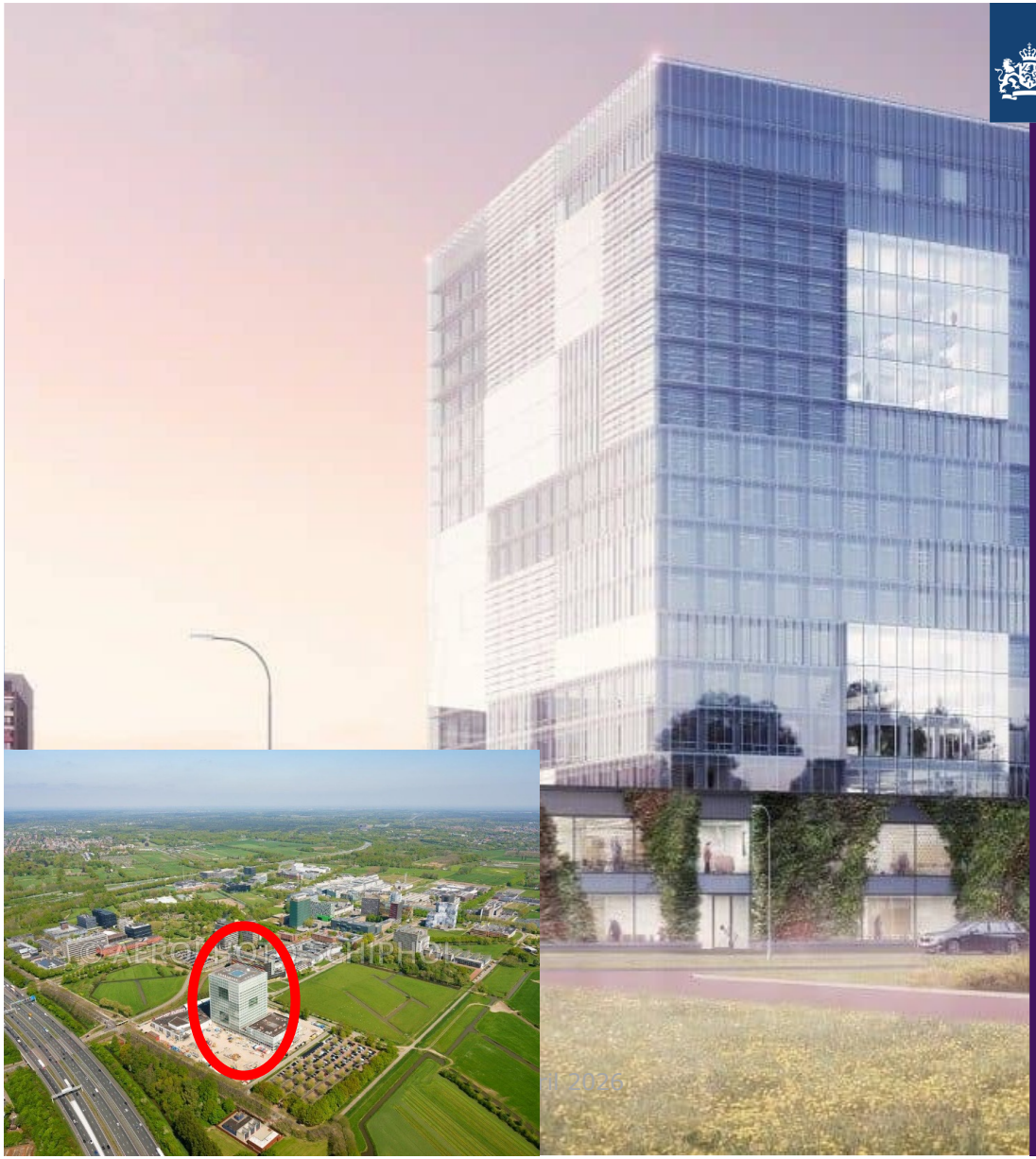
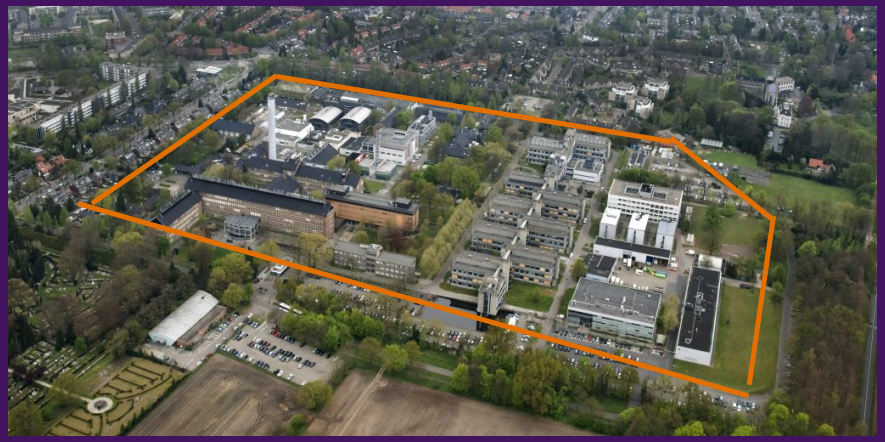


Utrecht University

Institute for Risk Assessment Sciences (IRAS)

Luchtverontreiniging nog een problem?

Flemming R. Cassee, PhD ERT



Air pollution and mortality

World-wide air pollution is responsible for over 7 million premature deaths every single year

Estimates and 25-year trends of the global burden of disease attributable to ambient air pollution: an analysis of data from the Global Burden of Diseases Study 2015

Aaron J Cohen, Michael Brauer*, Richard Burnett, H Ross A*
Lalit Dandona, Rakhi Dandona, Valery Feigin, Greg Freedma
Lidia Morawska, C Arden Pope III, Hwashin Shin, Kurt Straif,
Theo Vos, Christopher J L Murray, Mohammad H Forouzanf

2015 rank	
1	High systolic blood pressure
2	Smoking
3	High fasting plasma glucose
4	High total cholesterol
5	Ambient particulate matter pollution
6	Diet high in sodium
7	High body-mass index
8	Diet low in whole grains
9	Diet low in fruits
10	Household air pollution from solid fuels
11	Impaired kidney function
12	Alcohol use
13	Diet low in nuts and seeds
14	Diet low in vegetables
15	Low physical activity
16	Diet low in seafood omega3 fatty acids
17	Unsafe sex
18	Childhood undernutrition
19	Unsafe water source
20	No handwashing with soap

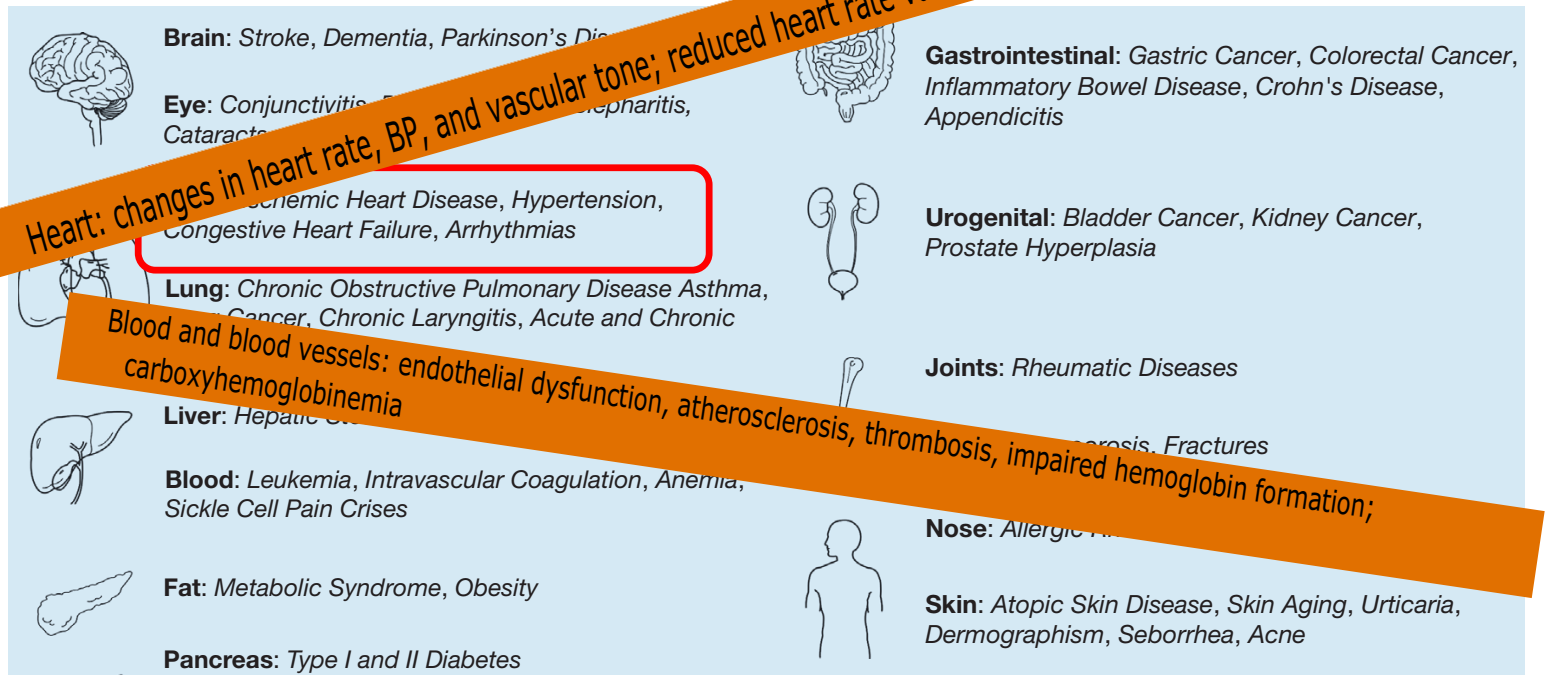
Outdoor air pollution

Cohen et al. 2017. Lancet 389: 1907-18

Systemic effects of air pollution (II)

Schraufnagel et al. 2019. Air Pollution and non-communicable diseases [illegible] Chest 155 : 409-41

Schraufnagel et al. 2019. Air Pollution and non-comm[illegible]ases, Part 2: Chest 155 : 417-42



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Aaron J Cohen, Lalit Dandona, R Lidia Morawska, Theo Vos, Christ*

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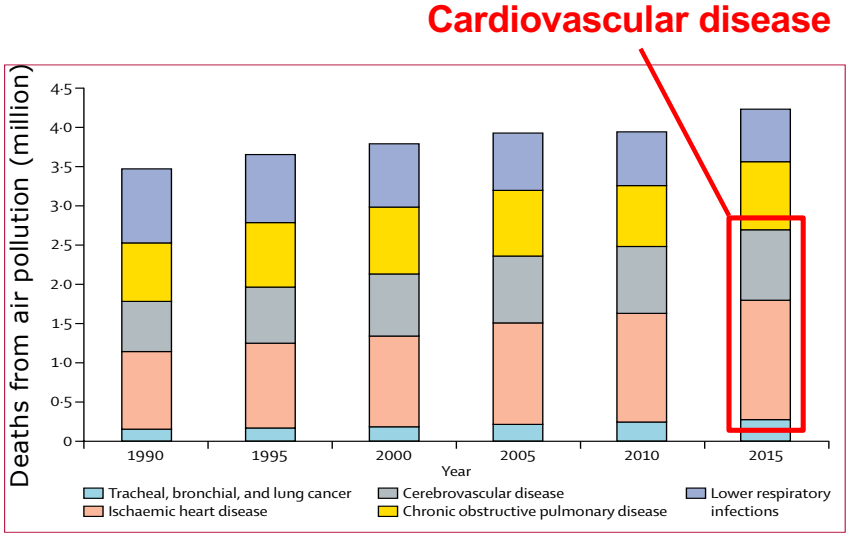
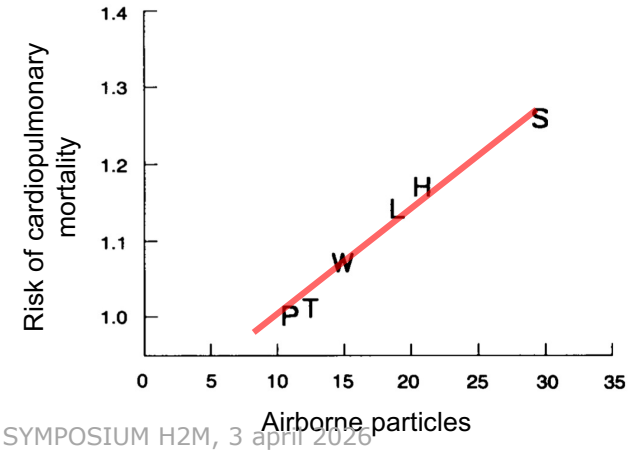


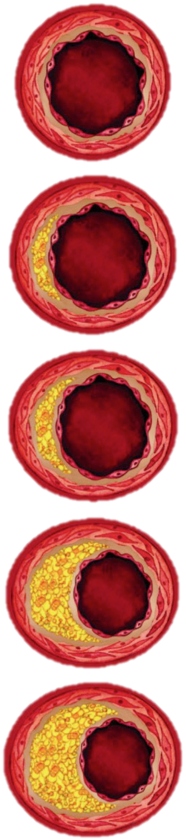
Cohen et al. 2017. Lancet 389: 1907-18

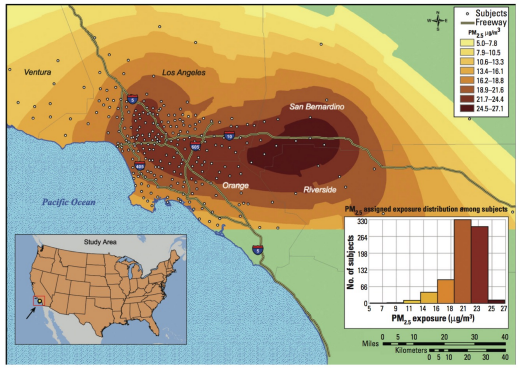
Particulate air pollution and cardiovascular mortality and morbidity

