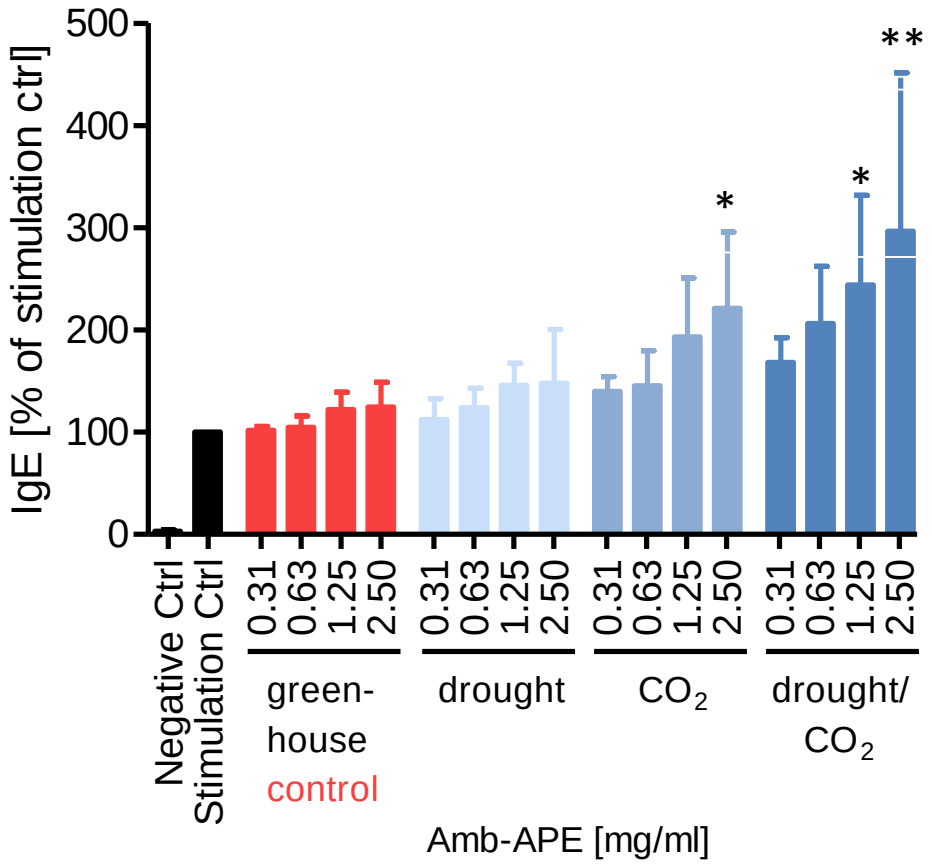
down-regulated



Zhao et al. 2015 PCE, in revision

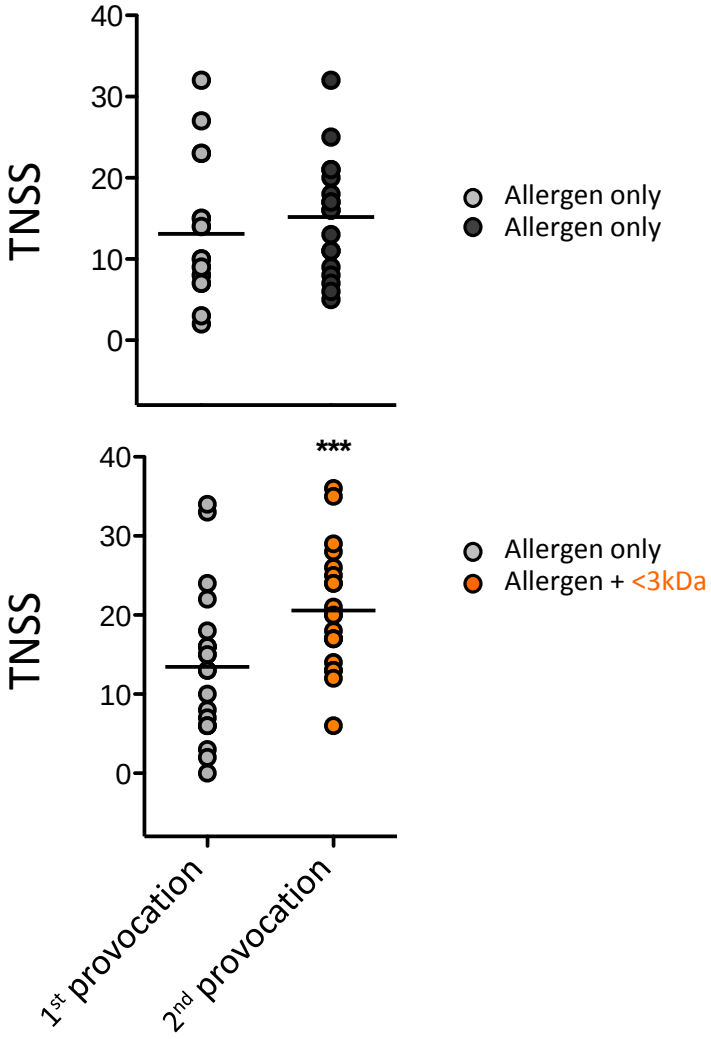
U. Frank, PDS4

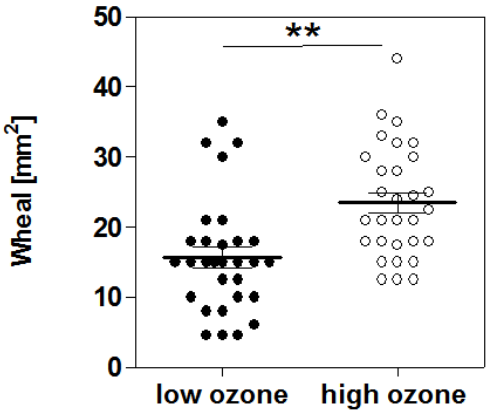
Effect of Climatic Conditions of Ambrosia Pollen

