Thinking outside the box: how to use the existing science on ultrafine particles to protect against them?

Lidia Morawska

Queensland University of Technology

World Health Organization

Collaborating Centre for Air Pollution and Health

Working groups

Exposure:

- **Lidia Morawska**, QUT
- **Aneta Wierzbicka**, Lund U
- **Aurelio Tobias**, IDÆA
- **Xavier Querol, ID/EA**
- **Giorgio Buonanno**, U Cassino
- **Hicran Altug**, U Hospital Düsseldorf
- **Josef Cyrys**,
- **Jürgen Schnelle-Kreis**, CMA Munich
- **Karin Hougaard**, APHA
- **Michal Kowalski**, EPI Munich
- **Micheal Riediker**, SCOEH
- **Per Schwarze**, NIPH
- **Regina Pickford**, EPI Munich
- **Wolfram Birmili**, UBA, Germany

Toxicology:

- **Flemming Cassee**, RIVM
- **Ali Önder Yildirim**, HMGU Munich
- **Alison Elder**, URMC
- **Dietrich Plaß**, UBA, Germany
- **Je Yu**, KEMTI
- **Johan Øvrevik**, NIPH
- **Otmar Schmid**, ILBD
- **Steffen Loft**, U Copenhagen
- **Tobias Stöger**, U Copenhagen

Epidemiology:

- **Annette Peters**, EPI Munich
- **Susanne Breitner**, EPI Munich
- **Timo Lanki**, NIHW Finland
- **Enembe Okokon**, NIHW Finland
- **Regina Pickford**, EPI, Helmholtz Center Munich
- **Evangelia Samoli**, U Athens
- **Tamara Schikowski**, IUF Düsseldorf
- **Massimo Stafoggia**, Lazio Region Health Service
- **Alexandra Schneider**, EPI Munich
- **Siqi Zhang**, EPI Munich
- **Barbara Hoffmann**, U Hospital Düsseldorf
- **Kai Chen**, EPI Munich
- **Kathrin Wolf**, EPI Munich
- **Nino Künzli**, Swiss TPH
- **Ron Kappeler**, Swiss TPH
- **Sarah Lucht**, U Hospital Düsseldorf

How did this work start?

5th Workplace and Indoor Aerosol Conference, Cassino, Italy, April 2018

Lidia's presentation: *Ultrafine particles: two decades of research and the debate is still on!*

Decision: to do something about this!

As an adviser to the minister of health/environment…

….how would you answer the questions:

- What are the concentration trends of UFP in your city/country (going up or down)?
- What is their source apportionment?
- How to measure them?
- Do UFP cause health effects?
- What standard values would you recommend?

Health guidelines for UFP?

"While there is a considerable toxicological evidence of potential detrimental effects of UFP on human health, the existing body of epidemiological evidence is insufficient to conclude on exposure/response relationship to UF particles"

WHO 2005

WHO: revision of the air quality health guidelines

WHO Guidelines Development Group, Bonn, September 2015

Next meeting: 4-6 June, Bonn

New WHO AQ Guidelines: 2020?

Will they include UFP?

Randomized control trials?

The Parachute

Parachutes reduce the risk of injury after gravitational challenge, but their effectiveness has not been proved with randomised controlled trials

Hazardous journeys

Parachute use to prevent death and major trauma related to gravitational challenge: systematic review of randomised controlled trials

Gordon C S Smith, Jill P Pell

BMJ: firs

Conclusions As with many interventions intended to prevent ill health, the effectiveness of parachutes has not been subjected to rigorous evaluation by using randomised controlled trials. Advocates of evidence based medicine have criticised the adoption of interventions evaluated by using only observational data. We think that everyone might benefit if the most radical protagonists of evidence based medicine organised and participated in a double blind, randomised, placebo controlled, crossover trial of the parachute.

Smith and Pell, BMJ, 327, 20–27, 2003

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The Team:
Thinking outside the box

How do we work?

Meetings in Munich:

- 5 Nov 2018
- 15 Feb 2019

Support:

- Helmholtz Zentrum München, German Research Center for Environmental Health (GmbH)
- International Laboratory for Air Quality and Health, QUT

Three subgroups:

- Exposure
- Toxicology
- Epidemiology

Progress to date

Focus of this presentation

Sections of the paper

Current state of knowledge

The White Paper – highly advanced

Epi meta analyses – starting before summer, manuscripts ready by the end of this year

Update of the 2008 review paper – starting before summer

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Morawska et al, Ambient nano and ultrafine particles from motor vehicle emissions: characteristics, ambient processing and implications on human exposure. Atmospheric Environment, 42: 8113-8138, 2008.