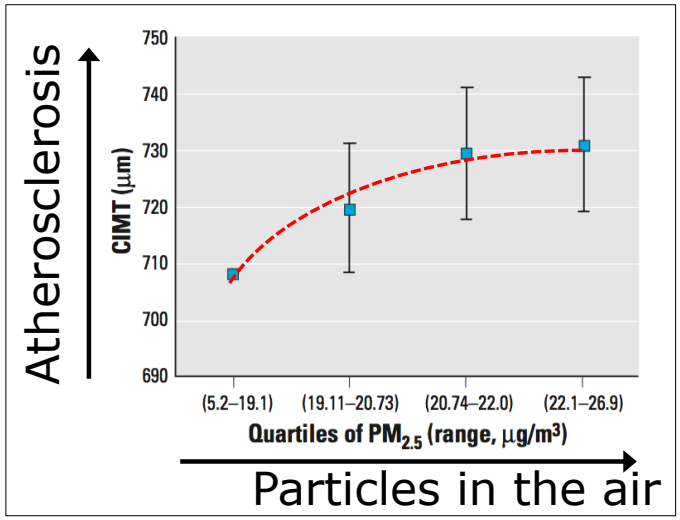
The Six Cities Study (1993)



Dockery (1993) N Engl J Med

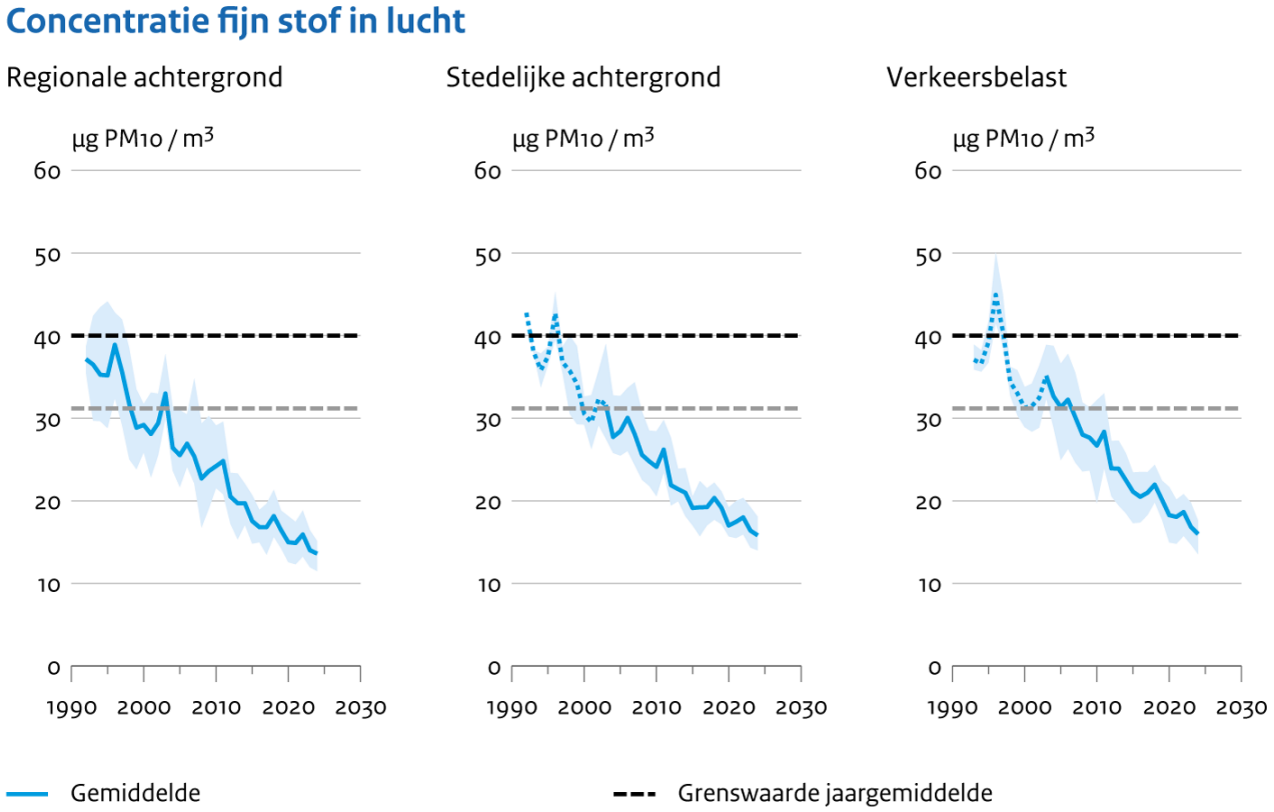




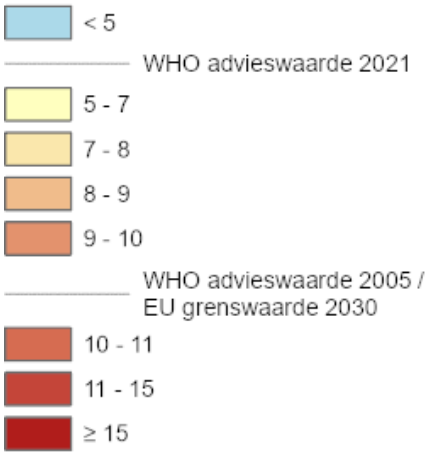


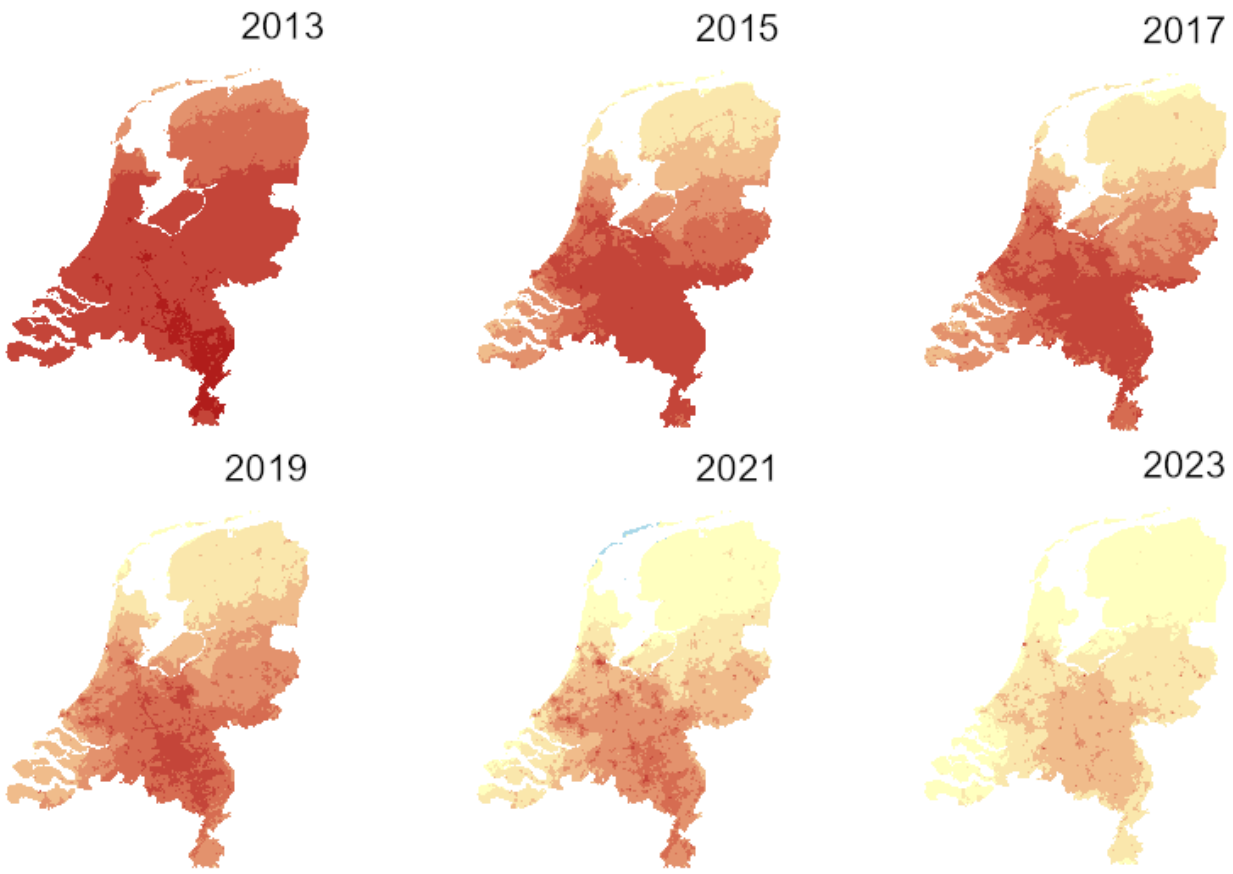
Kunzli (2005) Environ Health Perspect 113

Hoe staan we er voor?



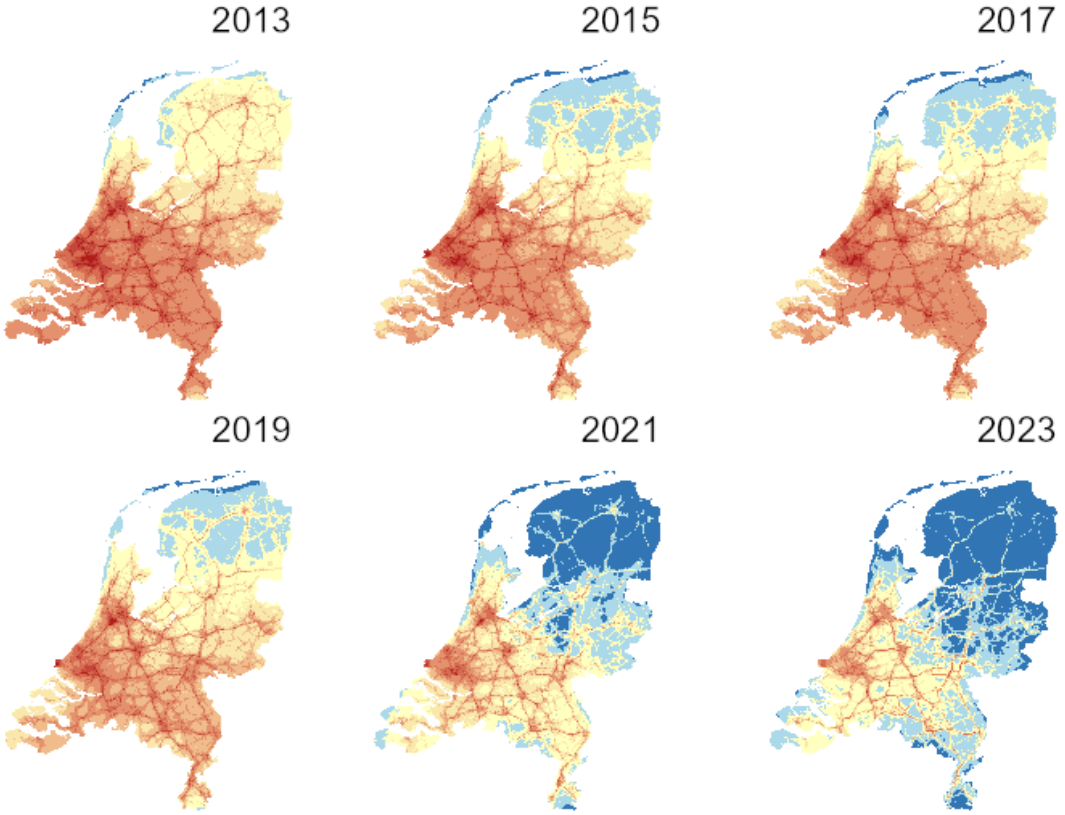
Fijnstof (µg PM2,5/m^3)