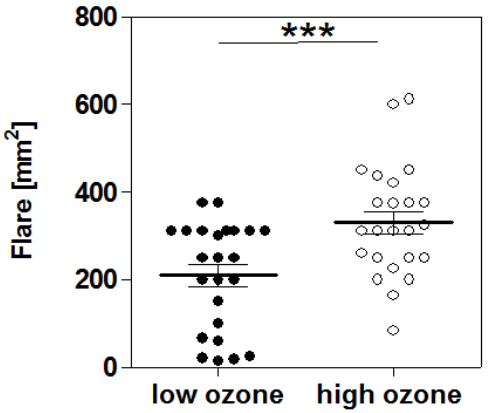


Öder et al., unpublished 2015

Testing pollen allergenicity in vivo

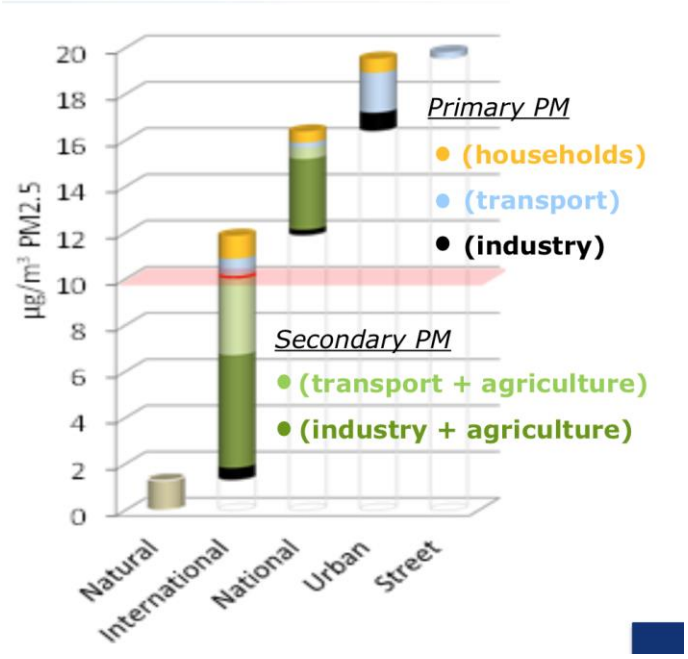






