# Efectos de la Contaminación Atmosferica en la Salud Cardiovascular

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ISGlobal
Institut de Salut Global Barcelona
Una iniciativa de:

Institució CERCA
Centres de Recerca de Catalunya

OCTAVAS JORNADAS CIENTÍFICAS DEL
CEIPV
Comité Español Interdisciplinario para la Prevención Vascular

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9 out of 10 people in the world breath polluted air (WHO)
What is air pollution?
Chris_LeBoutillier

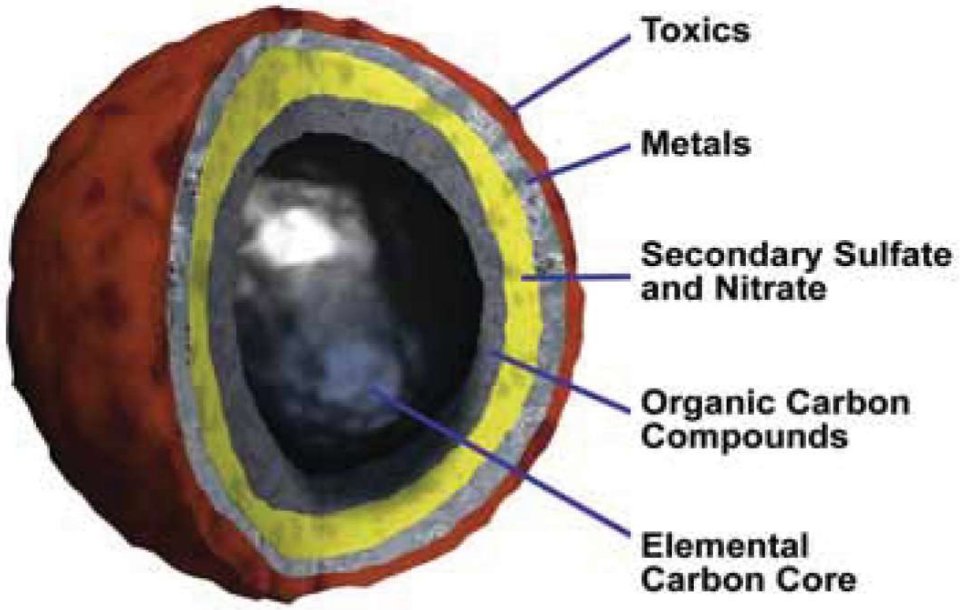
# Air pollutants

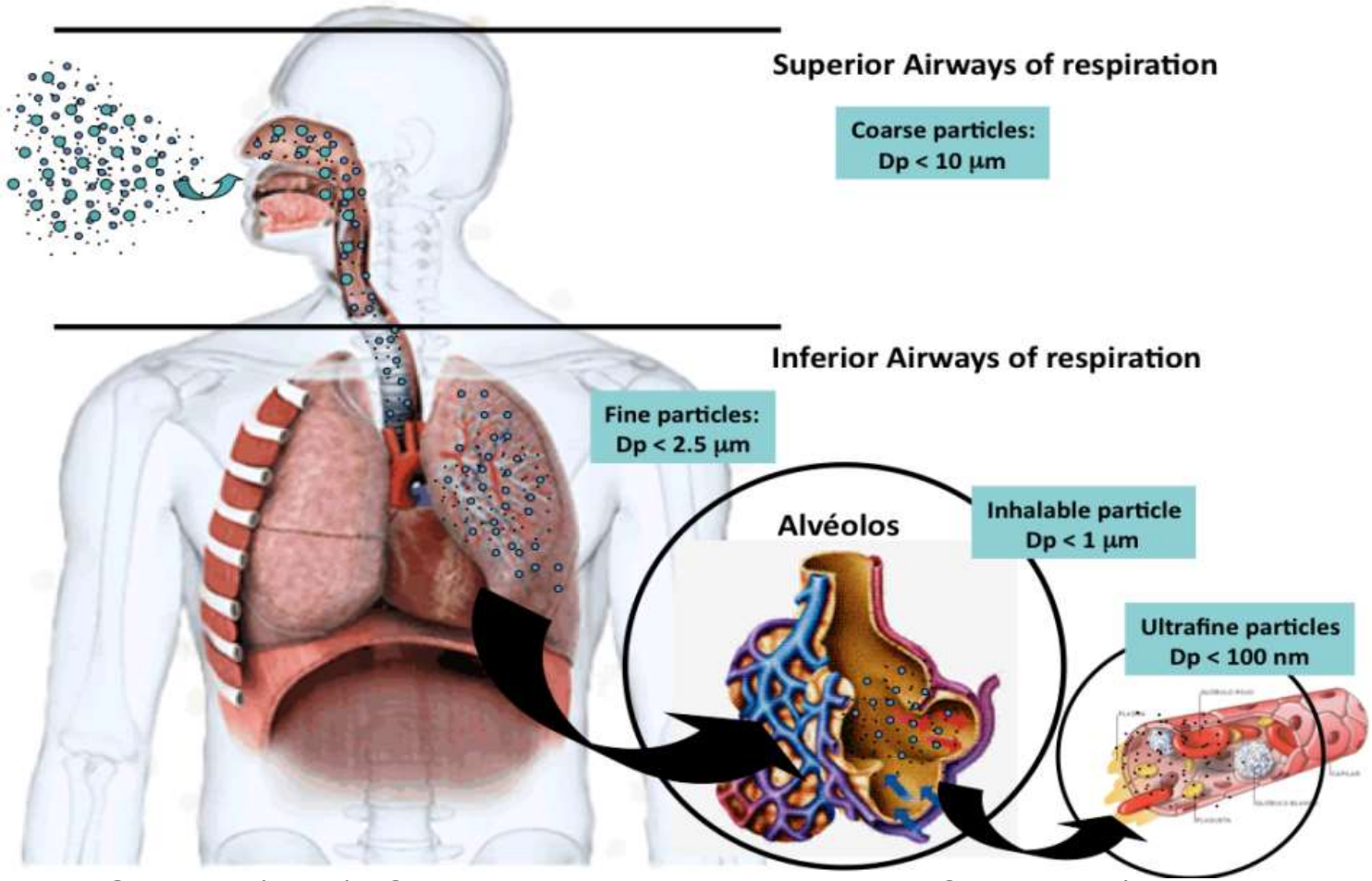
- Particulate matter ($PM_{10}$, $PM_{2.5}$, components e.g. OC, BC)
- Nitrogen dioxide ($NO_2$)
- Carbon dioxide ($CO_2$)
- Ozone
- Sulfur dioxide ($SO_2$)

# Particulate matter

- Complex mix of particles in solid and liquid phase which dimentions can span from few nm to 100 µm.