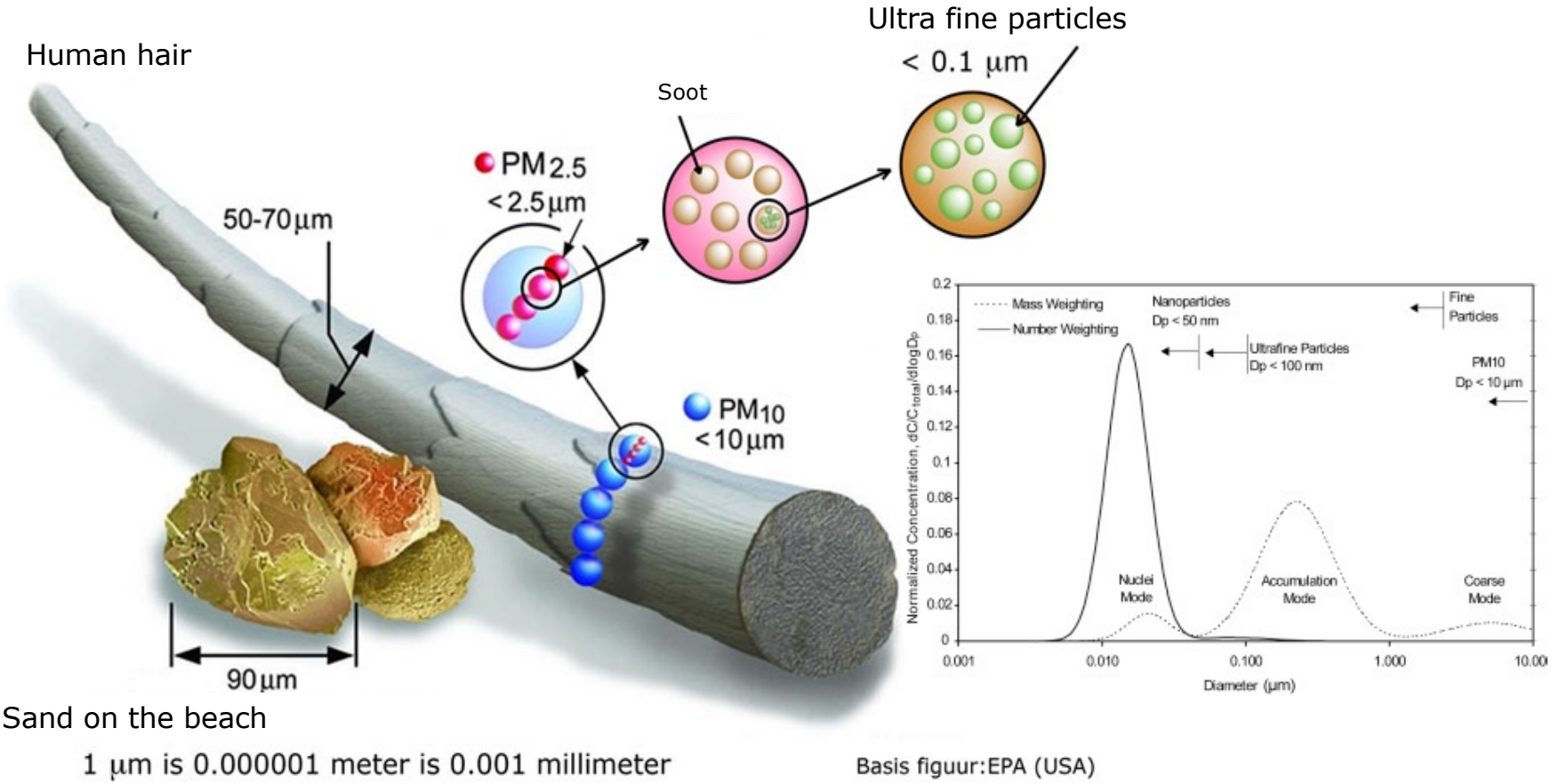




Stikstofdioxide (µg/m^3)

- < 8
- 8 - 10
- WHO advieswaarde 2021
- 10 - 12
- 12 - 14
- 14 - 16
- 16 - 20
- WHO advieswaarde 2005 / EU grenswaarde 2030
- 20 - 25
- 25 - 30
- ≥ 30



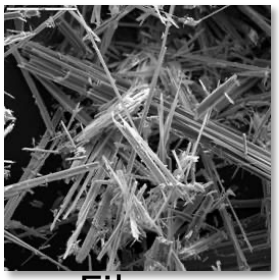


1 µm is 0.000001 meter is 0.001 millimeter

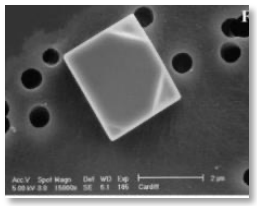
Basis figuur:EPA (USA)

What can be detected in air?

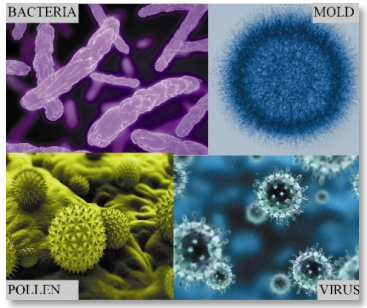
Metal

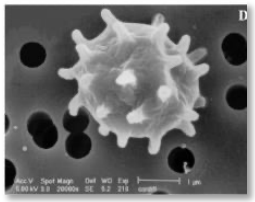


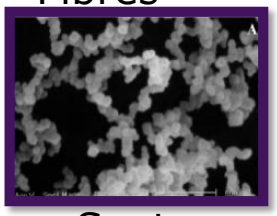
Fibres



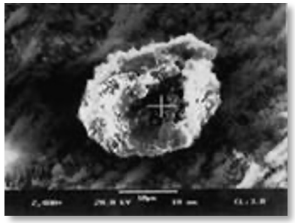
Sea salt

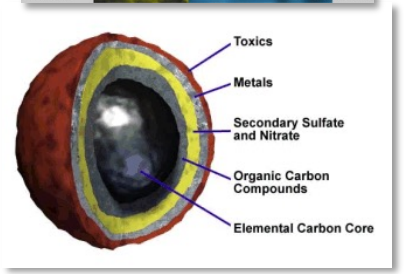


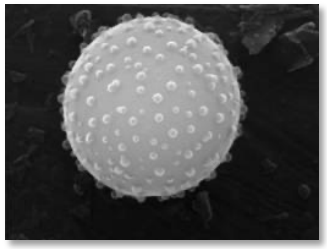


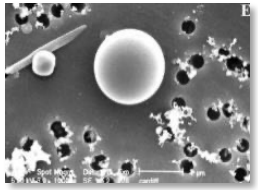


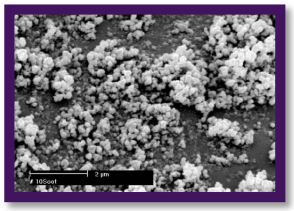
Soot











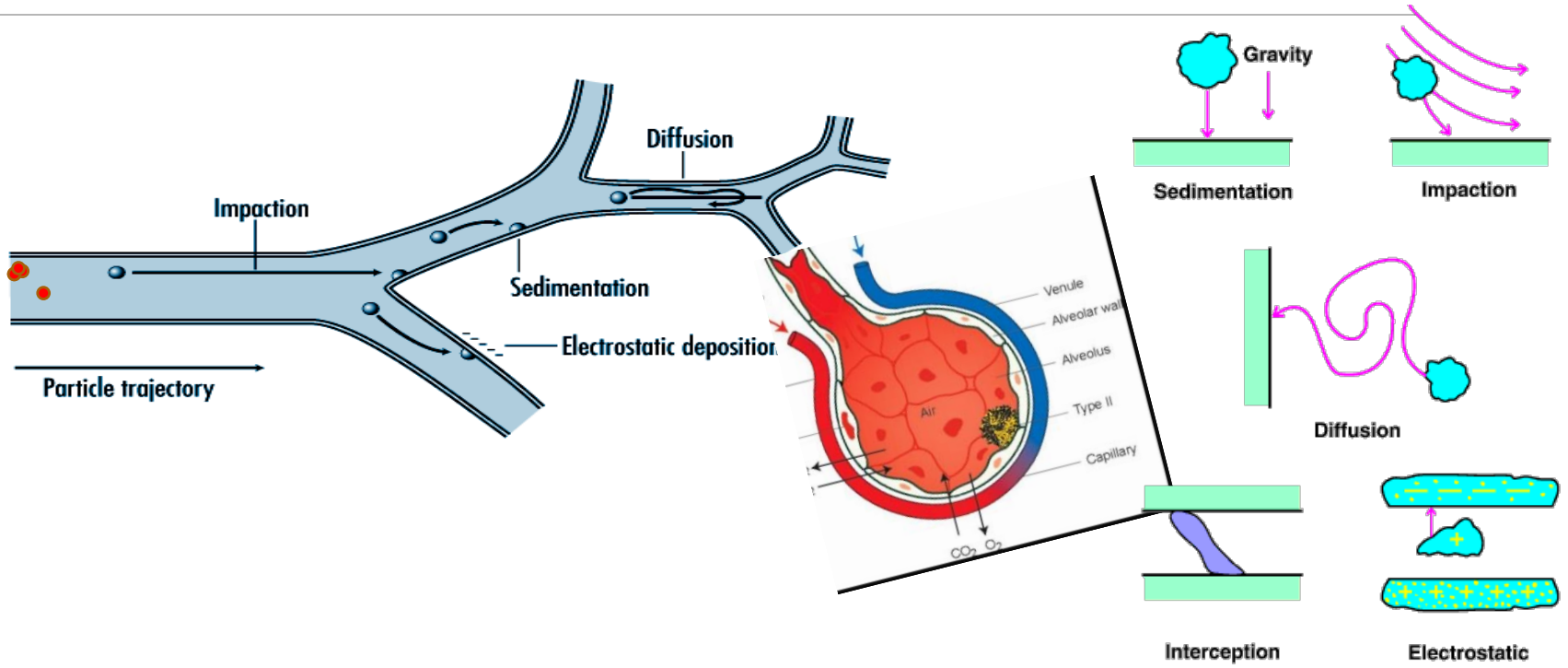
Plastics

Utrecht University

Institute for Risk Assessment Sciences (IRAS)

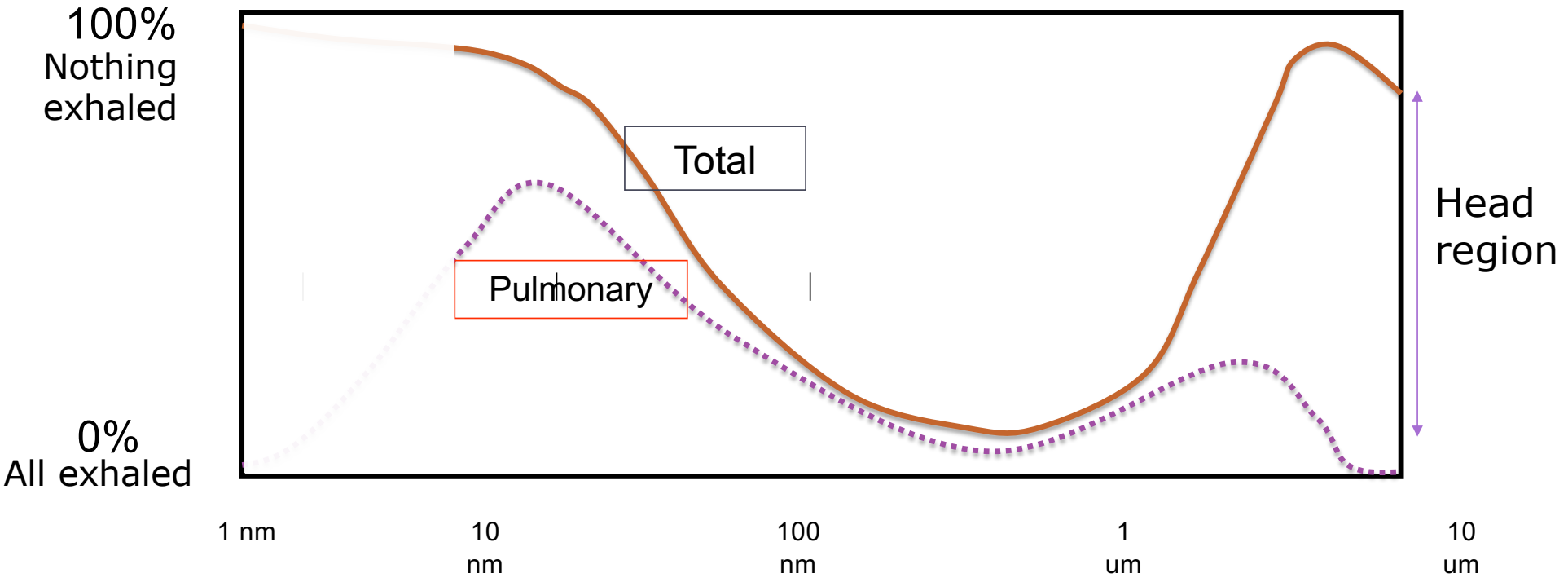
National Institute for Public Health and the Environment
Ministry of Health, Welfare and Sport

Mechanisms of particle deposition in the lung



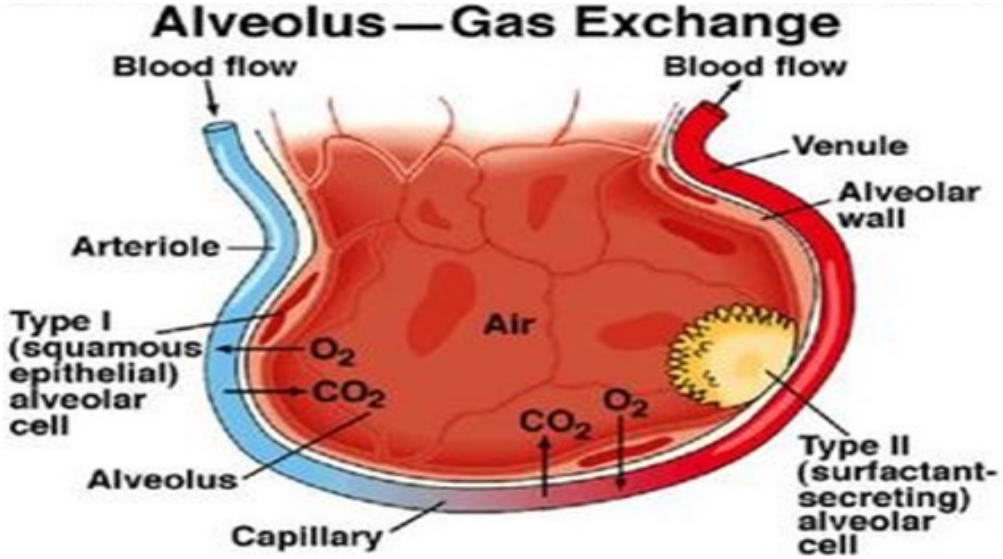
Deposition after inhalation

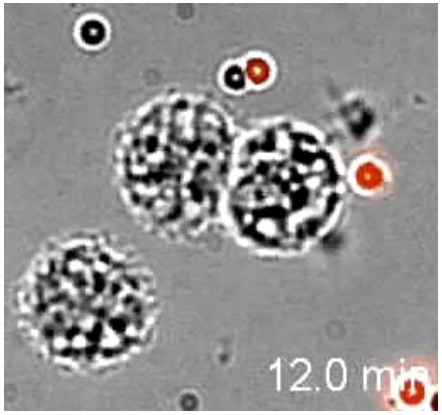
MPPD
MULTIPLE-PATH PARTICLE DOSIMETRY MODEL
VERSION 2.0
Co-developed RIVM
v 3.04