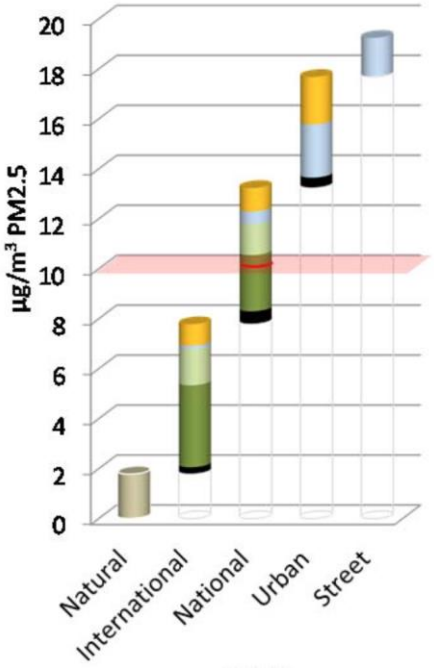
Beck et al., PLoS One 2013

Urban $PM_{2.5}$ concentrations



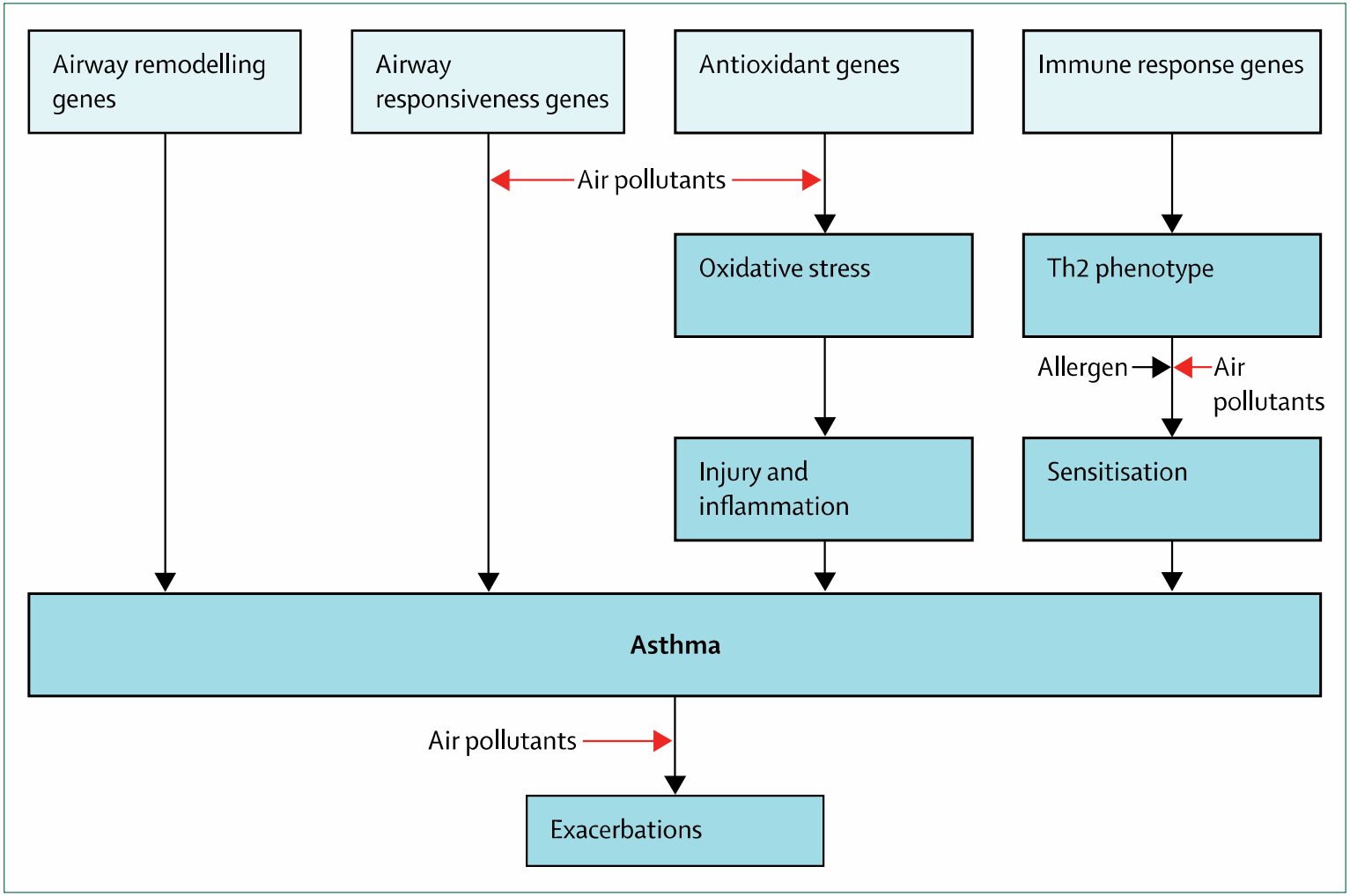
Austria (29 stations)