General

What are ultrafine particles?

Why are ultrafine particles important?

Why are ultrafine particles a special challenge?

Exposure: source emissions

Current state of knowledge

The theories underpinning UFP emission and formation process are generally well developed;

Local understanding of the origin of UFP (secondary/primary, specific sources), or their chemical composition (solid/liquid, organic carbon/elemental carbon, metals, etc.) is generally very limited;

UFP and precursor emission inventories hardly exist.

Exposure: UFP concentrations and spatial/temporal variation in cities

Current state of knowledge

The mechanisms/conditions affecting particle concentrations/trends ➔in general well understood;

A general agreement on what are low versus high concentrations (clean versus polluted) ➔ recommendation about ‘normal’ versus ‘abnormal’ concentrations;

There is typically limited local data on UFP spatial and temporal concentrations.

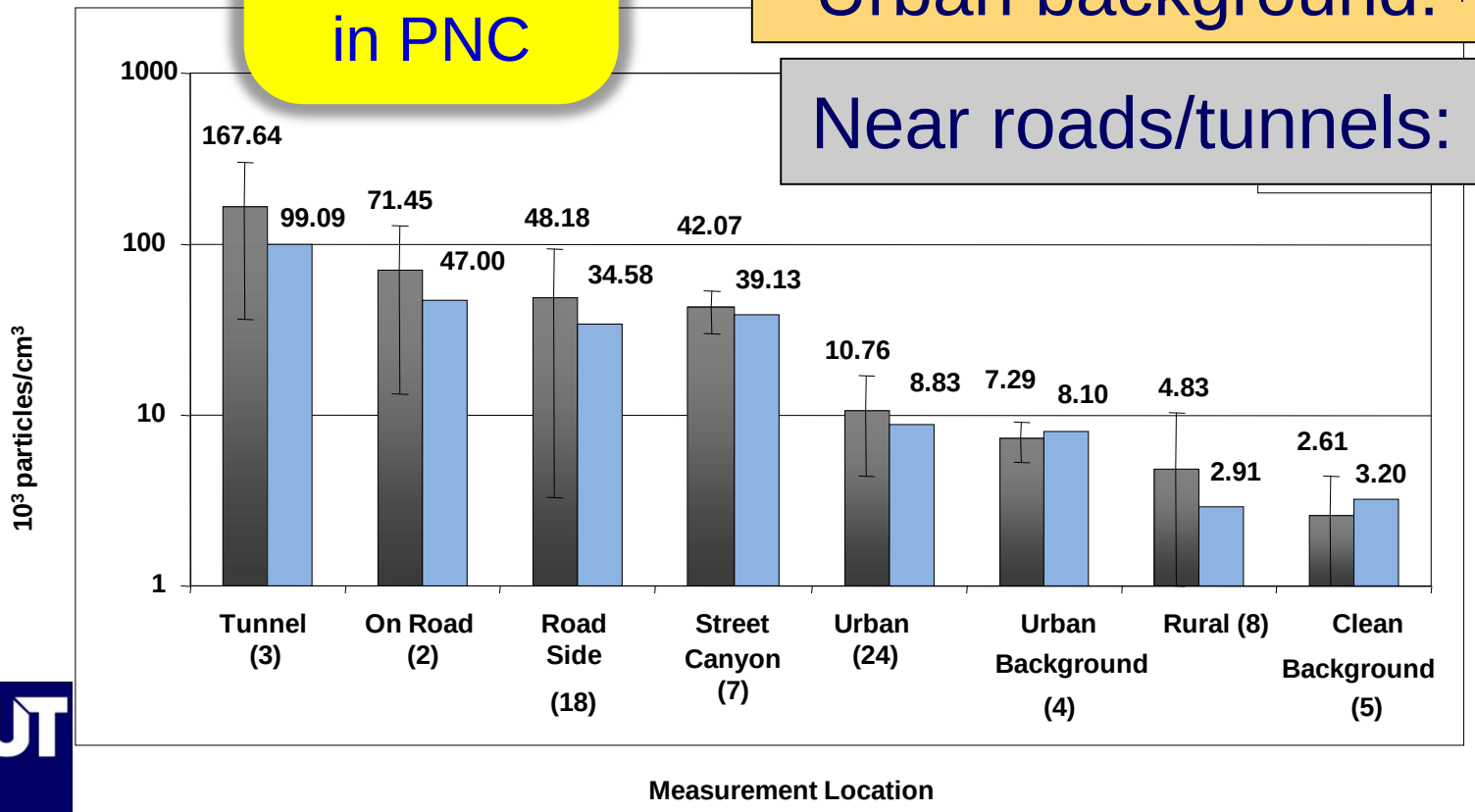
Particle number concentrations in different environments: 2008