Size affects the internal dose… and the choice of the in vitro model

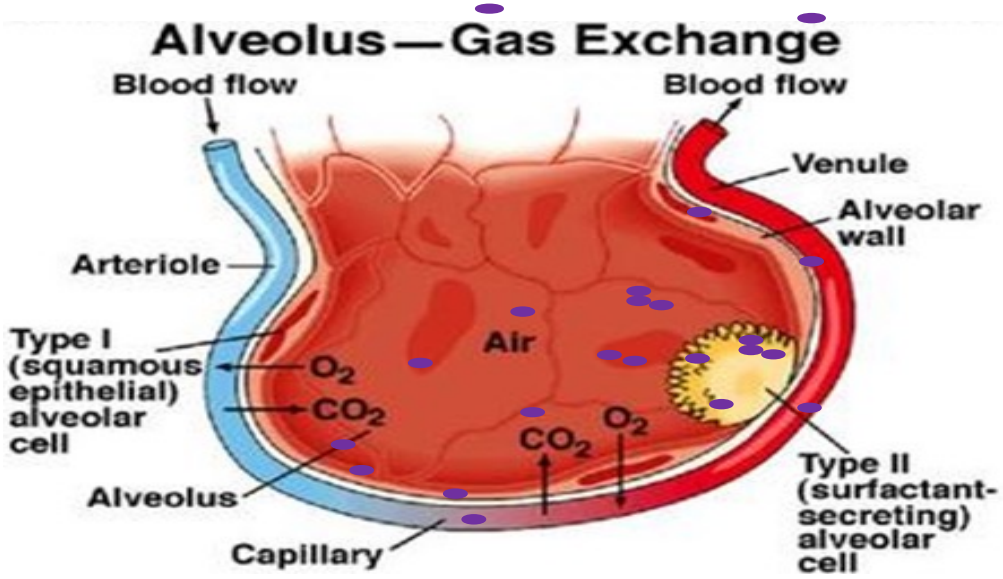
Size matters: micro particle external concentration x mg/m^3





Clearance micro-size particles within 6-14 hr

Size matters: nanoparticle: ~~also~~ external concentration **x** mg/m^3

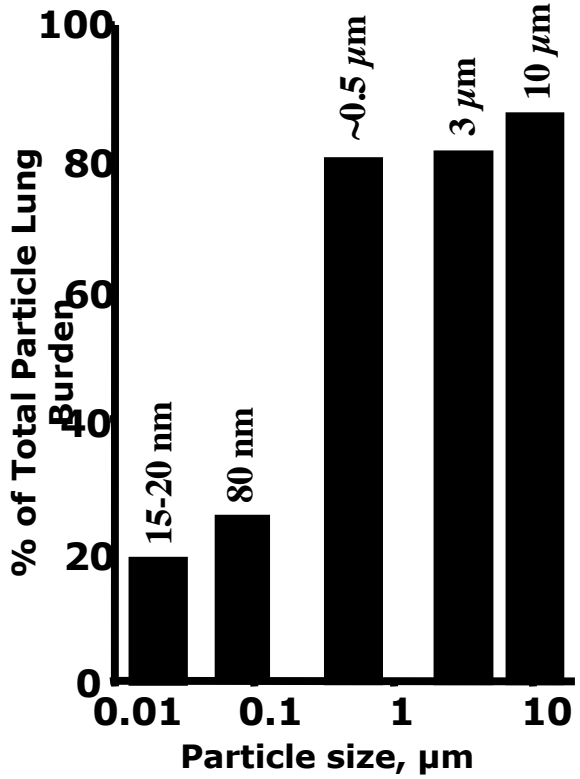


Ultrafine particle uptake by epithelial cells + interstitial translocation + lack of macrophage recognition

Compartmentalized Retention of Particles in Rat Lungs

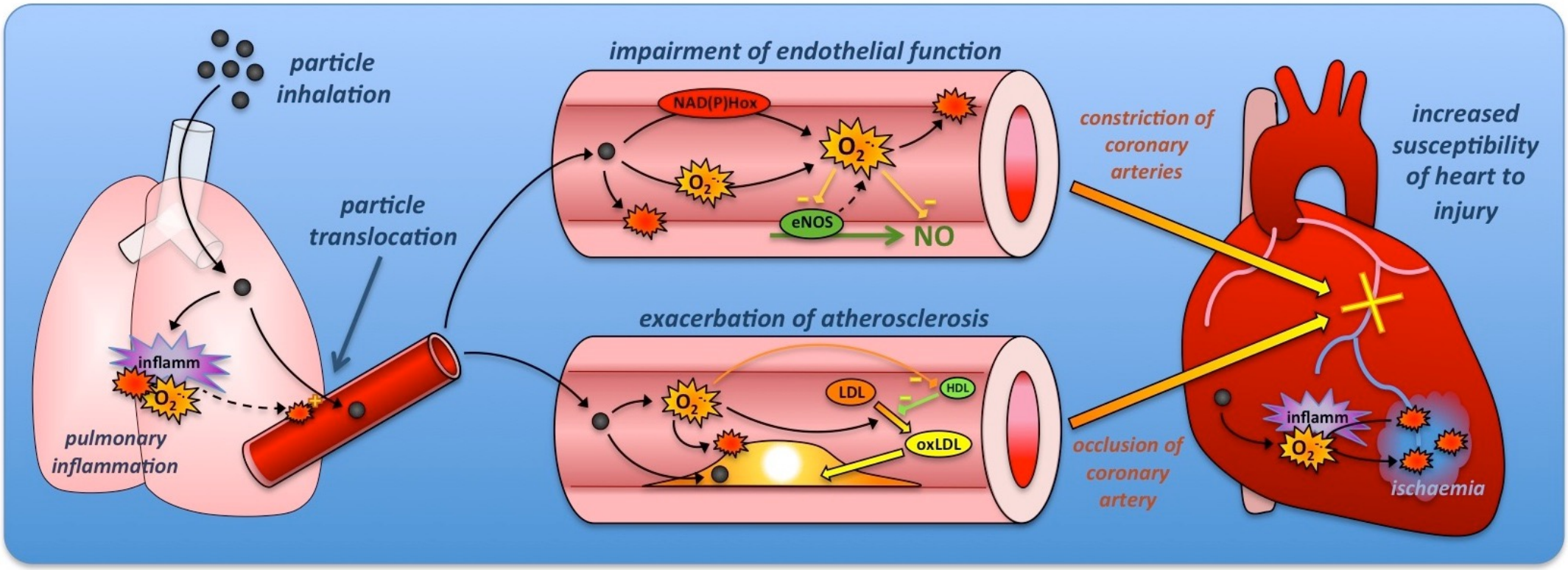
24 hrs post-exposure, extensive lavage

Alveolar Macrophages



m Oberdörster, 2004

1. Cardiovascular



Courtesy Mark Miller,
Miller (2014). Biochem Soc Trans 42:1006-11

Diesel, particle trap and thrombus formation
A study in volunteers

Increase thrombus

Decrease thrombus

Particle Traps Prevent Adverse Vascular and Prothrombotic Effects of Diesel Engine Exhaust Inhalation in Men

Andrew J. Lucking, MD*; Magnus Lundbäck, MD, PhD*; Stefan L. Barath, MD; Nicholas L. Mills, MD, PhD; Manjit K. Sidhu, MD; Jeremy P. Langrish, MD; Nicholas A. Boon, MD; Jamshid Pourazar, PhD; Juan J. Badimon, MD, PhD; Miriam E. Gerlofs-Nijland, PhD; Flemming R. Cassee, PhD; Christoffer Boman, PhD; Kenneth Donaldson, PhD; Thomas Sandstrom, MD, PhD; David E. Newby, MD, PhD; Anders Blomberg, MD, PhD

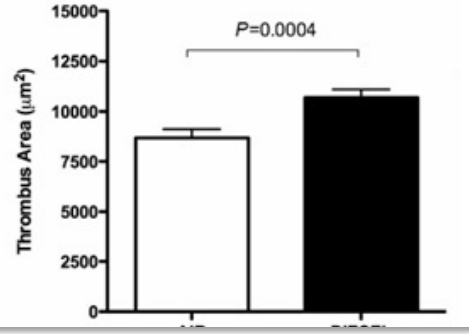
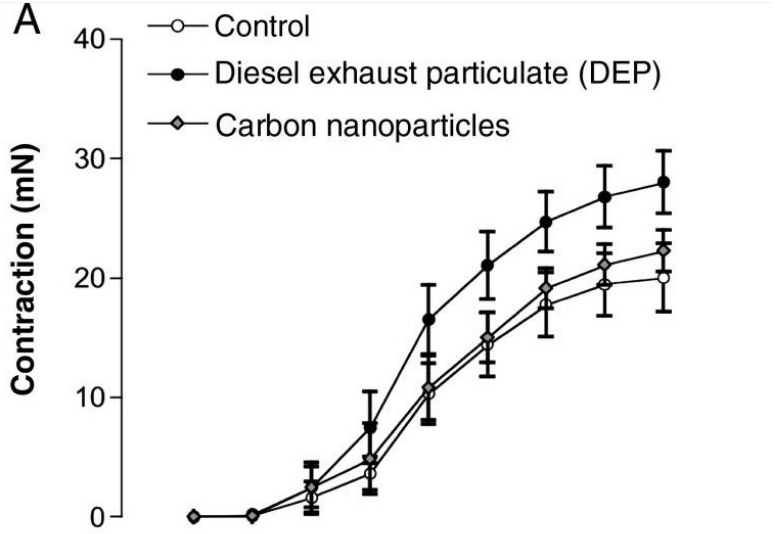


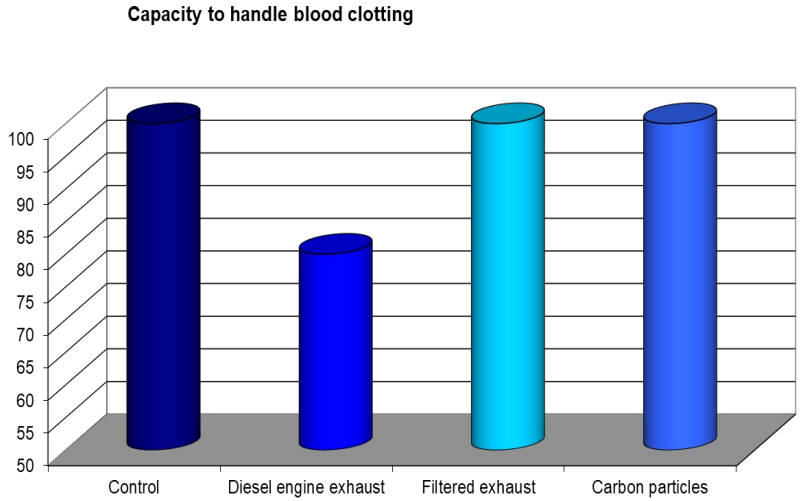
Figure 4. Ex vivo thrombus formation assessed with the Badimon chamber at 2 hours after exposure. Data from the low-shear chamber are shown in the top

Clean air Diesel Diesel Filtered

2 hr exposures

Contraction of blood vessel (ex vivo)





Similar observations arterial stifness

Absorbed components on ultrafineparticles seem to drive the response

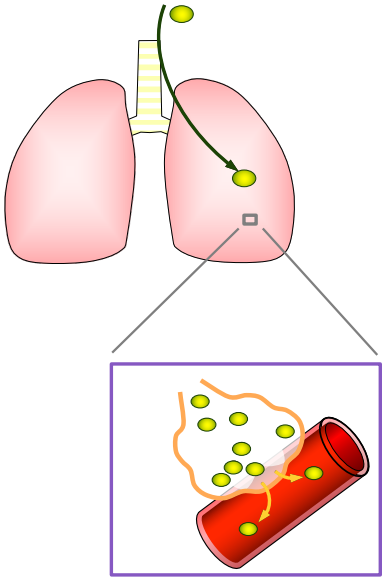
Characterization of exposure conditions

2 hr exposures

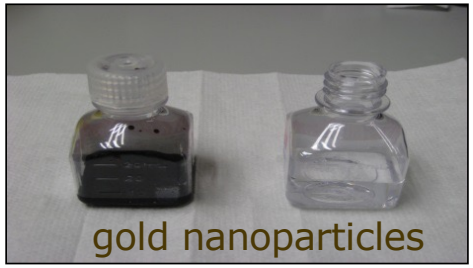
	Filtered air	Diesel exhaust	Filtered exhaust	Carbon
PM (teflon filter), $\mu g/m^3$	<1	348 ± 64	6 ± 16	70 ± 28
Particle number, $\times 1000/cm^3$	<1	1198 ± 204	2 ± 4	3865 ± 424
Particle diameter, nm	–	67 ± 4	–	37 ± 4

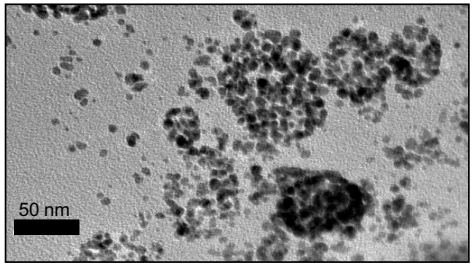
Mills et al., Eur Heart J. 2011 Nov; 32(21): 2660–2671.

Waar gaan de ultrafijne deeltjes naar toe?