A. 2009

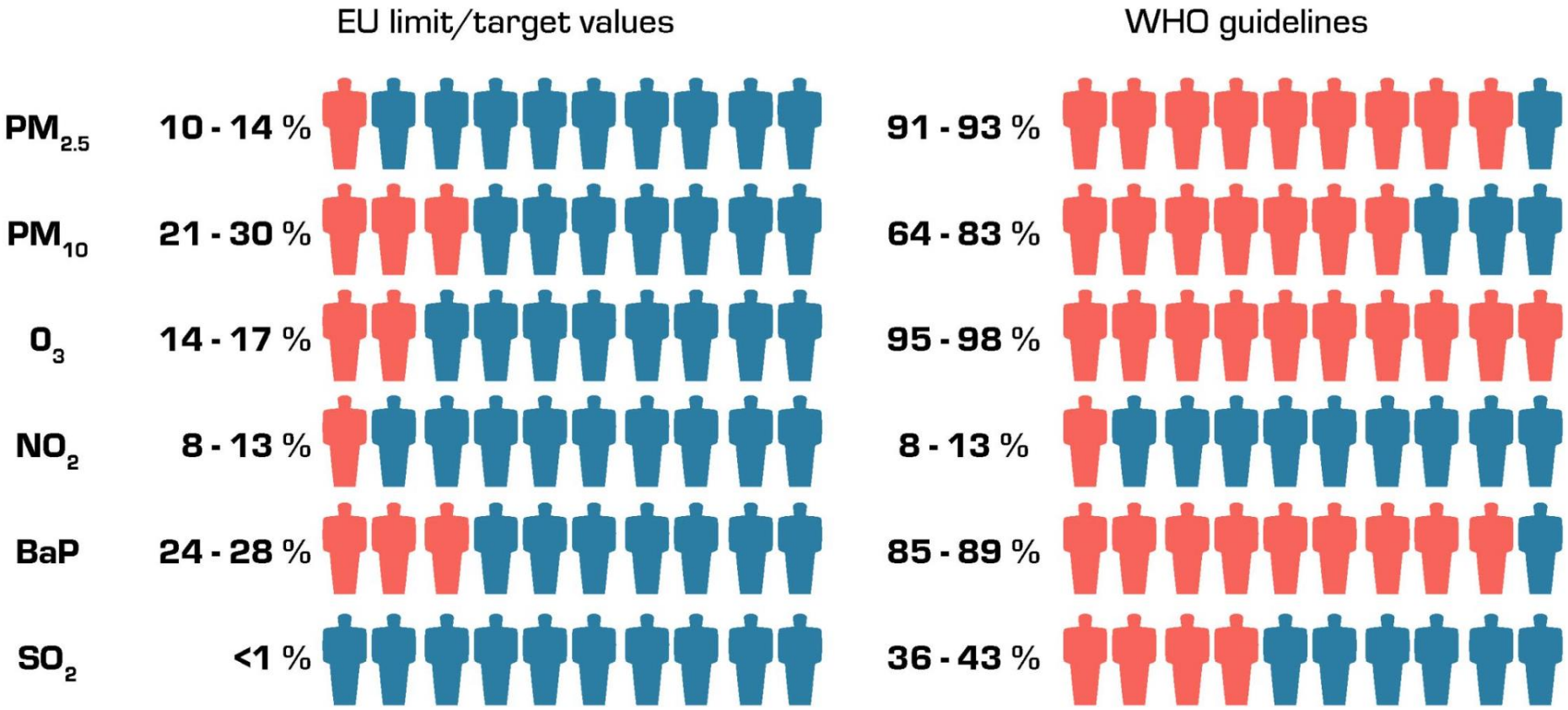


Kiesewetter 2014

Air pollutants and asthma



Guarnieri & Balmes, Lancet, 2014


EU limit/target values
WHO guidelines
PM2.5
10 - 14 %
91 - 93 %
PM10
21 - 30 %
64 - 83 %
O3
14 - 17 %
95 - 98 %
NO2
8 - 13 %
8 - 13 %
BaP
24 - 28 %
85 - 89 %
SO2
<1 %
36 - 43 %

- Air Pollution
- Air Pollution and Pollen
- Air Pollution and Allergy

- Air Pollution
  - Motor vehicles
  - Wood combustion
  - Ships
  - Gases vs particles
- Air Pollution and Pollen
  - more pollen
  - new pollen
  - changed pollen
- Air Pollution and Allergy
  - Combustion pollution
  - Arylhydrocarbon Receptor (AhR)