Hence: spatial variation in PNC

Clean environments: < 10^3

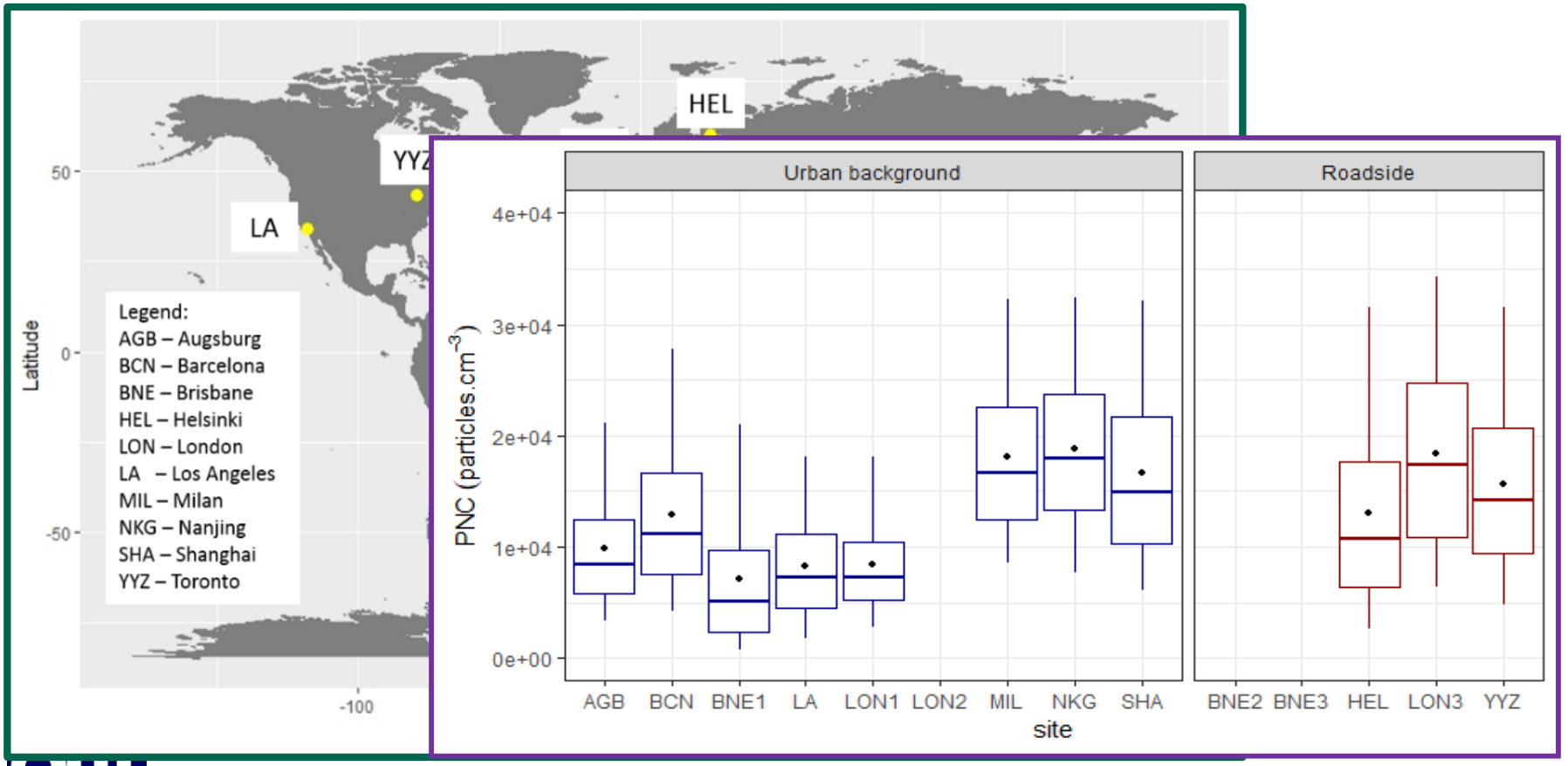
Urban background: ~ 10^4

Near roads/tunnels: > 10^5



Morawska, et al. *Atmospheric Environment,* 42: 8113-8138, 2008

Particle number concentrations in different environments: 2019



De Jesus et al. *Ultrafine particles and $PM_{2.5}$ in the air of cities around the world: how similar or different are their drivers?* *Environment International, Accepted 9 May 2019*