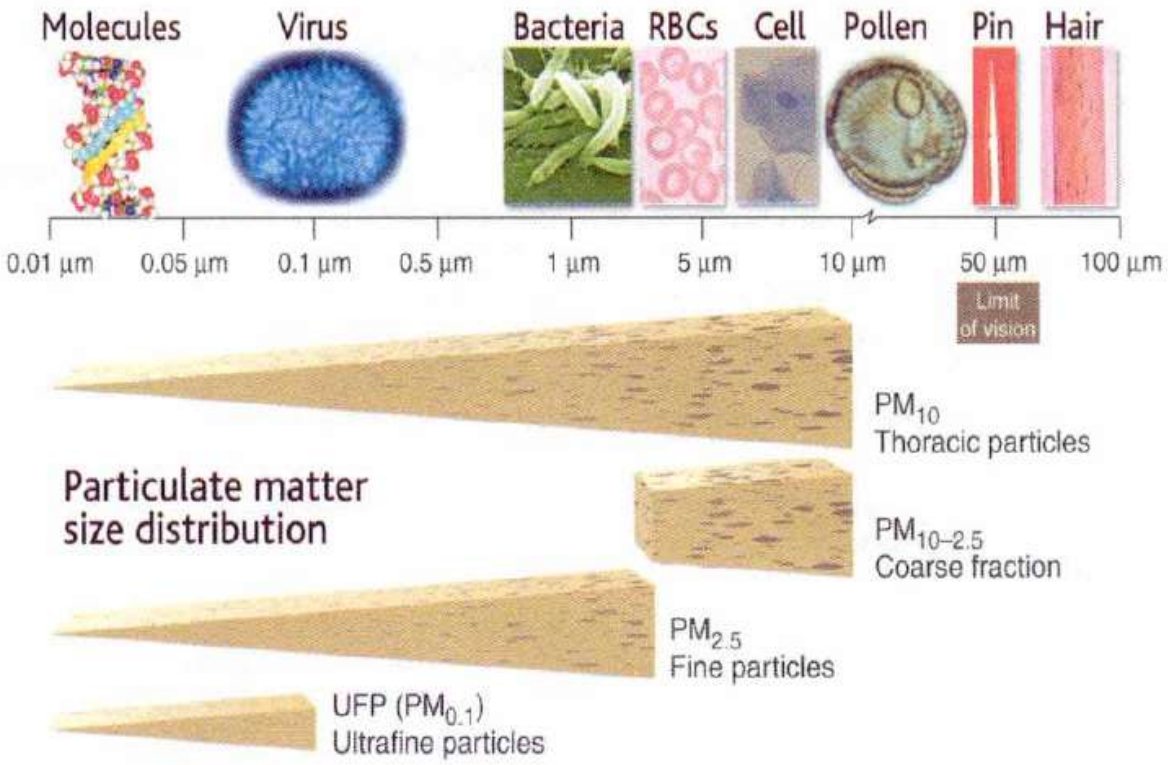
- Aerodinamic equivalent diameter

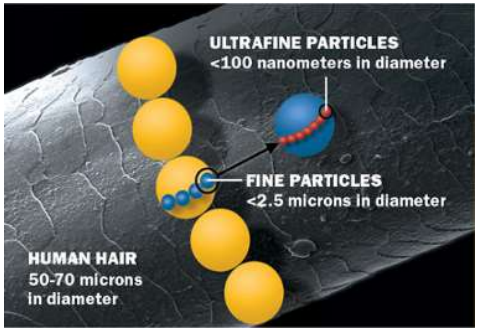




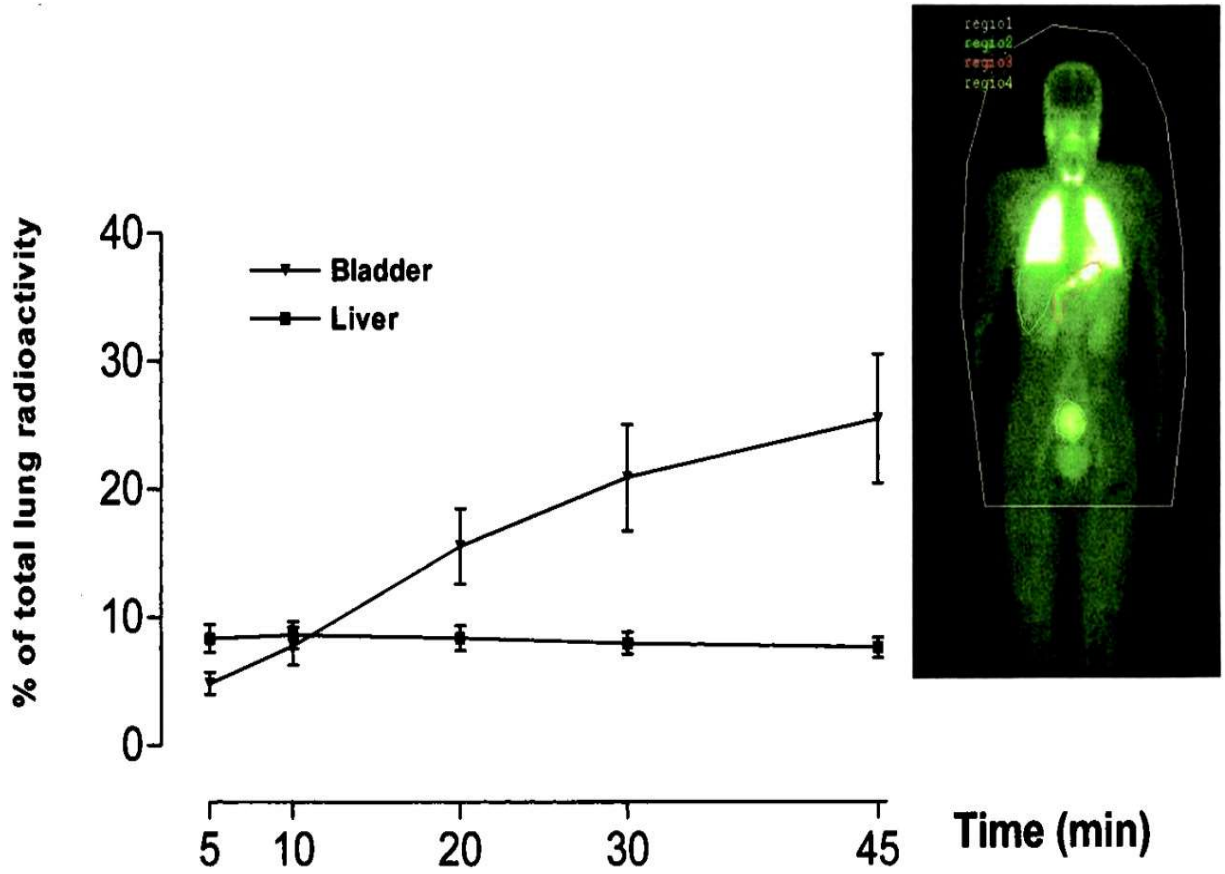

Lefol Nani Guarieiro (2013). ISBN: 978-953-51-0950-1, InTech, DOI: 10.5772/52513.

# Particulate matter – $PM_{10}$, $PM_{2.5}$, Coarse particles, UFP



# UFPs passage in the blood stream




*Da Nemmar et al. Circulation 2002;105:411*




Source: WHO website

**Particulate matter**




Source: WHO website

**Particulate matter – $PM_{2.5}$**




Source: WHO website

$NO_2$




Source: WHO website

## Ozone

Secondary pollutant → produced when carbon monoxide (CO), methane, or VOCs are oxidized in the presence of nitrogen oxides and sunlight.

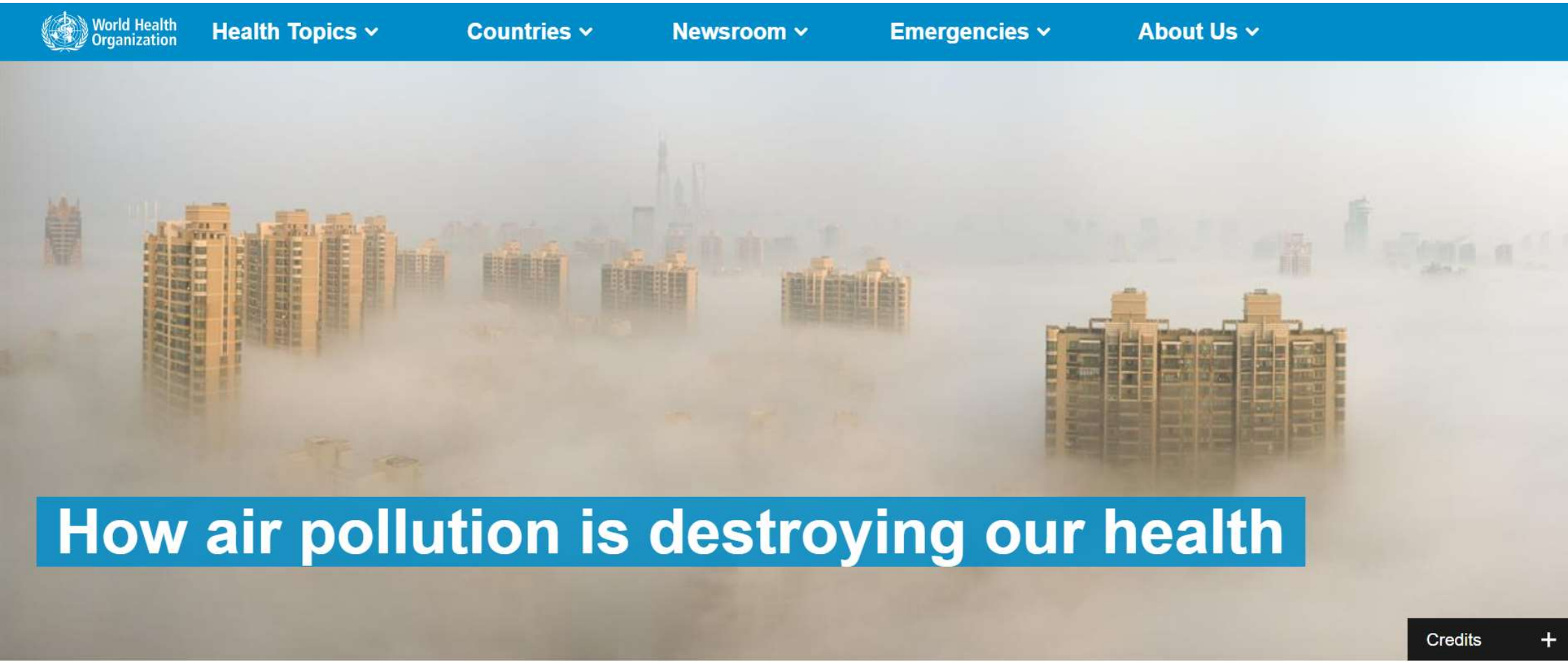



Source: WHO website

$SO_2$



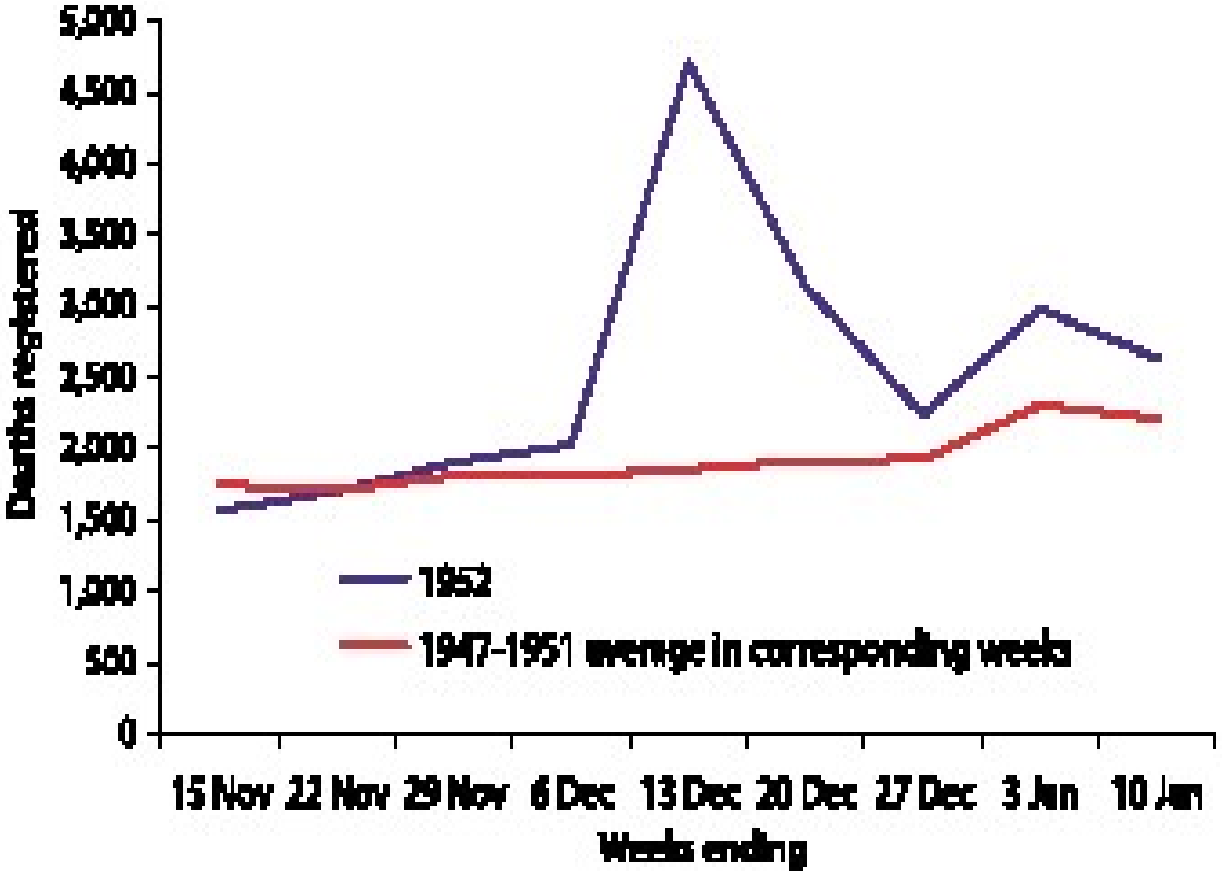

Source: WHO website

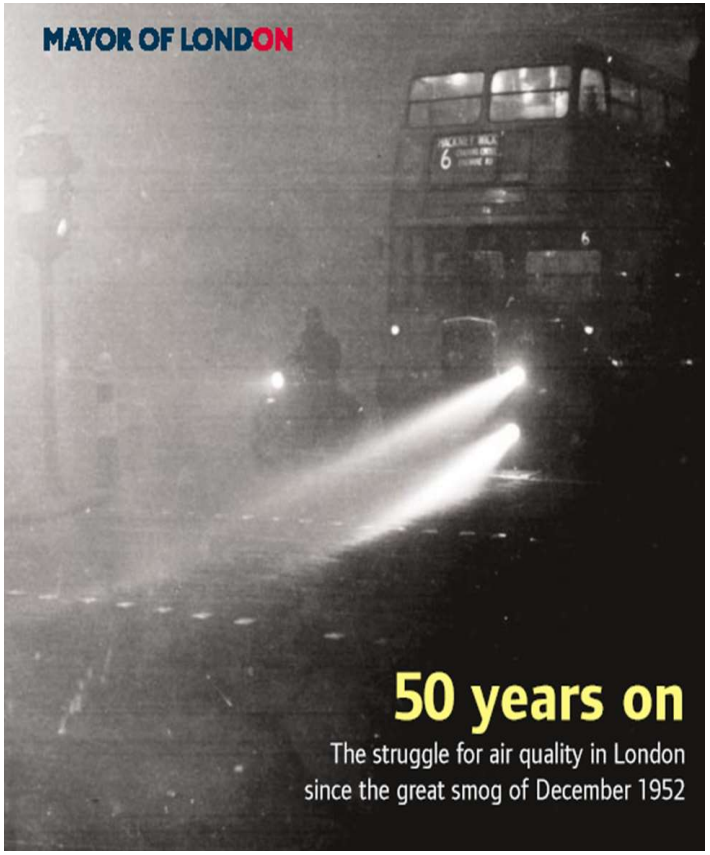

World Health Organization
Health Topics
Countries
Newsroom
Emergencies
About Us
How air pollution is destroying our health
Credits