Soot hard to trace

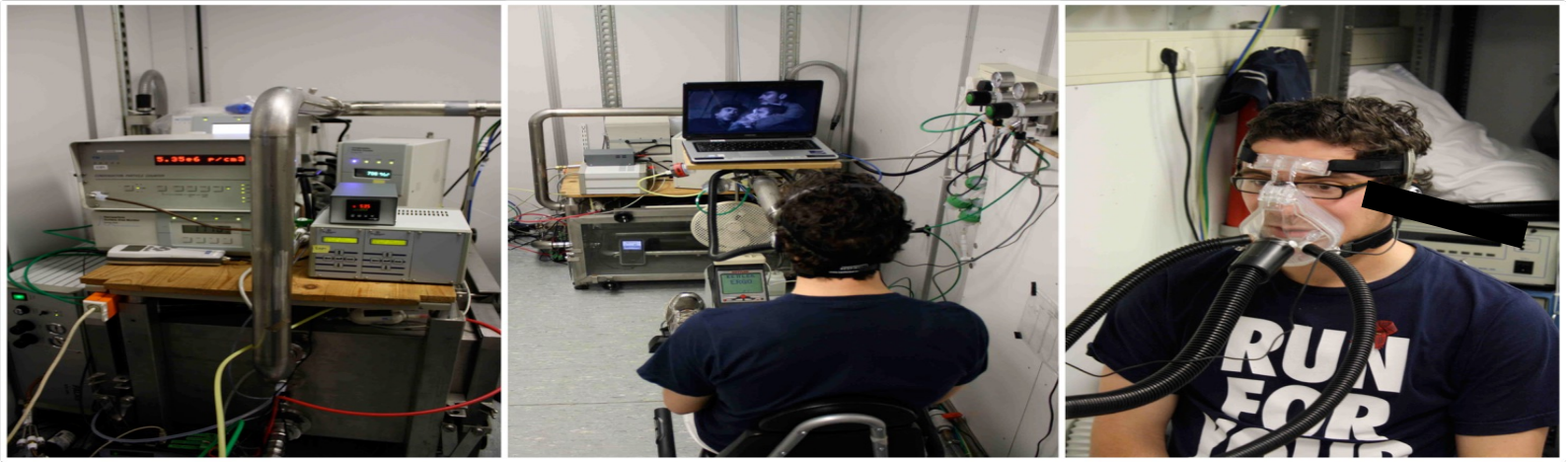




Why use gold?

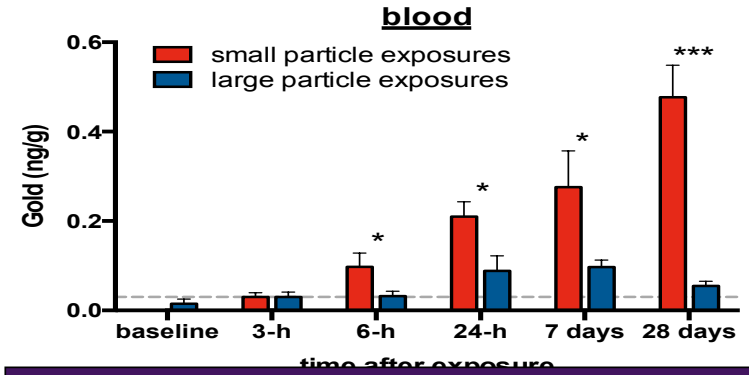
- Very small size available
- Safe to use
- Techniques to measure very low levels
- Low levels of gold in the body (background)

Inhalation of gold nanoparticles



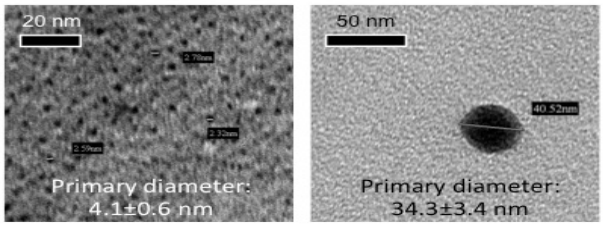
- 16 healthy volunteers
- 2-hour inhalation of gold nanoparticles : 5-15 nm; 5. 10^6 per cc
- Measure gold in blood and urine after the exposure
- Paralel study in mice: more sizes, IT

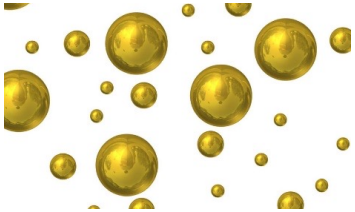
Using gold particles for tracing



17.8 ± 1.2

52.4 ± 1.4

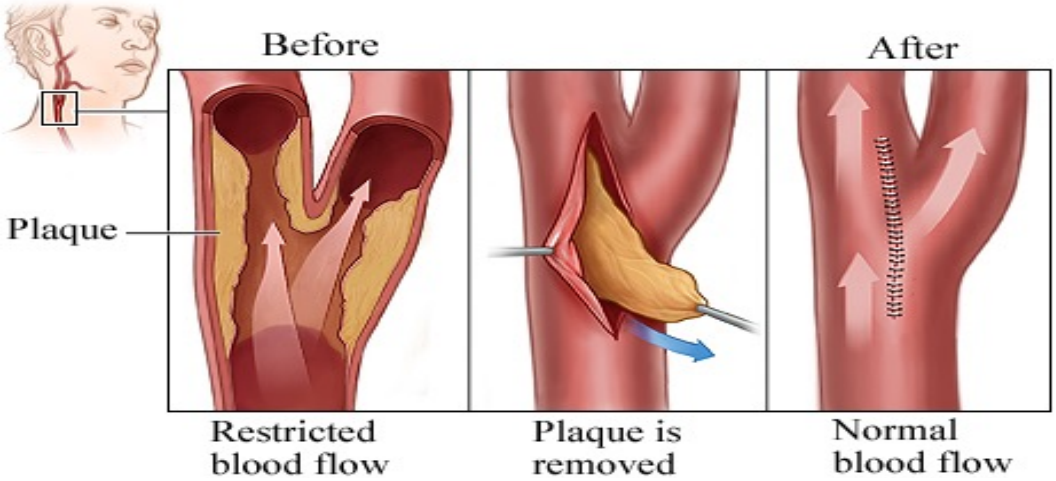


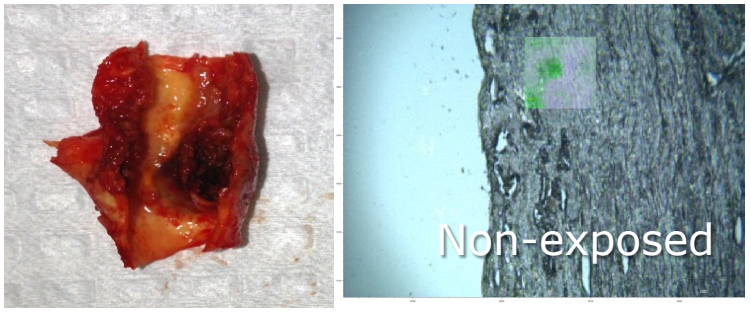


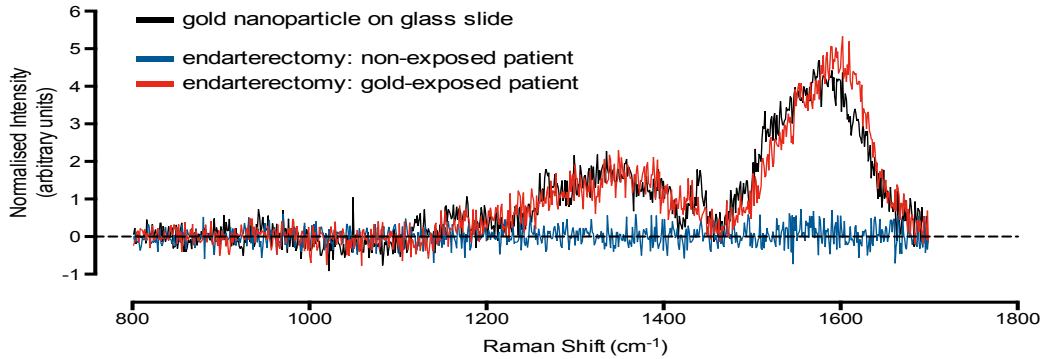
Clinical

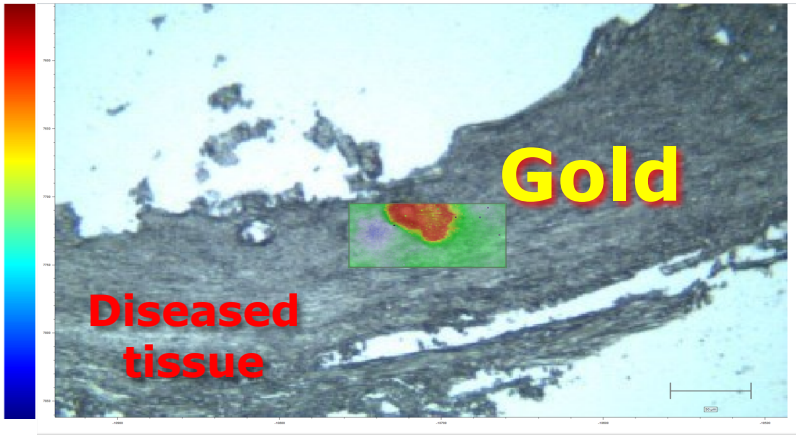
Size dependent particle translocation from the lung

Gold nanoparticles reach areas of vascular disease

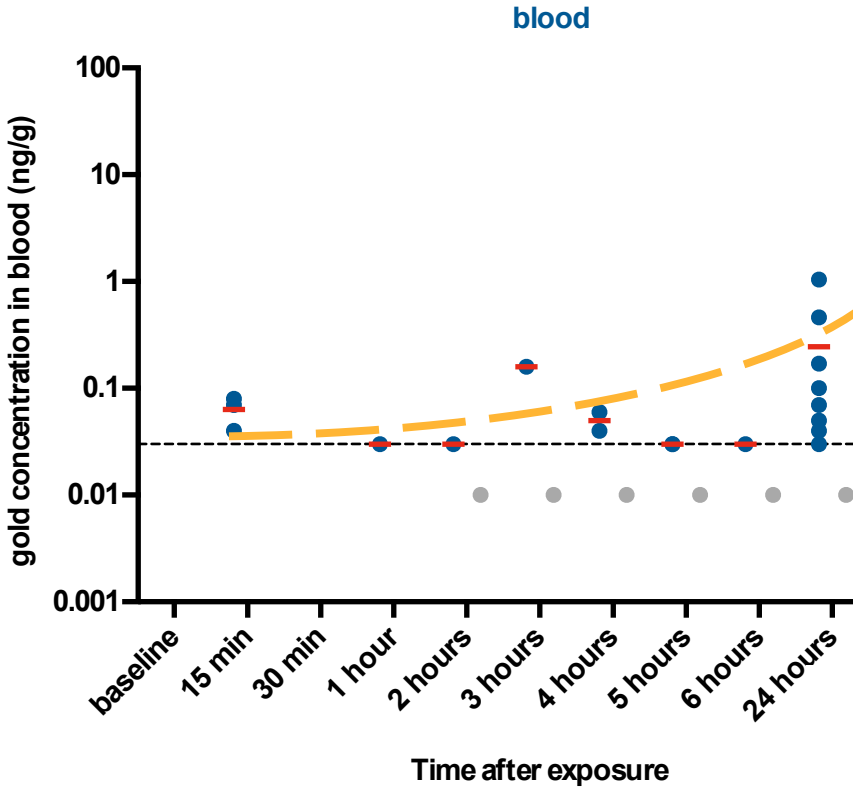




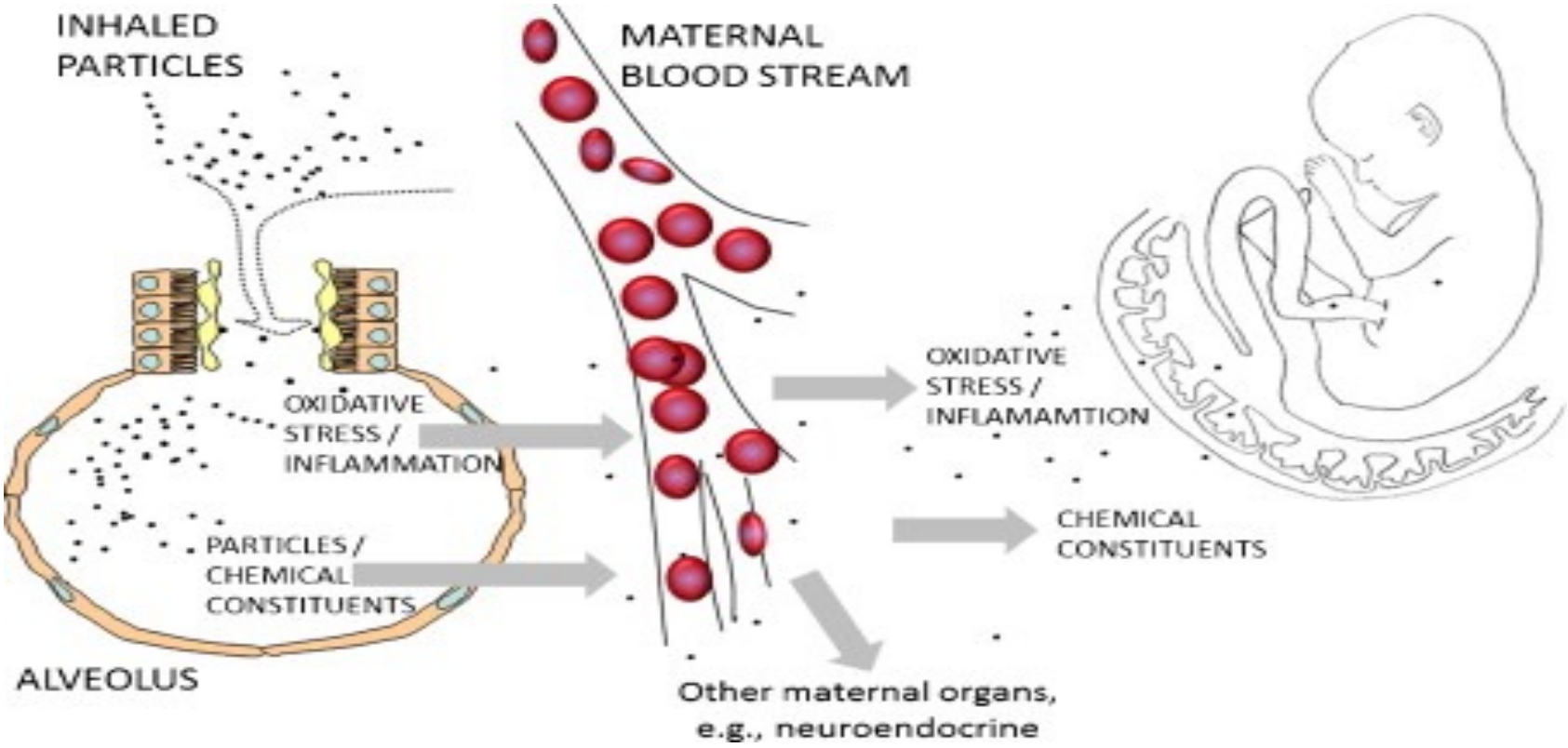




Gold nanoparticles reach the systemic circulation



2. Reproduction and development



nature COMMUNICATIONS

ARTICLE

https://doi.org/10.1038/s41467-019-11654-3 OPEN

Ambient black carbon particles reach the fetal side of human placenta

Hannelore Bové[1,2,3,6], Eva Bongaerts[1,6], Eli Slenders[2], Esmée M. Bijnens[1], Nelly D. Saenen[1], Wilfried Gyselaers[4], Peter Van Eyken[4], Michelle Plusquin[1], Maarten B.J. Roeffaers[3], Marcel Ameloot[2] & Tim S. Nawrot[1,5]