Exposure: UFP measurement methods I

Current state of knowledge

PNC/PSD ➔ most commonly measured, relatively well established methods ➔ no standard methods selected;

Proposal ➔ instruments measuring at least down to 10 nm, no upper limit restriction. An error/uncertainly due to missing the first few nm needs to be established;

An uncertainty due the lack of absolute calibration methods for of instruments measuring PNC (of the order of 10% ➔ can be quantified);

How to transform the inter-quantitative data, or a factor converting this to say, 10^4 particles/cm^3 based on the measurement device?

Exposure: UFP measurement methods II

Due to the lack of adequate instrumental methods we cannot recommend UFP mass or surface area measurements as routine approaches;

We call for establishing of “supersites”.

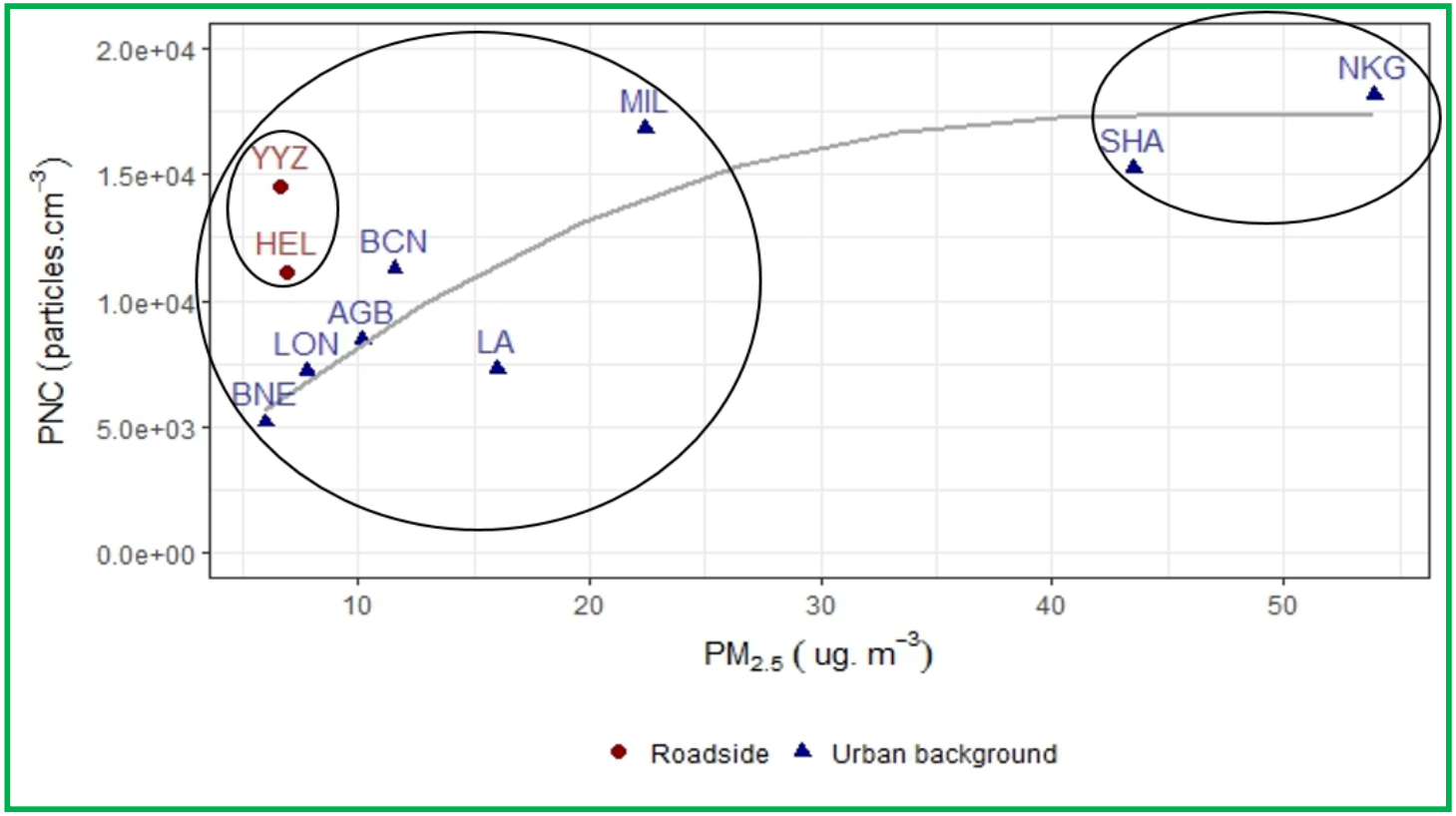
Exposure: relationship between UFP, other particle metrics and gaseous pollutants