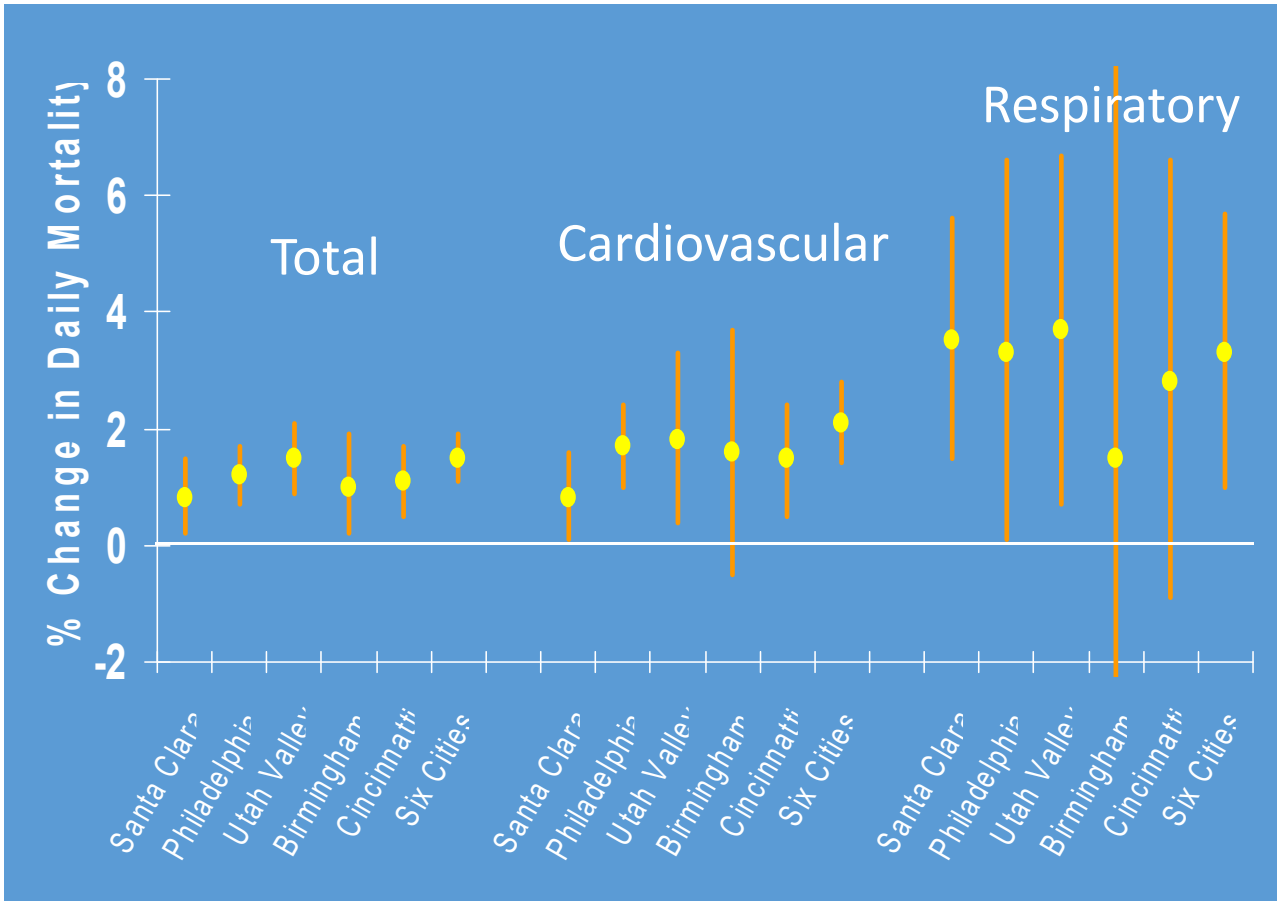
*House of Parliament*, Claude Monet (1904)

# The London's Great Smog – Winter 1952



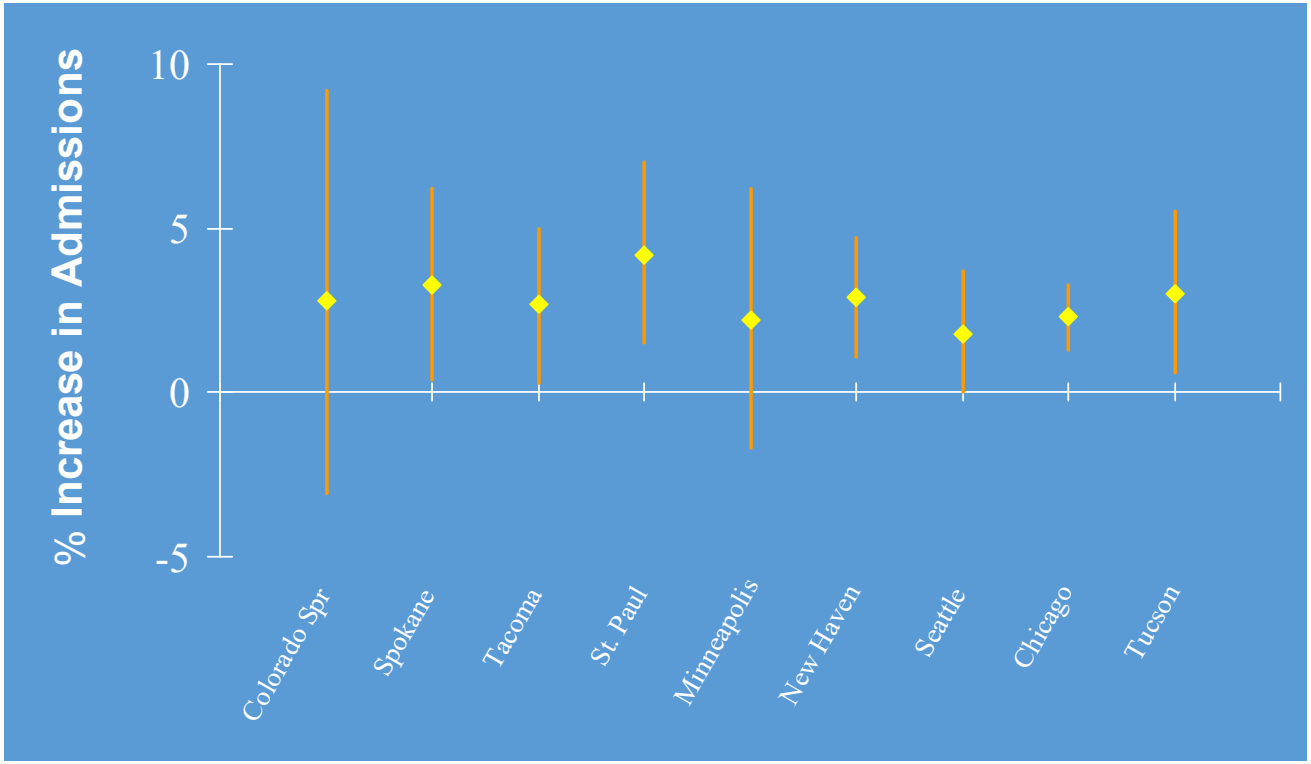



# Six Cities Study: Effect on mortality of a daily increase of 10 $\mu g/m^3$ in $PM_{10}$



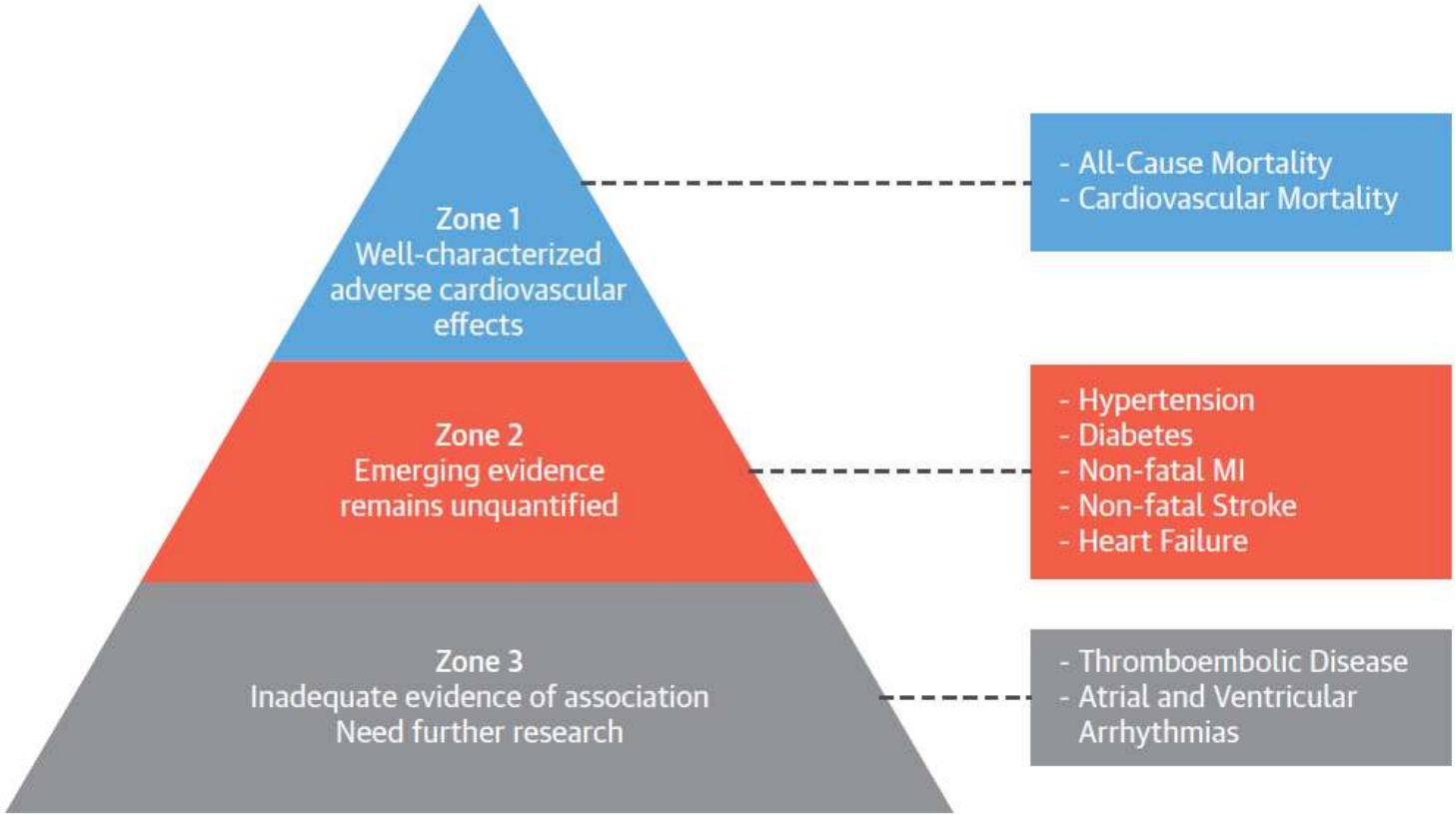

Adapted from Dockery D.W. (1993). N. Engl. J. Med, 329: 1753-1759.