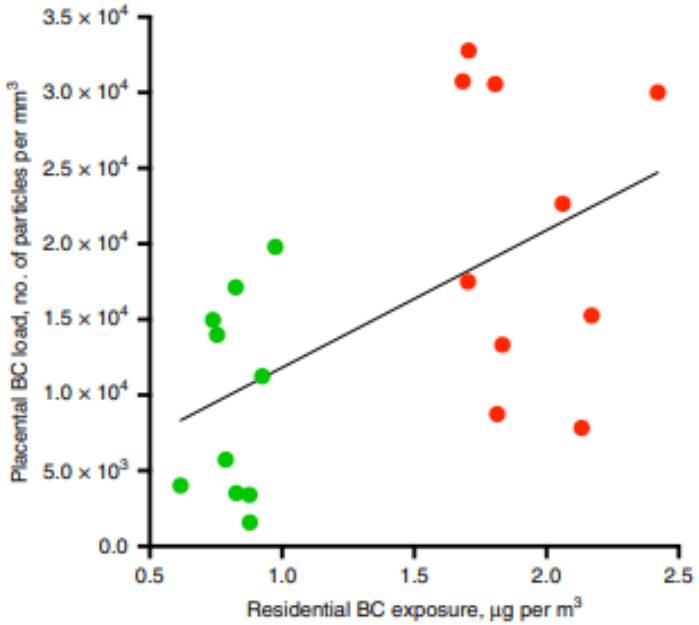
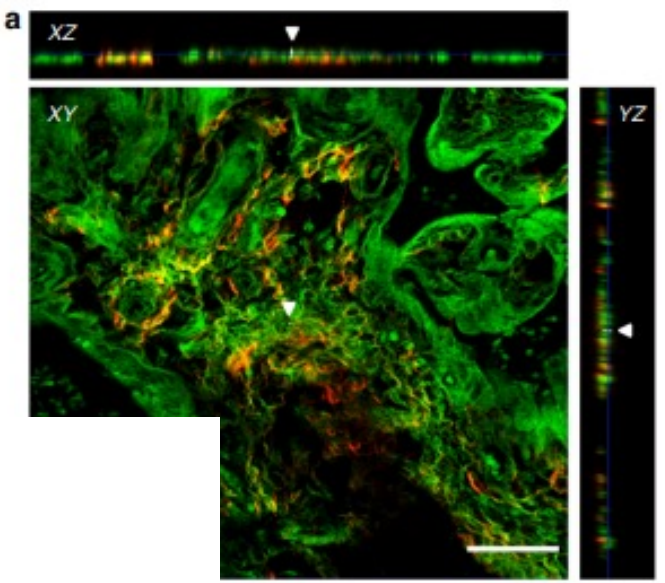


Fig. 4 Correlation between placental BC load and residential BC exposure averaged over the whole pregnancy. The line is the regression line. Green and red dots indicate low ($n = 10$ mothers) and high ($n = 10$ mothers) exposed mothers. Pearson correlation $r = 0.55$, $P = 0.012$ and corresponding Spearman's Rank correlation $r = 0.43$, $P = 0.06$. Source data are provided as a Source Data file



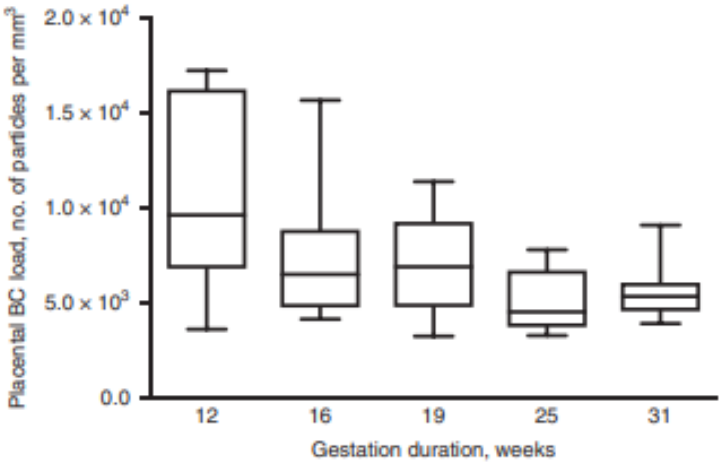


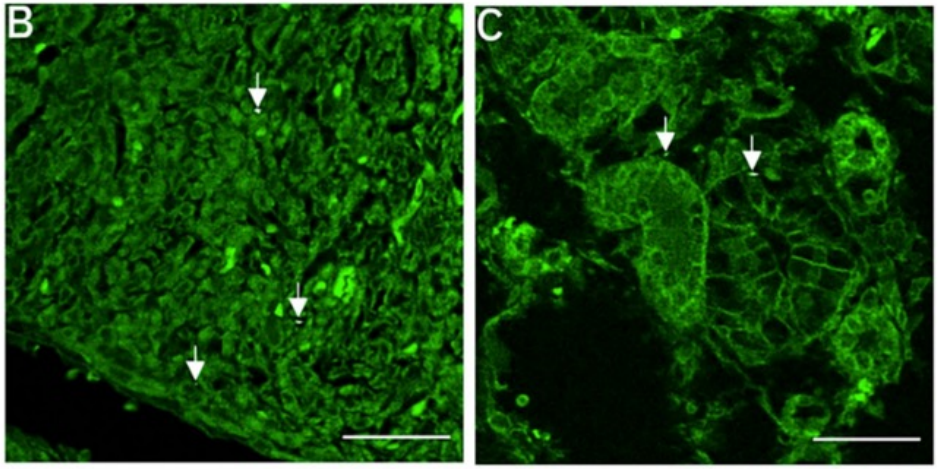
Fig. 5 BC load in placentae from spontaneous preterm births ($n = 5$). The whiskers indicate the minimum and maximum value and the box of the box plot illustrates the upper and lower quartile. The median of spreading is marked by a horizontal line within the box. Source data are provided as a Source Data file

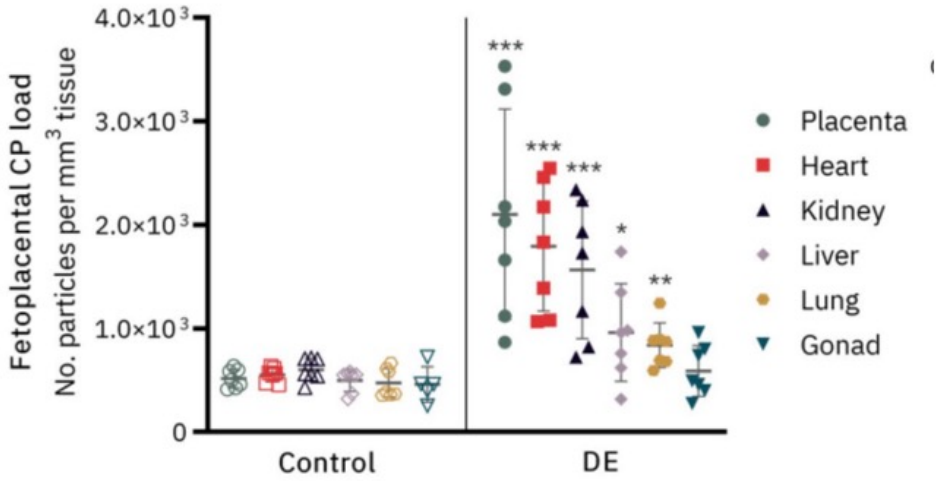
Bongaerts et al. Particle and Fibre Toxicology (2023) 20:20
https://doi.org/10.1186/s12989-023-00531-z
Particle and Fibre Toxicology

RESEARCH Open Access

Placental-fetal distribution of carbon particles in a pregnant rabbit model after repeated exposure to diluted diesel engine exhaust

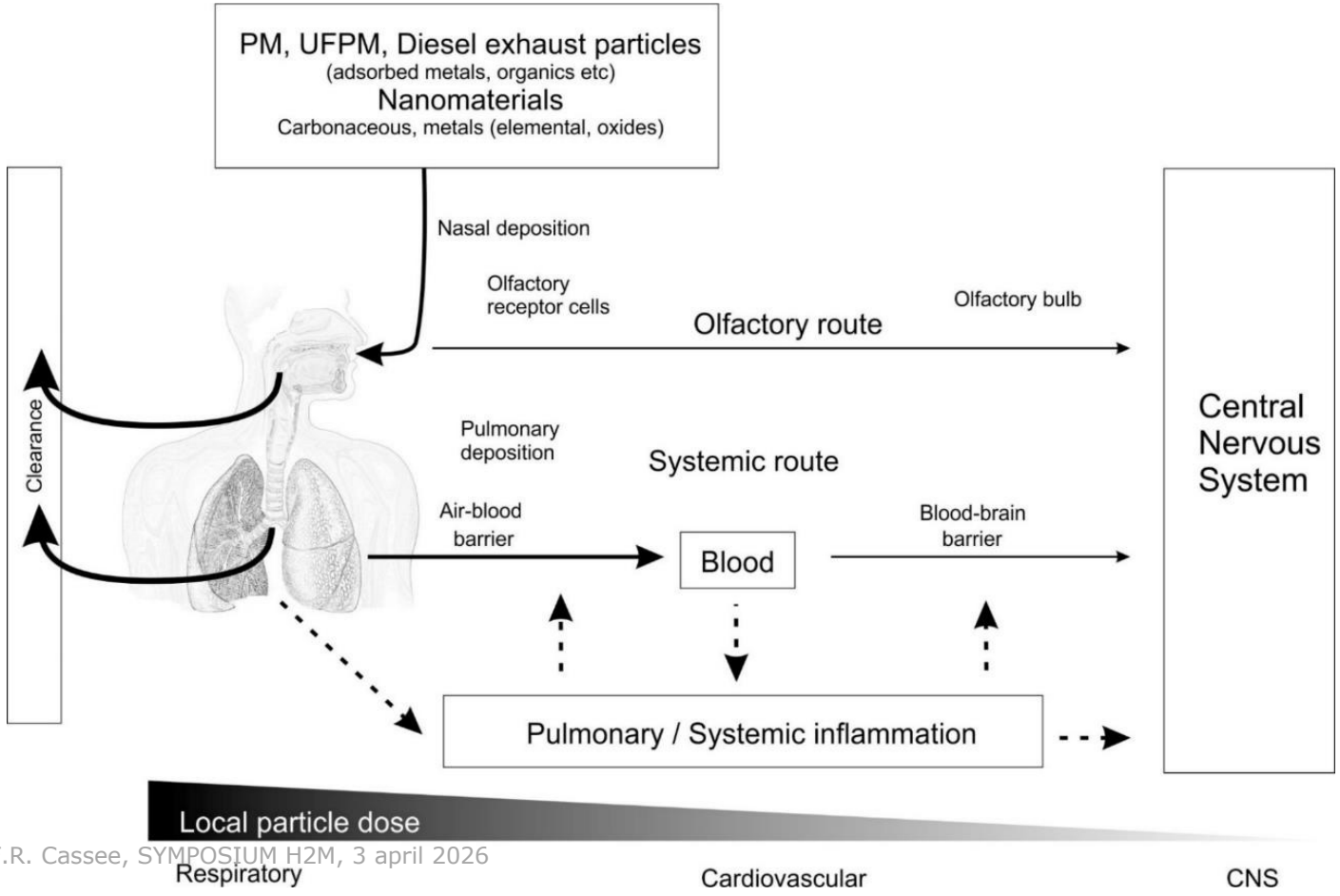
Eva Bongaerts[1], Tim S Nawrot[1,2*], Congrong Wang[1], Marcel Ameloot[3], Hannelore Bové[1], Maarten BJ Roeffaers[4], Pascale Chavatte-Palmer[5,6], Anne Couturier-Tarrade[5,6] and Flemming R Cassee[7,8]





Carbon Particles were present (white and further indicated with white arrowhead) (B) heart, (C) kidney, Magnification x20. Scale bars: 50 µm.