# Effect of a daily increase of 10 μg/m$^3$ in $PM_{10}$ and admissions cardiovascular diseases




Schwartz J, *Epidemiology* 1999

**FIGURE 2** The Zones of Evidence Linking Air Pollution and CV Disease




Adapted from Landrigan et al. (1). CV = cardiovascular; MI = myocardial infarction.

Rajagopalan JACC 2018;72(17):2954-70




Source: WHO website

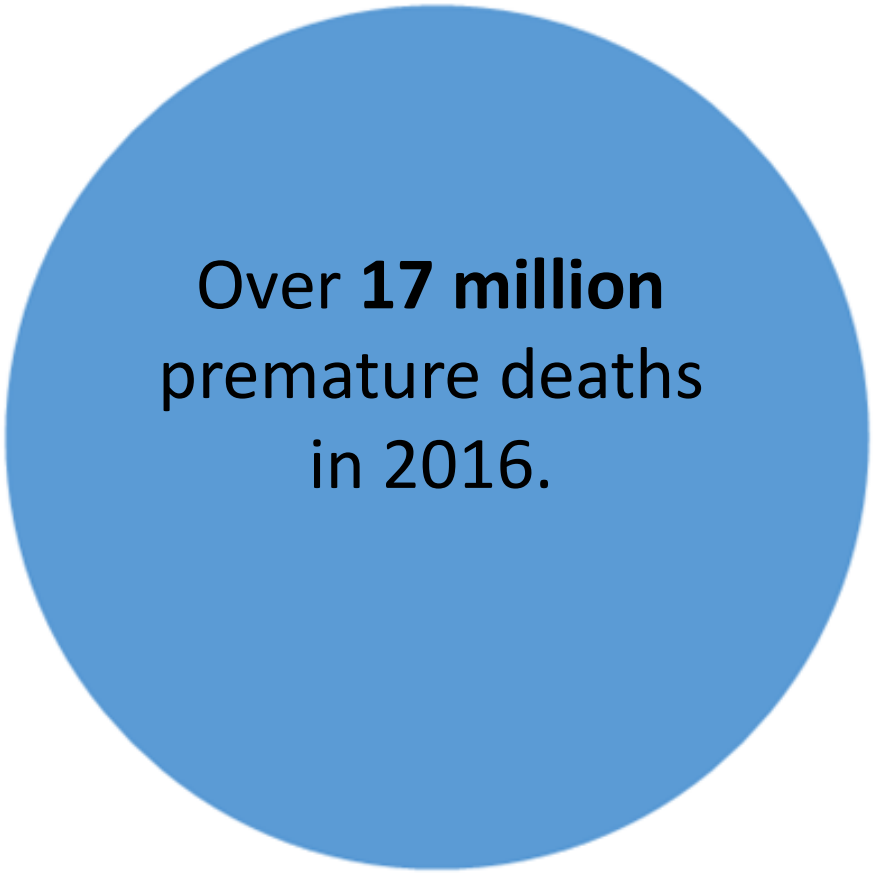
# SUSTAINABLE DEVELOPMENT GOAL 3

## Ensure healthy lives and promote well-being for all at all ages

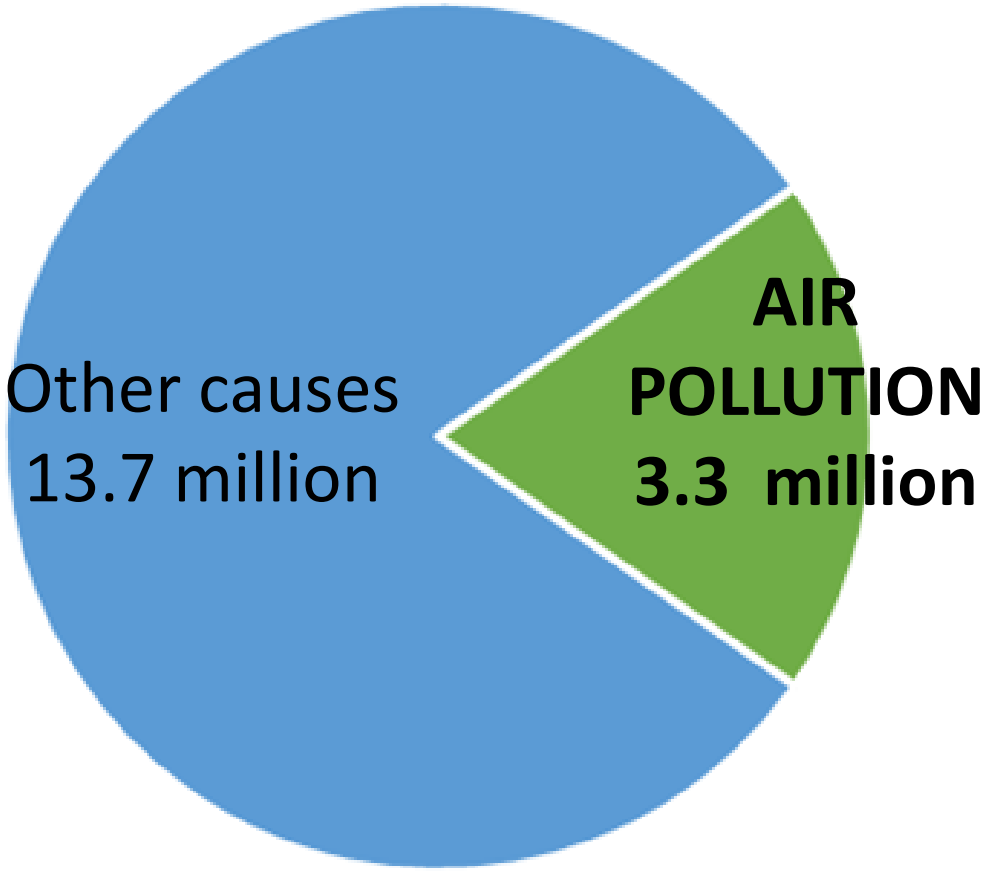


| | | | |
|---|---|---|---|
| **3.9** | By 2030, substantially reduce the number of deaths and illnesses from hazardous chemicals and air, water and soil pollution and contamination | **3.9.1** | Mortality rate attributed to household and ambient air pollution |
| | | **3.9.2** | Mortality rate attributed to unsafe water, unsafe sanitation and lack of hygiene (exposure to unsafe Water, Sanitation and Hygiene for All (WASH) services) |
| | | **3.9.3** | Mortality rate attributed to unintentional poisoning |

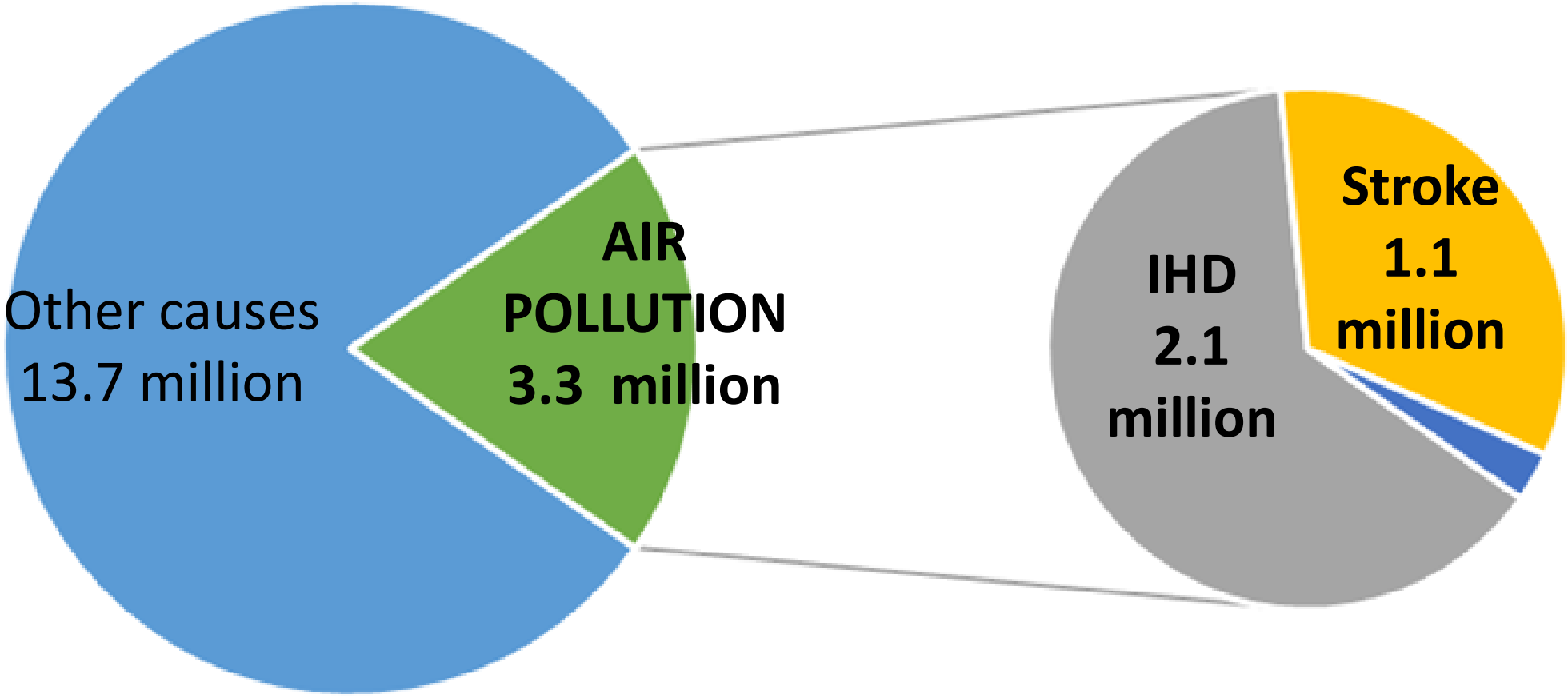
**Cardiovascular disease → leading cause of death**



**Exposures to air pollution** was responsible of 19% of these deaths (http://ghdx.healthdata.org/gbd-results-tool; GBD Lancet. 2017;390:1345–1422.)



**Exposures to air pollution** was responsible of 19% of these deaths (http://ghdx.healthdata.org/gbd-results-tool; GBD Lancet. 2017;390:1345–1422.)



## HEART

**Myocardial infarction:** More than 1.1 million deaths every year.

According to WHO, myocardial infarctions lead to 26% of annual premature deaths caused by the exposure to household air pollution from solid fuel combustion.

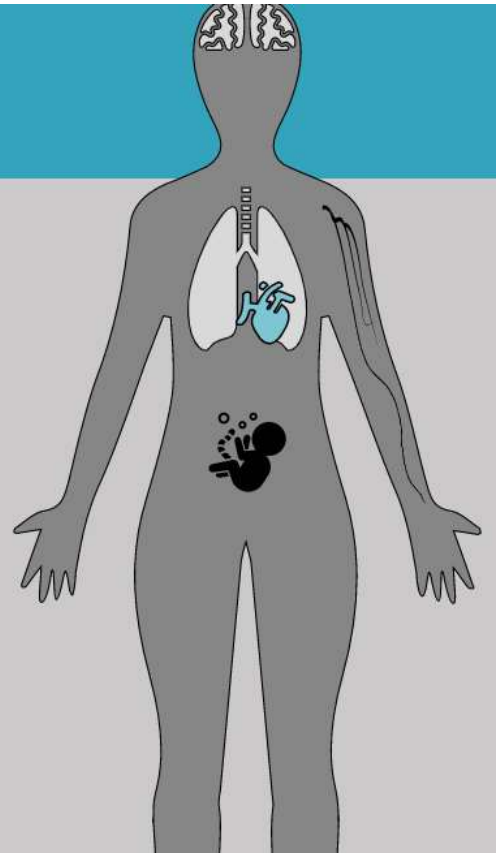
*Source: http://www.who.int/mediacentre/factsheets/fs292/es/*

**Arrhythmia:** Triggering factor of arrhythmias.

*Source: Circulation 2010;121;2331-2378.*

**Congestive heart failure:** Growing evidence links air pollution with cardiovascular mortality and morbidity.

*Source: Circulation 2010;121;2331-2378.*



Source: ISGlobal website

## ARTERIES

**Hypertension:** Higher risk of hypertension.

*Source: Circulation 2010;121;2331-2378.*

**Systemic inflammation:** Higher risk of chronic inflammation.

*Source: Circulation 2010;121;2331-2378.*

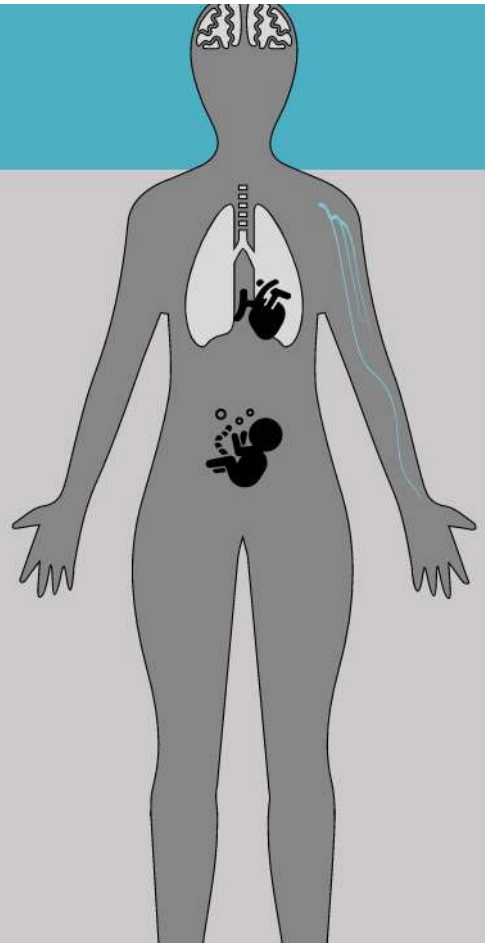
**Deep venous thrombosis:** Evidence suggesting a 70% risk increase.

A study performed in Lombardy, Italy, found that a long-term increase in exposure to PM10 particles is associated with a 70% increase in the risk of developing deep venous thrombosis.

*Source: Circulation 2010;121;2331-2378.*

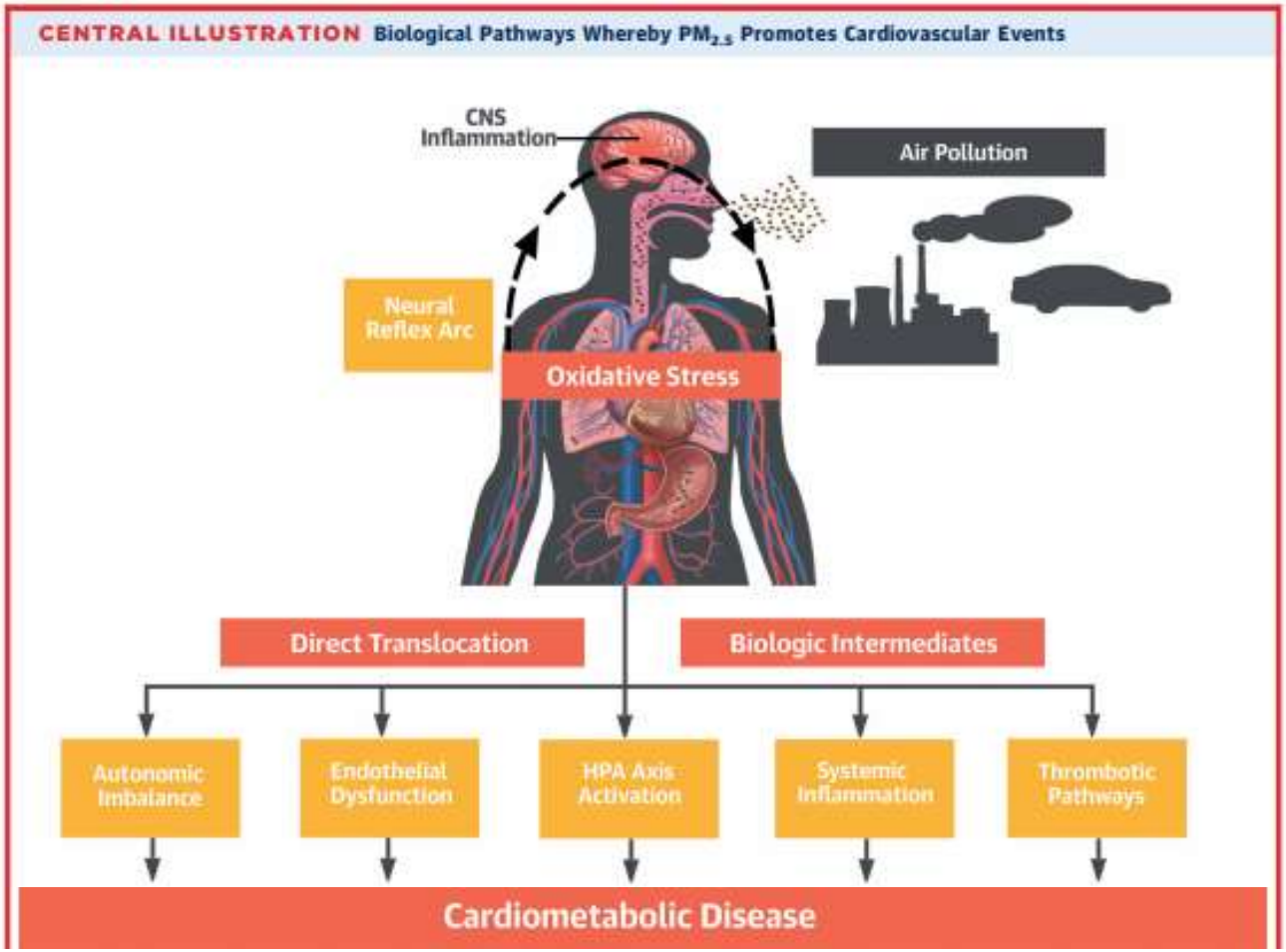
**Diabetes:** Increased risk of type 1 and type 2 diabetes and of insulin resistance.

*Source: http://www.diabetesandenvironment.org/home/conta...*



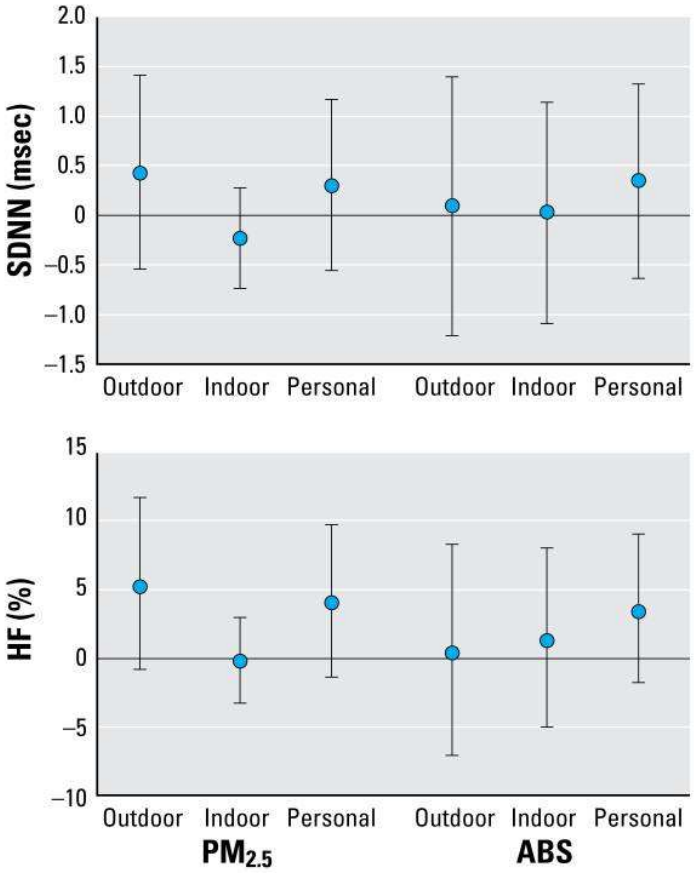
Source: ISGlobal website

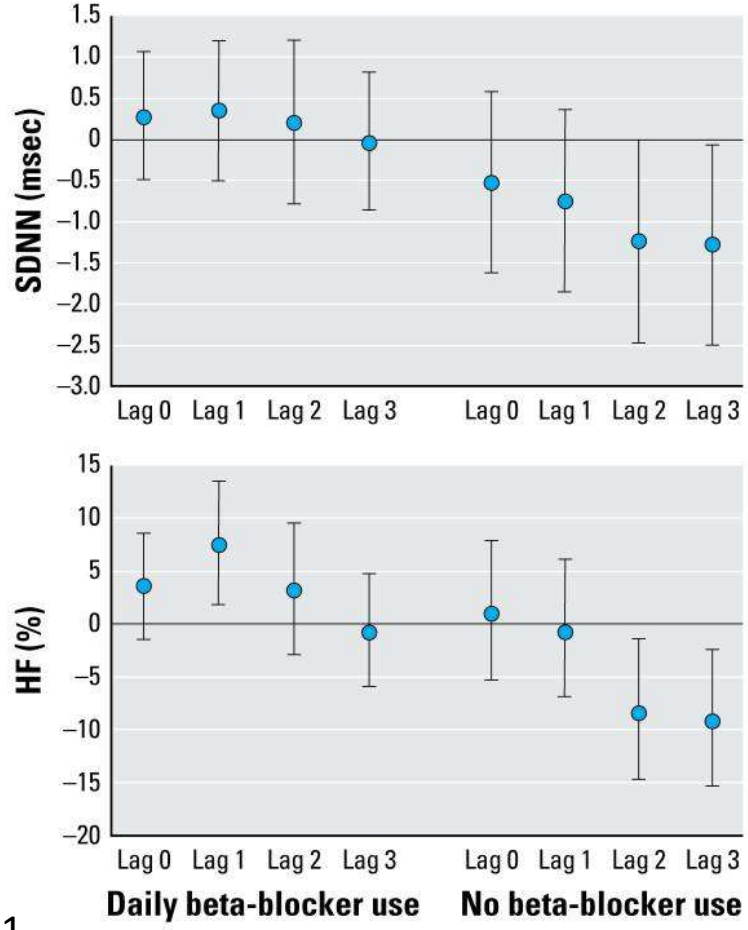
# Biological Pathways Whereby $PM_{2.5}$ Promotes Cardiovascular Events