3. Neurodegeneration & Alzheimer's disease



Heusinkveld HJ, Wahle T, Campbell A, Westerink RHS, Tran L, Johnston H, Stone V, Cassee FR, Schins RPF. Neurodegenerative and neurological disorders by small inhaled particles. ***Neurotoxicology*** 2016;56:94-106.

doi: 10.1016/j.neuro.2016.07.007

Traffic-related air pollution exposure

Air inlet at a busy street.

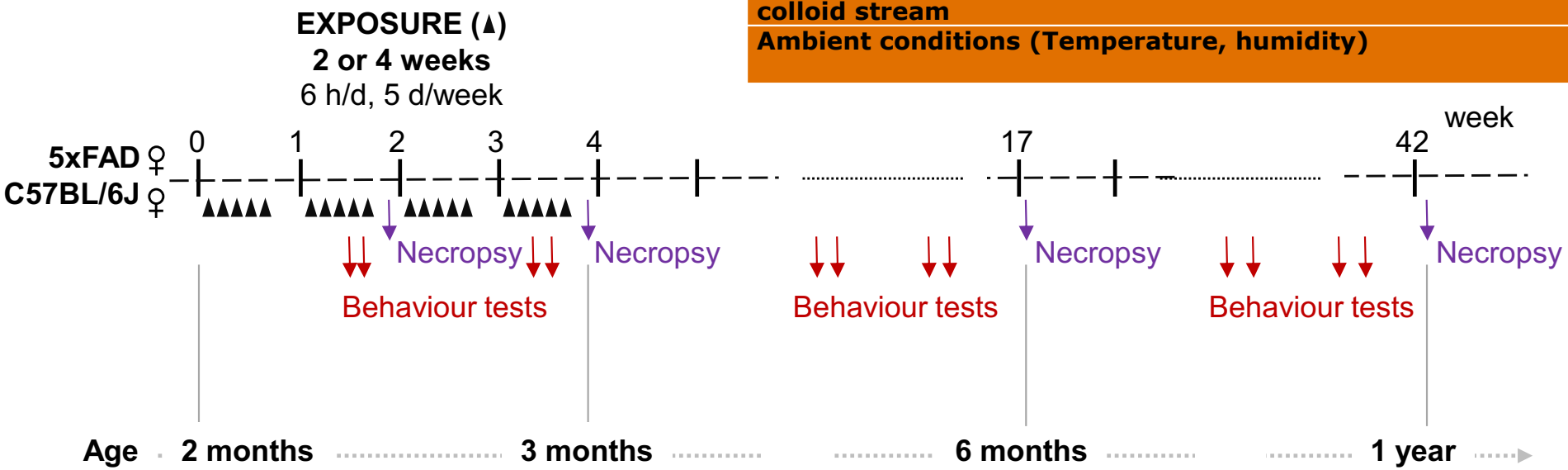
Whole body single housing inhalation exposure units

alzheimer nederland

Alzheimer Forschung Initiative e.V.

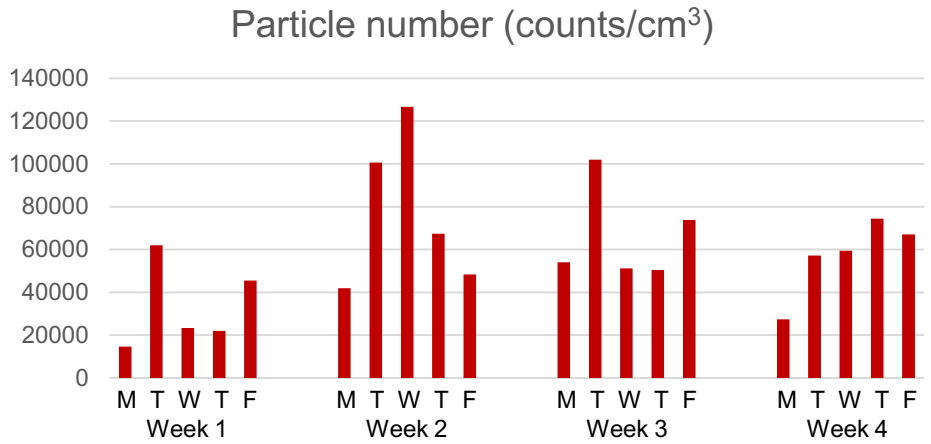
Study design

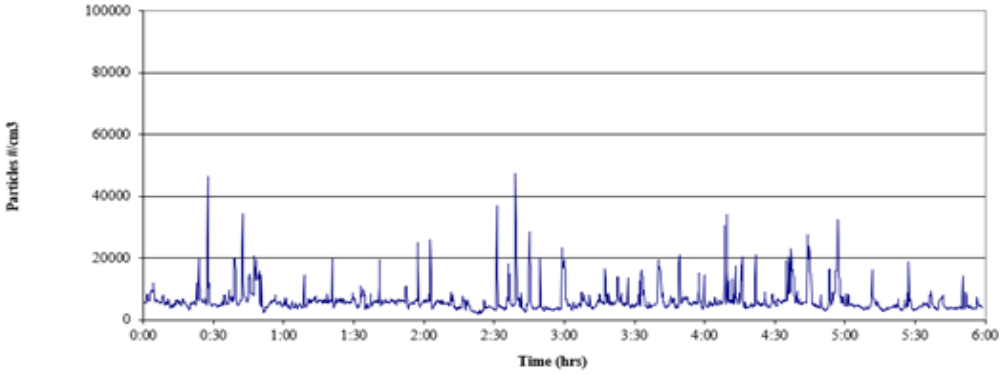
Substance
Nitrogen oxides : NOx, NO and NO_2
Carbon monoxide
Ozone
Particle number using a condensation particle counter
Particle mass
Temperature and humidity in the chamber
Optically absorbing ('black smoke') suspended particulates in a gas colloid stream
Ambient conditions (Temperature, humidity)



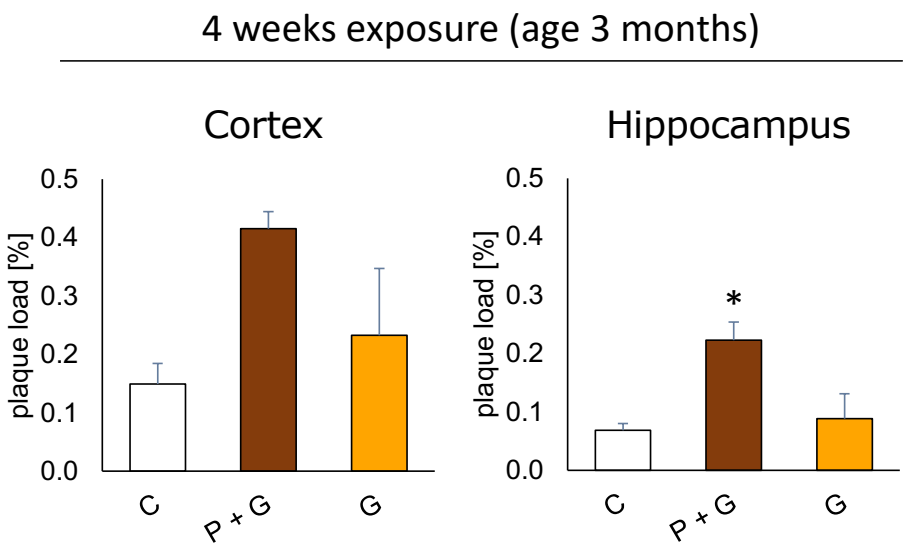
Exposure characteristics – concentrated PM

Date	Counts per cm^3	Mass $\mu g/m^3$	NO_2 $\mu g/m^3$	O_3 $\mu g/m^3$	temp	RH
Average	58460	109	50	35	26.1	72.6
StDev	28187	76	11	22	1.7	5.2





β-Amyloid pathology



*p<0.05 (ANOVA, Dunnett post-hoc testing).

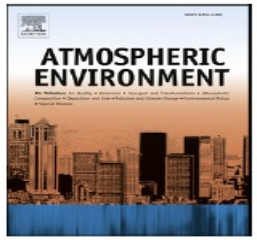
Conclusion Alzheimer’s disease PM study

- Accelerated β-amyloid plaque formation in 5xFAD mice exposed to traffic-related air pollution particles and gases but not for gases alone

The findings of our ongoing research support a role of exposure to traffic-related air pollution particles in the pathogenesis of Alzheimer's disease

4. Aviation and UFP

F.R. Cassee, SYMPOSIUM H2M, 3 april 2026



HIGHLIGHTS

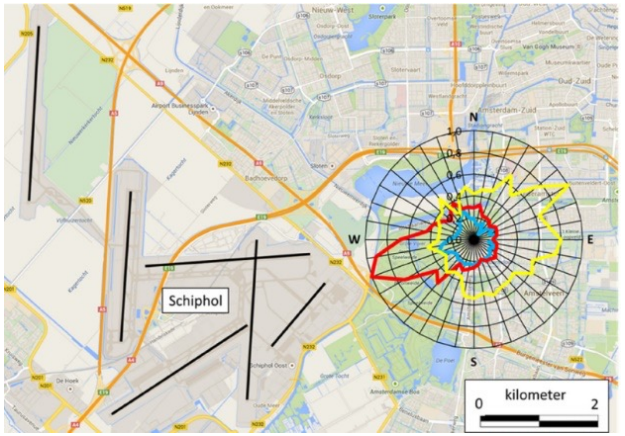
- Ultrafine particles are a factor 3 elevated 7 km downwind Schiphol airport.
- The size-distribution of these particles is dominated by particles of 10–20 nm.
- 45,000/60,000 addresses exposed to 5–10,000 (annual)/10–20,000 (hourly) #/cm^3.

Background

- Elevated concentrations of UFP near airports, including Schiphol Airport (Keuken et al, Atm Env 2015)
- Little is known about the health effects of ultrafine particles from aviation.

➢ **5 year research program into the health risks of ultrafine particles around Schiphol Airport.**

1. **Studies on health effects of short-term exposures**
2. Measurements & modelling of long-term concentrations
3. Studies on health effects of long-term exposures

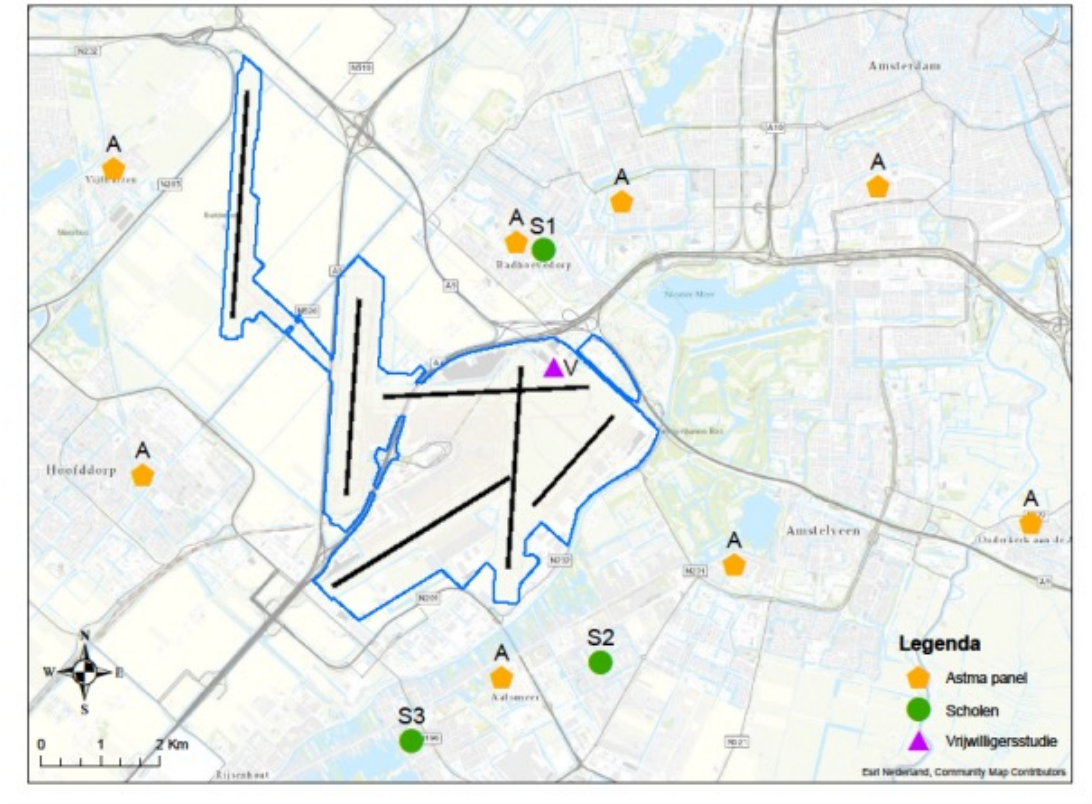


UFP (daytime) UFP (night) BC

Research questions

1. *What are the health effects of short-term exposure to UFP in general and of UFP from aviation in particular?*
2. *How do these effects compare to effects of UFP from other sources (mainly road traffic)?*

3 studies with varying designs



Panel study (real-life concentrations)

- 161 children from 3 schools situated in Badhoevedorp (S1) and Aalsmeer (S2+S3) (school panel)
- 30 children with asthma from the wider area around Schiphol (asthma panel).