Adapted from Rajagopalan JACC 2018;72(17):2954-70

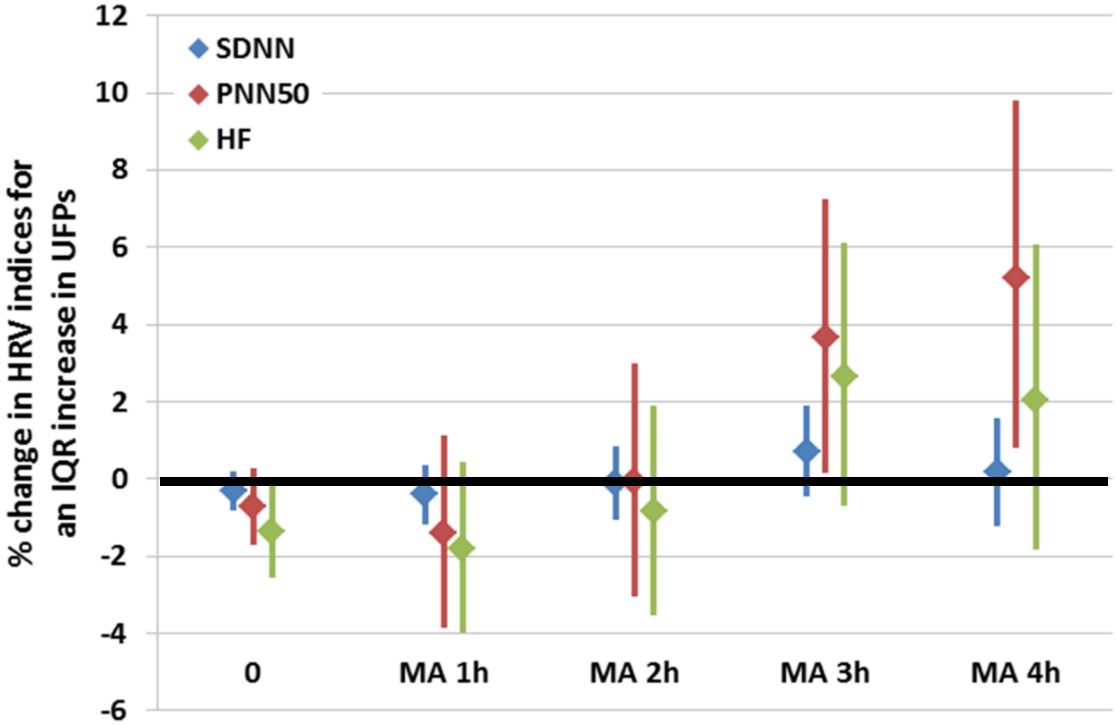
# Associations between $PM_{2.5}$ and Heart Rate Variability Are Modified by Beta-Blocker Use in Patients with Coronary Heart Disease

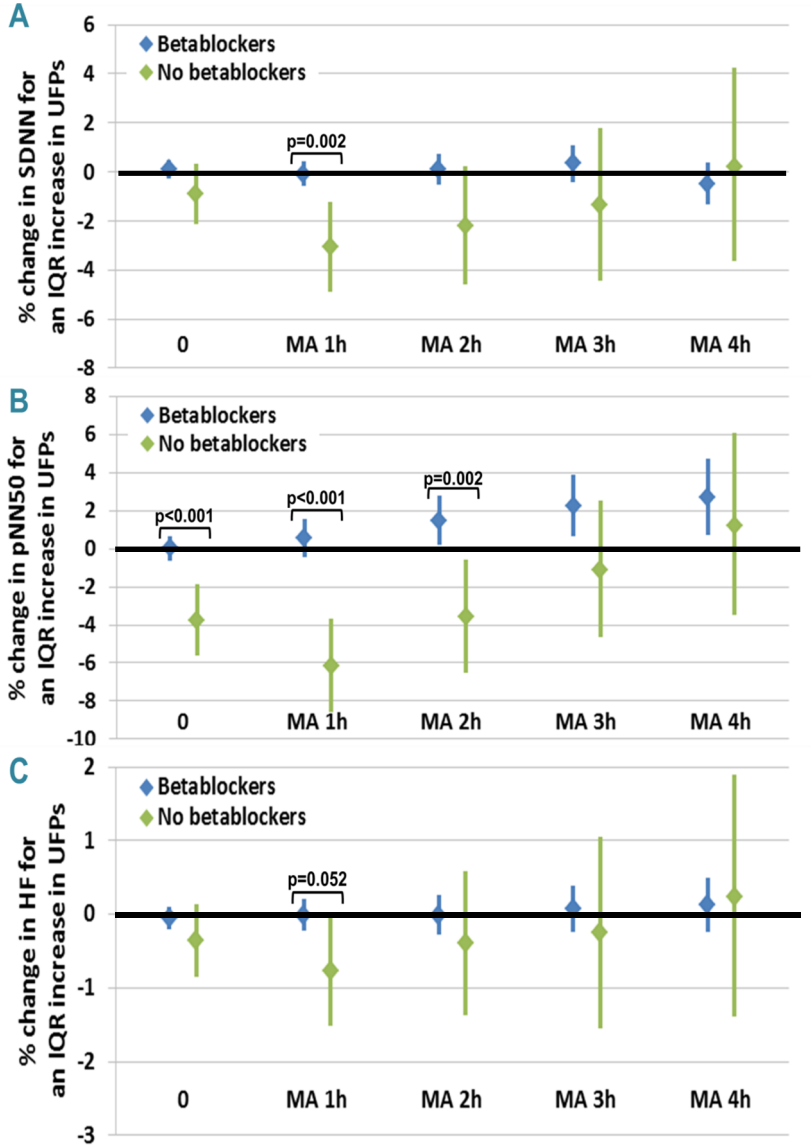



de Hartog et al Environ Health Perspect. 2009 Jan; 117(1): 105–111.

# Associations between UFP and Heart Rate Variability Are Modified by Beta-Blocker Use in Patients with Coronary Heart Disease

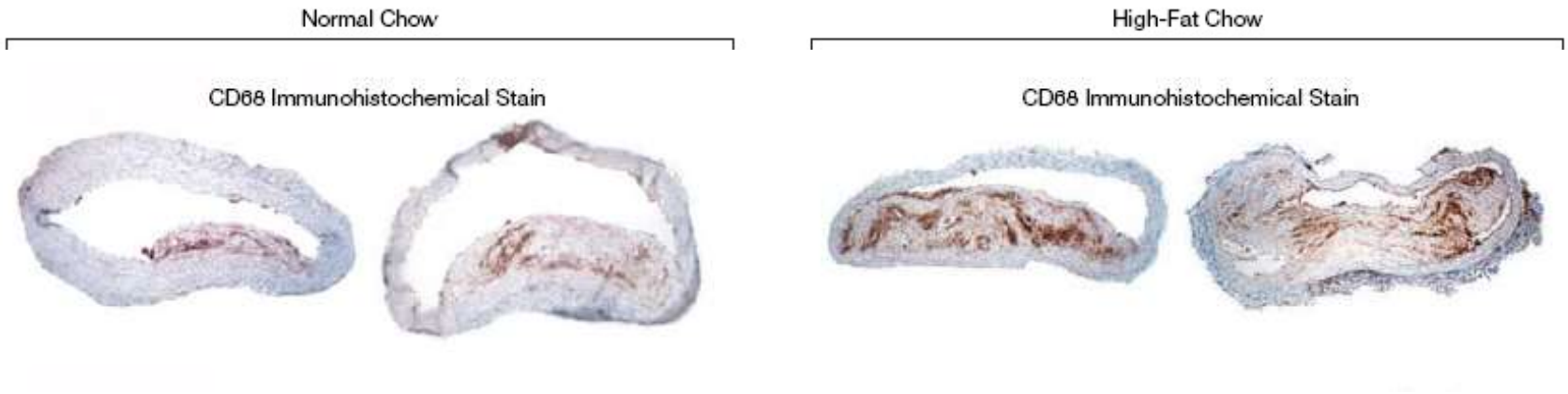


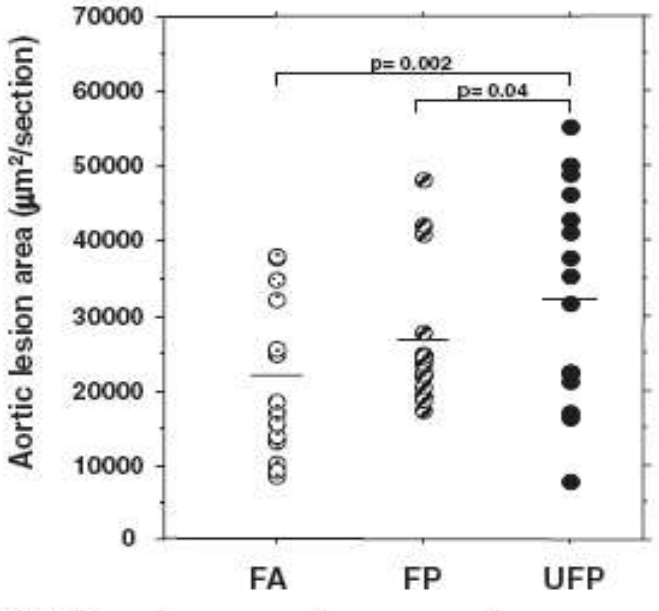

Fossati et al ISEE 2011

# Arterial plaques in mice after exposure to New York PM (Sun et al, JAMA Dec 2005)

**Figure 2.** Representative Photomicrographs of Hematoxylin-Eosin Staining and CD68 Immunohistochemical Staining of Abdominal Aortic Sections, and Oil Red-O Staining of Aortic Arch Sections



# Ultrafine particles (UFP) promote early atherosclerosis (Araujo, 2008)




| # sub-0.18 µm (particles/cm³) | ~ 5,000 | 3.88x10⁵ | 5.59x10⁵ |
|---|---|---|---|

**Figure 3.** UFP is the most proatherogenic PM fraction. Atherosclerotic lesions were quantitatively analyzed in serial aortic root sections and stained with oil red O. Lesional area was scored as square micrometer per section, averaged >25 sections per animal. Group averages are indicated by straight horizontal bars. One FA mouse was an obvious outlier in its group and removed from the atherosclerotic lesion analysis. However, its inclusion did not modify the overall significance. FA mice are represented by dotted circles (n=14), FPs by stripped circles (n=16), and UFPs by filled circles (n=15).

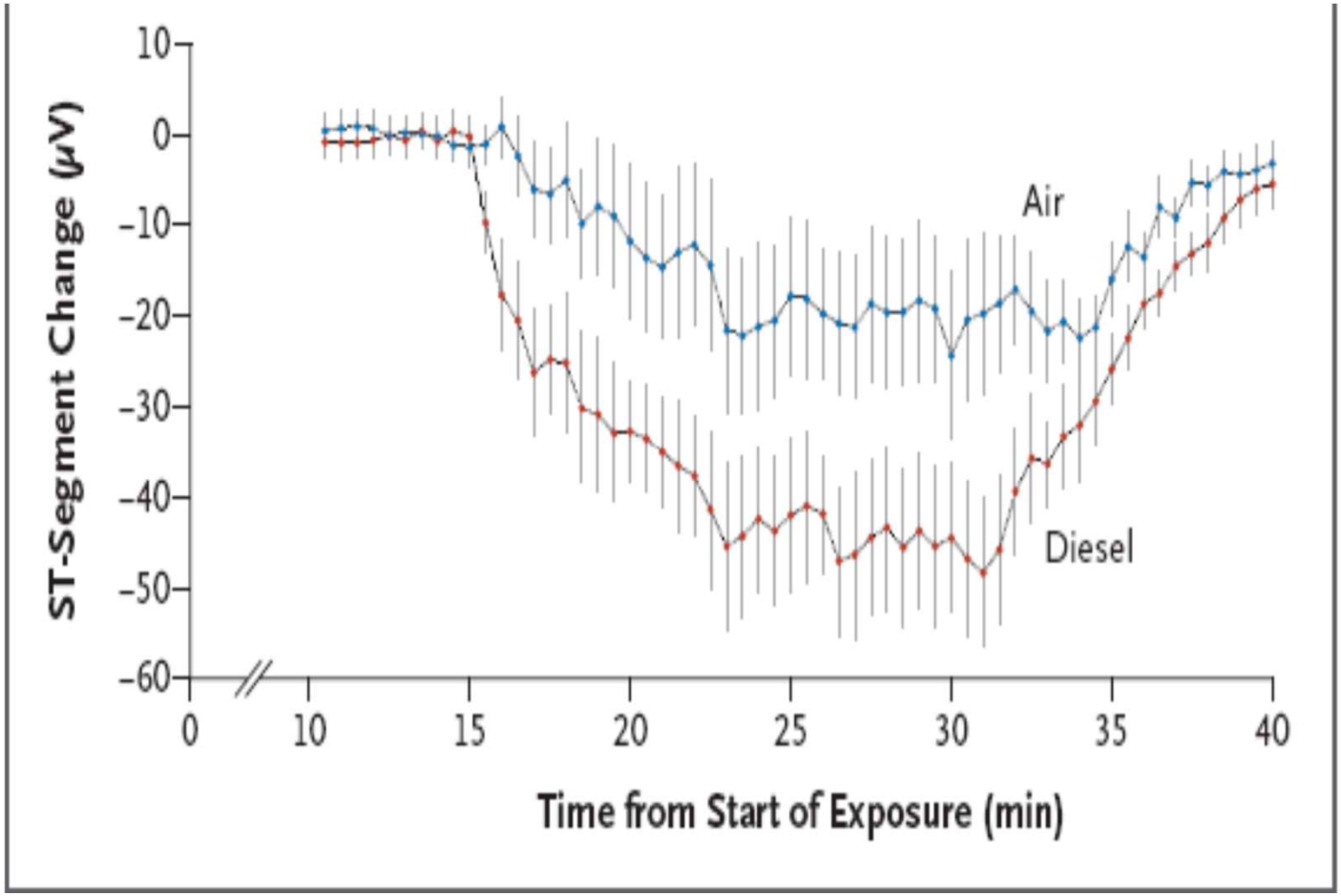
# Diesel exhaust exposure chamber



Slide courtesy of
Prof. Jordi Sunyer

**Mills et al, New England Journal of Medicine, 2007 (13.Sept)**

1 hour diesel exposure in a chamber in 20 IAM survivors
(Mills et al, N Engl J Med 2007)




Slide courtesy of
Prof. Jordi Sunyer

# Ambient Particulate Air Pollution and MicroRNAs in Elderly Men

*Serena Fossati,[a,b] Andrea Baccarelli,[a,c] Antonella Zanobetti,[a] Mirjam Hoxha,[d] Pantel S. Vokonas,[e] Robert O. Wright,[a,f] and Joel Schwartz[a,c]*

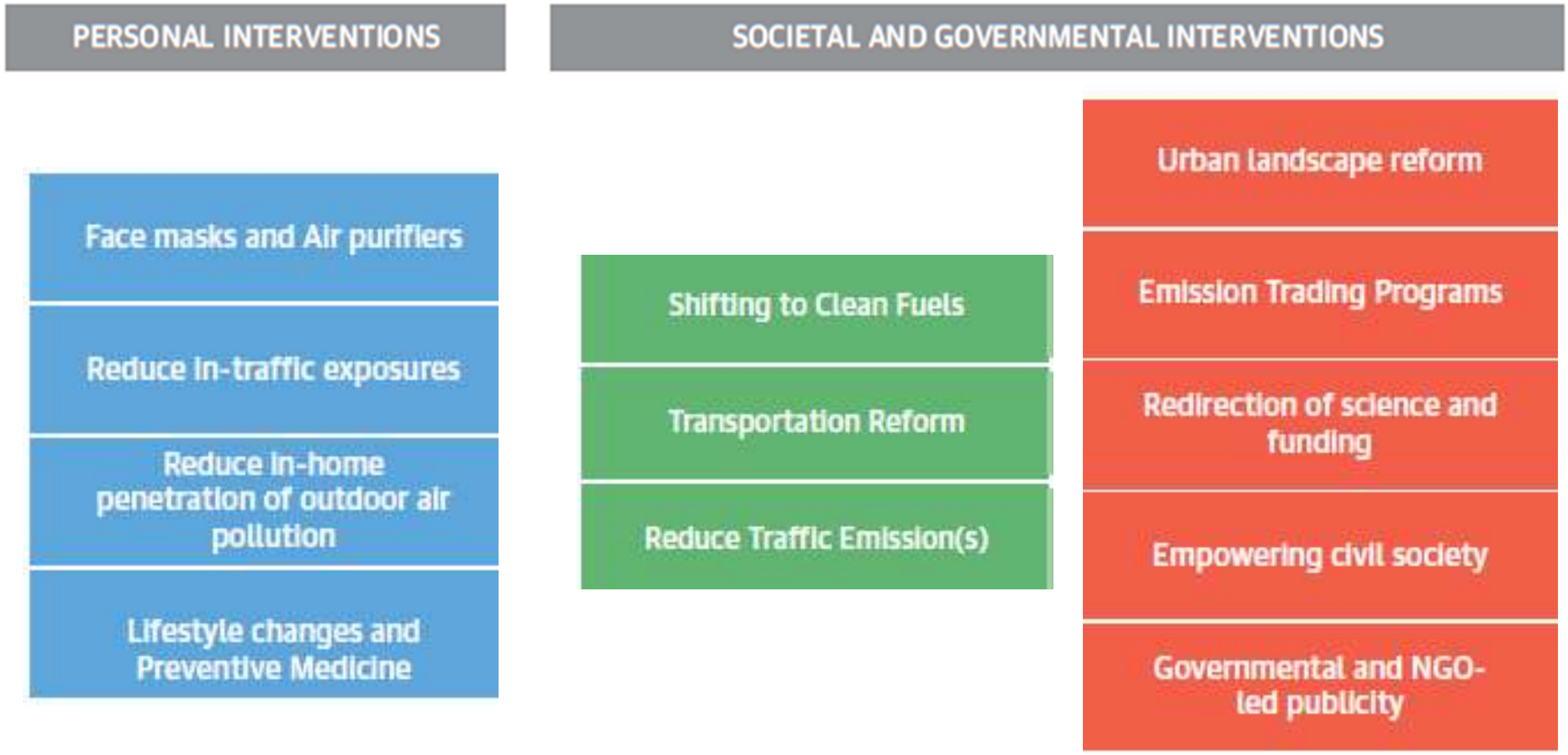
(*Epidemiology* 2014;25: 68–78)

Estimated Percentage Change[a] in MiRNAs for an Interquartile Range Increase in the Selected Exposure Window for Each Air Pollutant [b]
(n = 153, Except n=132 for Organic Carbon)

| MiRNA | % Change (95% CI) |
|---|---|
| $PM_{2.5}$ (3.83 μg/m³, 7-day) | |
| miR-1 | −33 (−50 to −10) |
| miR-126 | −25 (−38 to −8) |
| miR-135a | −29 (−43 to −12) |
| miR-146a | −34 (−48 to −17) |
| miR-155 | −21 (−33 to −7) |
| miR-21 | −35 (−48 to −18) |
| miR-222 | −20 (−33 to −4) |
| miR-9 | −22 (−34 to −8) |
| Black carbon | |
| miR-1 | −20 (−44 to 15) |
| miR-126 | −24 (−40 to −3) |
| miR-135a | −26 (−43 to −4) |
| miR-146a | −28 (−45 to −4) |
| miR-155 | −13 (−29 to 6) |
| miR-21 | −35 (−51 to −15) |
| miR-222 | −17 (−33 to 3) |
| miR-9 | −26 (−3 to −9) |

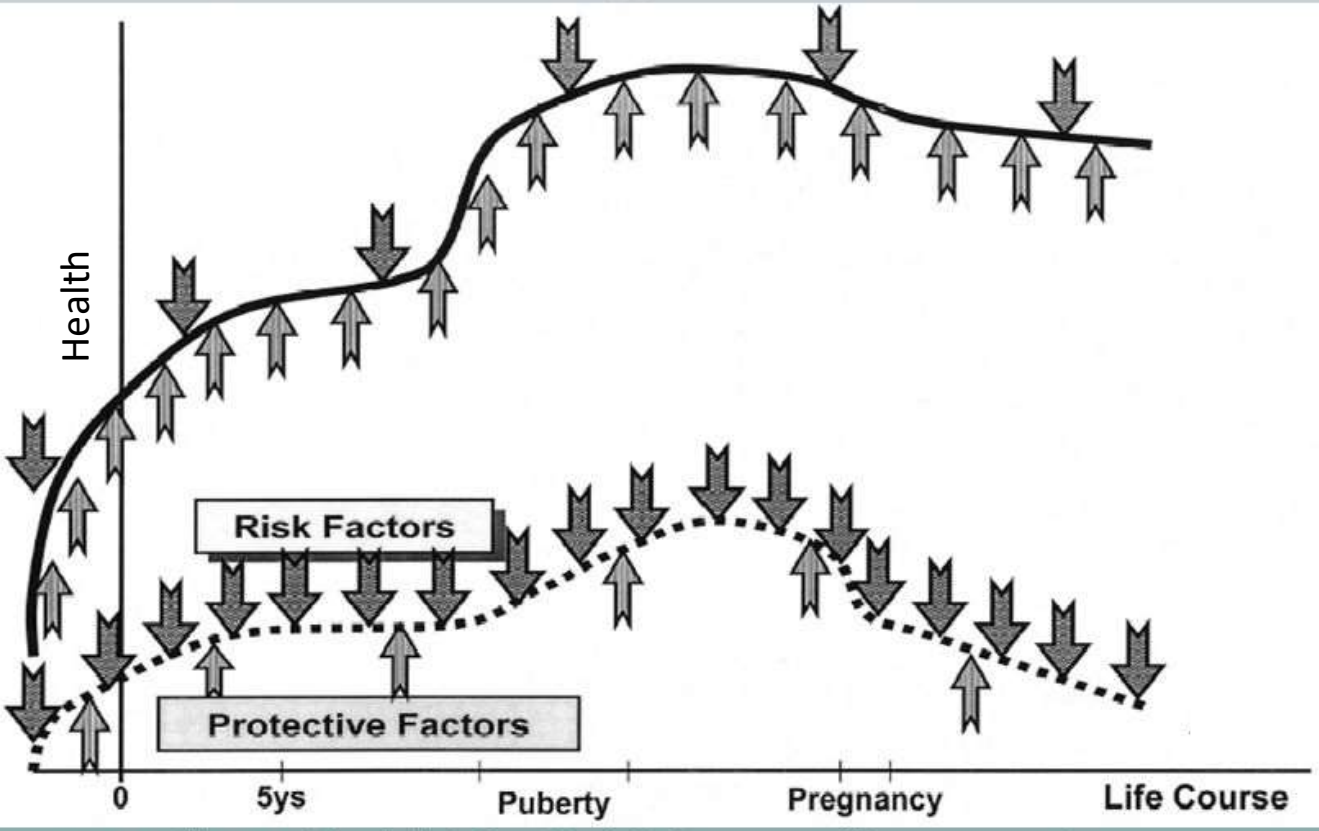
| MiRNA | % Change (95% CI) |
|---|---|
| Organic carbon | |
| miR-1 | −34 (−54 to −6) |
| miR-126 | −24 (−41 to −3) |
| miR-135a | −28 (−45 to −6) |
| miR-146a | −14 (−35 to 14) |
| miR-155 | −15 (−31 to 5) |
| miR-21 | −26 (−45 to −1) |
| miR-222 | −5 (−24 to 18) |
| miR-9 | −22 (−37 to −5) |
| $SO_4^{2-}$ | |
| miR-1 | −25 (−38 to −8) |
| miR-126 | −17 (−28 to −6) |
| miR-135a | −18 (−29 to −5) |
| miR-146a | −24 (−35 to −11) |
| miR-155 | −15 (−23 to −5) |
| miR-21 | −23 (−34 to −10) |
| miR-222 | −13 (−23 to −2.3) |
| miR-9 | −16 (−25 to −6) |