Volunteer study (high concentrations)

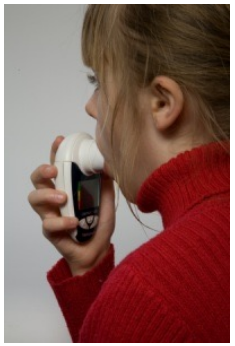
- 21 young healthy adults exposed in a mobile lab next to the airport (V)

Toxicological study (in-vitro)

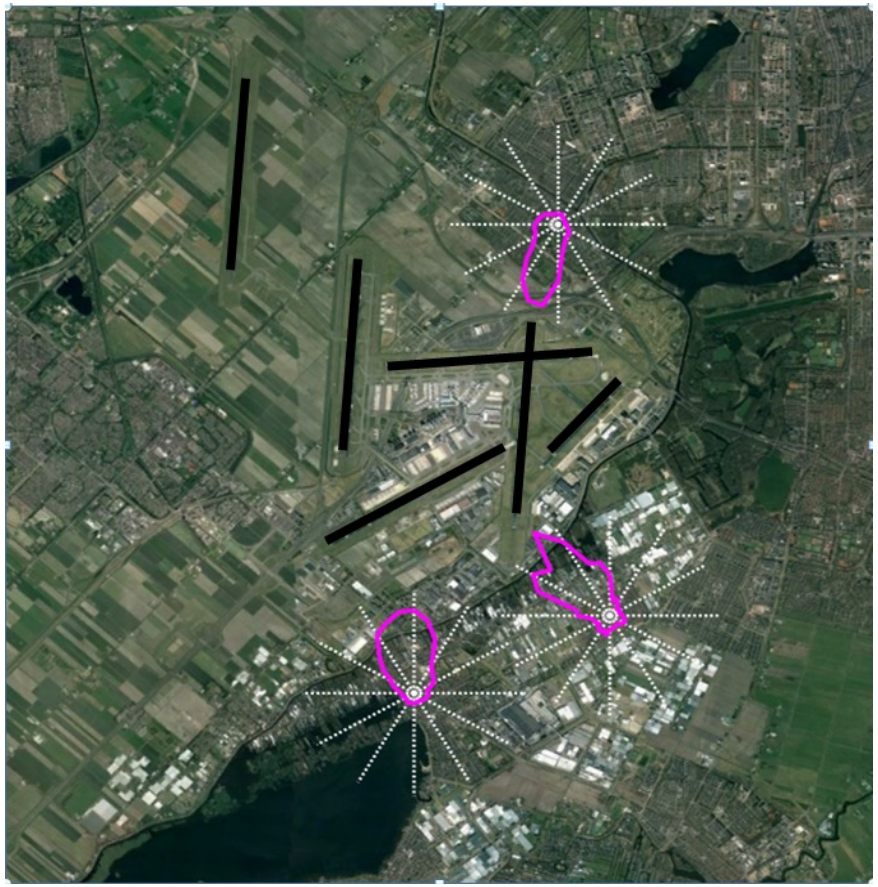
- Lung cells, exposed to UFP collected at the site of the volunteer study and directly from the exhaust of a turbine engine.

Panel study

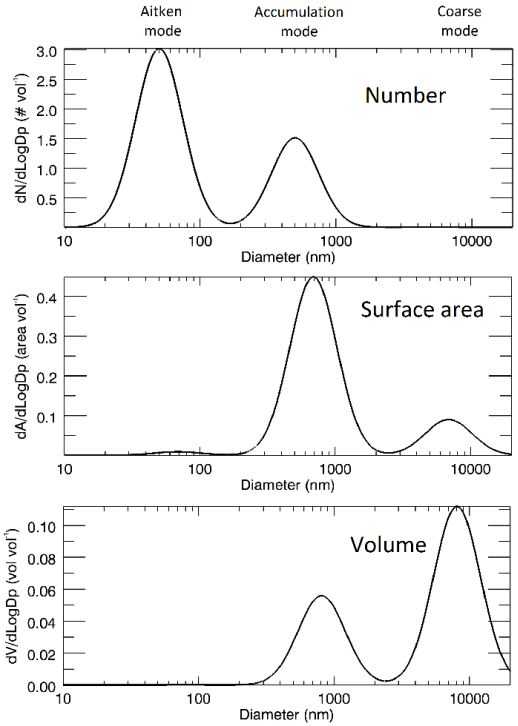
- Wekelijkse longfunctie- en uitgeademde NO-metingen op school (161 kinderen) en dagelijkse longfunctie- en symptoomregistratie thuis (alle 191 kinderen).
- Elk kind nam twee tot drie maanden deel aan het onderzoek; 4 onderzoeksperiodes
- Continue metingen van UFP (totaal aantal deeltjes + grootteverdeling) en roet op de schoolpleinen van de scholen.
- Onderzoek of veranderingen in UFP-concentraties verband hielden met veranderingen in de gezondheid van de luchtwegen.
- Uitgedrukt als het verschil tussen een gezondheidsmeting na een periode met hoge UFP en een gezondheidsmeting na een periode met lage UFP (p5-p95-toename).



Panel study (schoolyard measurements)



- PNC≤20nm used as an indicator for UFP mainly from aviation
- PNC>50nm used as an indicator for UFP mainly from road traffic
- PNC= particle number count, all particles in air
- UFP = ultrafine particles ~ <100 nm



Results panel study

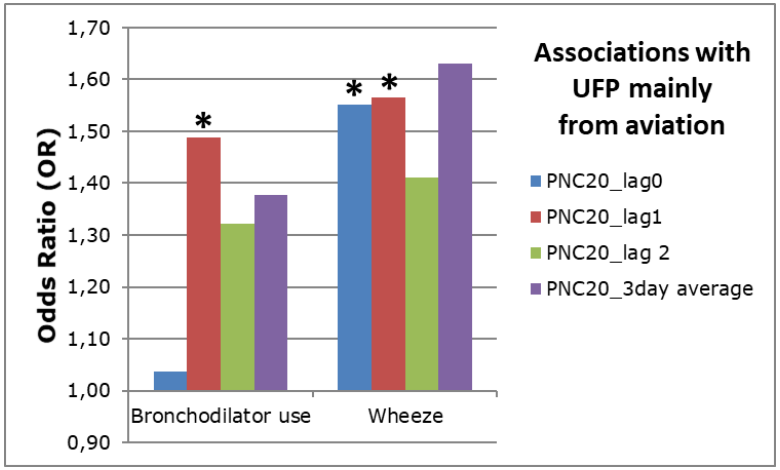
Respiratory symptoms and medication use

- Significant associations between exposure to UFP and an increase in daily respiratory symptoms (wheeze) and bronchodilator use.

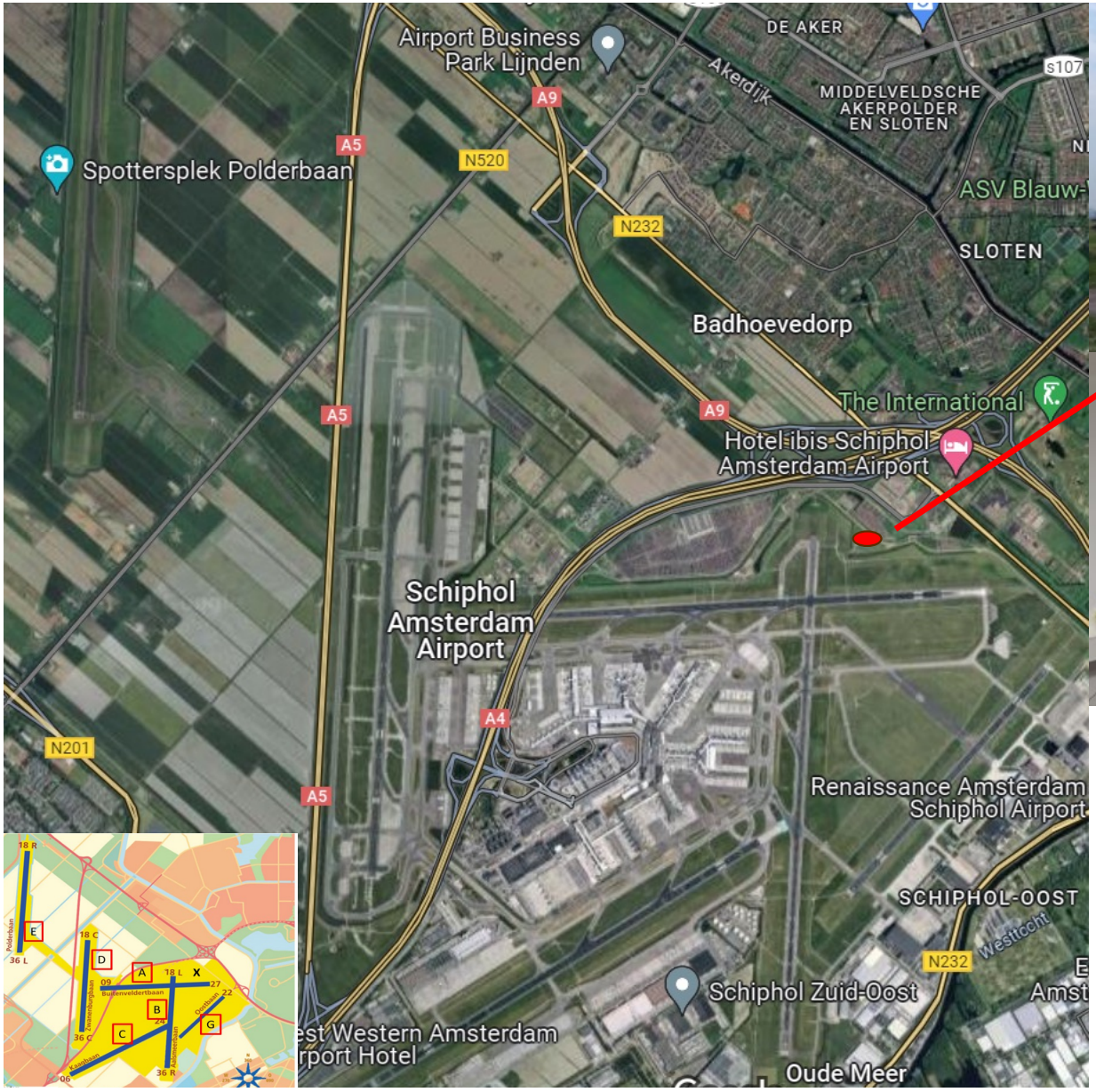
- For total UFP, for UFP mainly from aviation and for UFP mainly from road traffic.

Lung function and exhaled NO

- No associations between variations in UFP and lung function measurements and exhaled NO (indicator inflammation)

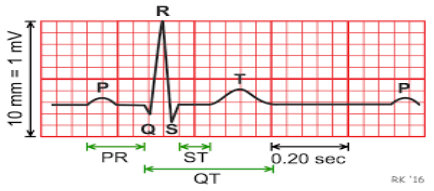


*Adjusted associations between 24-h exposure to UFP mainly from aviation (PNC20) and wheeze and bronchodilator use, combined school and asthma panel (n=191). ORs are expressed per p5-p95 increment (12.000 p/cm^3 for lag0, lag1 and lag2; 9.500 p/cm^3 for the 3-day average); * p<0,05*


Airport Business Park Lijnden
DE AKER
Akerdijk
MIDDELVELDSCHE AKERPOLDER EN SLOTEN
s107
A9
A5
N520
Spottersplek Polderbaan
ASV Blauw-
N232
SLOTEN
Badhoevedorp
A5
A9
The International
Hotel ibis Schiphol Amsterdam Airport
Schiphol Amsterdam Airport
A4
N201
A5
Renaissance Amsterdam Schiphol Airport
SCHIPHOL-OOST
N232
Schiphol Zuid-Oost
Oude Meer

Volunteer study

- 21 healthy volunteers exposed for 5 hours in a mobile lab next to the airport
- Measurements of UFP and other air pollutants during the exposure
- 2-5 exposure per person; 32 exposure days (total 86 exposures)
  - ➢ Large variation in UFP (10.000-170.000 #/cm^3)
- Health measurements before and after the exposure (lung function, exhaled NO, ECG, blood pressure, oxygen saturation)



Results volunteer study

- Short-term (5 hour) exposure to UFP was associated with:
  - A decline in lung function (FVC)
  - A prolongation of the QTc interval (ECG)

- Both for total UFP and UFP mainly from aviation (PNC ≤ 20 nm)

- UFP from road traffic (PNC>50 nm) was significantly associated with an increase in blood pressure.

- For other lung and cardiac function parameters, exhaled NO and oxygen saturation, no statistically significant associations with UFP were observed

Effects of short-term exposures to ultrafine particles near an airport in healthy subjects

A. Lammers[a], N.A.H. Janssen[b], A.J.F. Boere[b], M. Berger[a], C. Longo[a], S.J.H. Vijverberg[a], A.H. Neerincx[a], A.H. Maitland - van der Zee[a], F.R. Cassee[b,c,*]

Environment International 141 (2020) 105779

Conclusies

Gaat steeds beter met de luchtkwaliteit

Geen grote verschillen in toxiciteit van ultrafijn stof van wegverkeer t.o.v. vliegverkeer

Kortdurende blootstelling aan hoge concentraties ultrafijnstof in verband gebracht met verminderde longfunctie en repolarisatie van het hart, oxidatieve stress en arteriële stijfheid direct na blootstelling bij volwassenen, wel reversibel.

Langdurige blootstelling aan ultrafijn stof van vliegverkeer heeft **mogelijk** effect op het hart- en vaatstelsel. In gebieden met hoge concentraties zijn bijvoorbeeld meer mensen medicijnen tegen hartaandoeningen gaan gebruiken dan in gebieden met lage concentraties.

Conclusies

Blootstelling aan ultrafijn stof is bij zwangere vrouwen **mogelijk** nadelig voor de ontwikkeling van het ongeboren kind. We spreken van mogelijk omdat er te veel onzeker is om definitief te kunnen concluderen dat er een oorzakelijk verband is.

Er is niet genoeg wetenschappelijk bewijs dat blootstelling aan ultrafijn stof van vliegverkeer effect heeft op het zenuwstelsel of diabetes veroorzaakt.

Aannemelijk dat ultrafijne deeltjes het hart en de hersenen kunnen beïnvloeden en zelfs de placenta kunnen passeren na inademing