Immune Response Related GeneGo Pathway Enriched in Target Genes of 5/8 miRNAs → HMGB1/RAGE signaling pathway

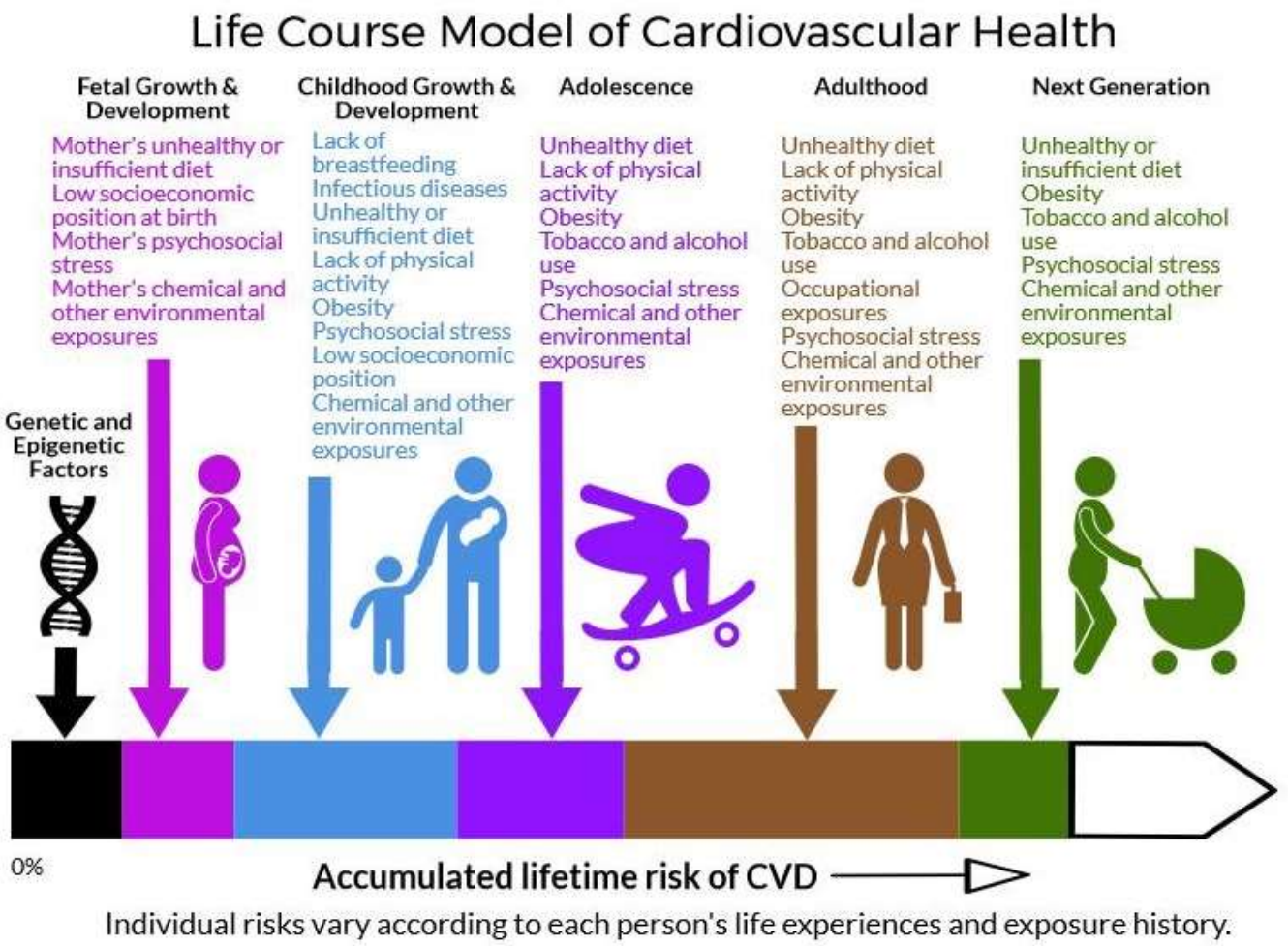



Adapted from Rajagopalan JACC 2018;72(17):2954-70

# Life Course Perspective




Adapted from Lu MC, Halfon N. Racial and ethnic disparities in birth outcomes: a life-course perspective. Matern Child Health J. 2003;7:13-30




A life course model, created by Nancy Hepp and Tom Austin from Berkman et al 2000; Hardy R, Lawlor DA, Kuh D. *Future Cardiology*. 2015;11(1):101-13; Aboderin I, et al 2001; WHO. 2002; Halfon N, et al. *Maternal and Child Health Journa*l. 2014 Feb;18(2):344-65; Hanson MA, et al. *Journal of Physiology*. 2016 Apr 15;594(8):2147-60.

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Review

# Environmental pollutants and child health—A review of recent concerns

Martine Vrijheid[a,b,c,*], Maribel Casas[a,b,c], Mireia Gascon[a,b,c,d], Damaskini Valvi[a,b,c,e], Mark Nieuwenhuijsen[a,b,c]

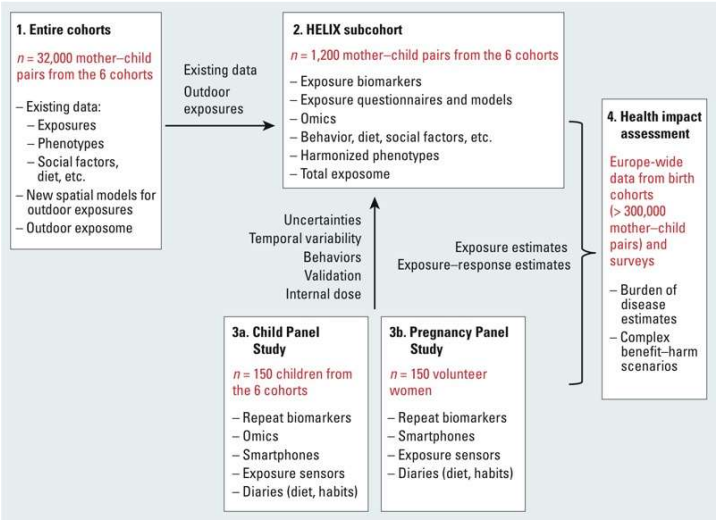
**Table 1**
Summary of the quality of evidence relating exposure to environmental chemicals to child health.

| | Foetal growth & prematurity | Neurodevelopment | Respiratory and immune health | Childhood growth and obesity |
|---|---|---|---|---|
| Outdoor air pollutants – $NO_2$, PM, ozone, $SO_2$, CO, PAHs | +++ | ++ | +++ | + |
| Heavy metals – Pb, Hg, Cd, As | ++ | +++ | 0 | + |
| Organochlorine compounds – PCBs, DDT/DDE, HCB, dioxins | ++ (+++ for PCBs) | +++ | ++ | +(++ for DDE) |
| Perfluoroalkyl substances (PFASs) – PFOS, PFOA, | + (++ for PFOA) | + | + | + |
| Polybrominated diphenyl ethers (PBDEs) | + | ++ | 0 | 0 |
| Currently used pesticides – organophosphates, pyrethroids | + | +++ | 0 | 0 |
| Phthalates | + | + | + | + |
| Bisphenol A | + | + | + | + |

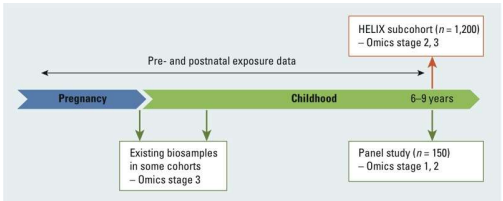
Quality of evidence.
+++ = Good evidence for an association based on consistent results from multiple studies and meta-analyses.
++ = Moderate evidence of an association based on multiple studies, but with some inconsistencies.
+ = Insufficient evidence. Evidence for an association based on only a few studies, or with substantial inconsistencies.
0 = No or very few studies.
*Abbreviations used:* $NO_2$: nitrogendioxide, PM: matriculate matter, $SO_2$: sulfurdioxide, PAHs: polycyclic aromatic hydrocarbons, Pb: lead, Hg: mercury, Cd: cadmium, As: Arsenic, PCBs: polychlorinated biphenyls, DDT/DDE: dichlorodiphenyl-trichloroethane/dichloroethylene, HCB: hexachlorobenzene, PFOS: perfluorooctane sulfonate, PFOA: perfluorooctanoate (PFOA), BPA: Bisphenol A.




| Cohort | Enrollment years | *n* subjects (total 32,000) |
|---|---|---|
| BiB—Born in Bradford, UK (Wright et al. 2013) | 2007–2010 | 14,000 |
| EDEN—Study of determinants of pre- and postnatal developmental, France (Drouillet et al. 2009) | 2003–2006 | 2,000 |
| INMA—Environment and Childhood, Spain (Guxens et al. 2012) | 2004–2006 | 2,500 |
| KANC—Kaunas Cohort, Lithuania (Grazuleviciene et al. 2009) | 2007–2009 | 4,000 |
| MoBa—The Norwegian Mother and Child Cohort Study, Norway (Oslo region) (Magnus et al. 2006) | 1999–2009 | 8,000 |
| Rhea—Mother–Child Cohort in Crete, Greece (Chatzi et al. 2009) | 2007–2008 | 1,500 |




HELIX BUILDING THE EARLY-LIFE EXPOSOME




Vrijheid et al. 2014

| Exposure groups |
|---|
| Built environment |
| Surrounding natural spaces |
| Meteorology |
| Ultraviolet (UV) |
| Outdoor air pollution |
| Traffic |
| Road traffic noise |
| Indoor air pollution |
| Tobacco smoking |
| Organochlorine compounds (OCs) |
| Polybrominated diphenyl ether (PBDEs) |
| Perfluoroalkyl substances (PFASs) |
| Metals and elements |
| Phthalate metabolites |
| Phenols |
| Organophosphate (OP) pesticide metabolites |
| Water disinfection byproducts (DBPs) |

# To wrap up

- Air pollution causes 3.3 milion premature cardiovascular deaths a year → they can be prevent!!
- Main source → traffic (diesel for UFP and $PM_{2.5}$)
- Its cardiometabolic effects start as early as in childhood
- Prevention strategies can be at different levels (individual and societal/governamental)
- Medical doctors can act as a lobby to reduce air pollution

# Thanks!

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