Current state of knowledge

Very little/no relationship between PNC and $PM_{2.5}$ ➔ due to their different sources and behaviour in ambient air. Therefore, they are not representative of each other (local combustion process ⇨ mainly UFP, and mechanical process and production of SOA at regional scale ⇨ mainly $PM_{2.5}$);

A better relationship between PNC and traffic emitted gaseous pollutants (CO and NO_x) and BC; but, the existence/degree of the relationship vary ➔is specific to different urban environments.

Annual median PNC and $PM_{2.5}$



De Jesus et al. *Ultrafine particles and $PM_{2.5}$ in the air of cities around the world: how similar or different are their drivers?* *Environment International, Accepted 9 May 2019*

Exposure: indoor versus outdoor UFP

Current state of knowledge

General understanding of the sources/processes leading to indoor UFP;

Some level of understanding of typical UFP concentrations in *typical* indoor environments (*typical* ➔ restricted to the countries/setting of the studies);

Often large differences in UPF concentration between specific and *typical* indoor environments (e.g. a *specific* and a *typical* school);

It is more logistically complicated to investigate UFP in indoor environments, however, since in general their sources are understood, recommendations can be provided regarding source control.

Exposure: assessment for epidemiological studies I

Current state of knowledge

The population exposure estimation to UFP in epi short/long-term studies ➔ significantly more complex than for $PM_{2.5}$/PM_{10}

For some cities the temporal correlation among monitoring sites ➔ comparable between $PM_{2.5}$ and UFP, for others < for UFP

PNC spatial variation across a city >> higher than of $PM_{2.5}$/PM_{10}

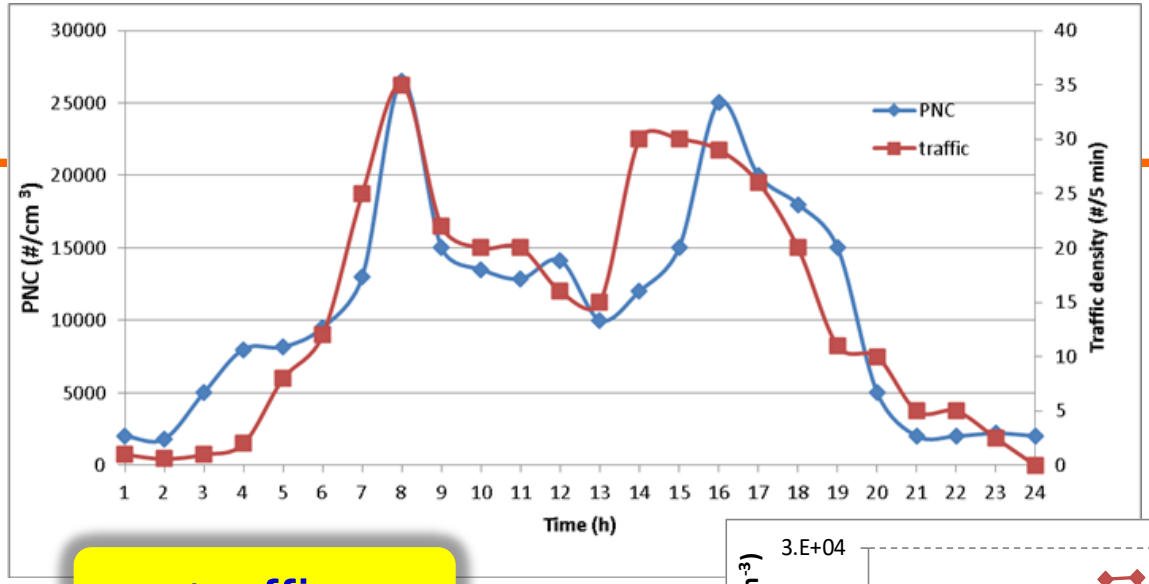
⬇

Epi long-term studies cannot adopt the approach of the $PM_{2.5}$ studies relying on single/few central sites

⬇

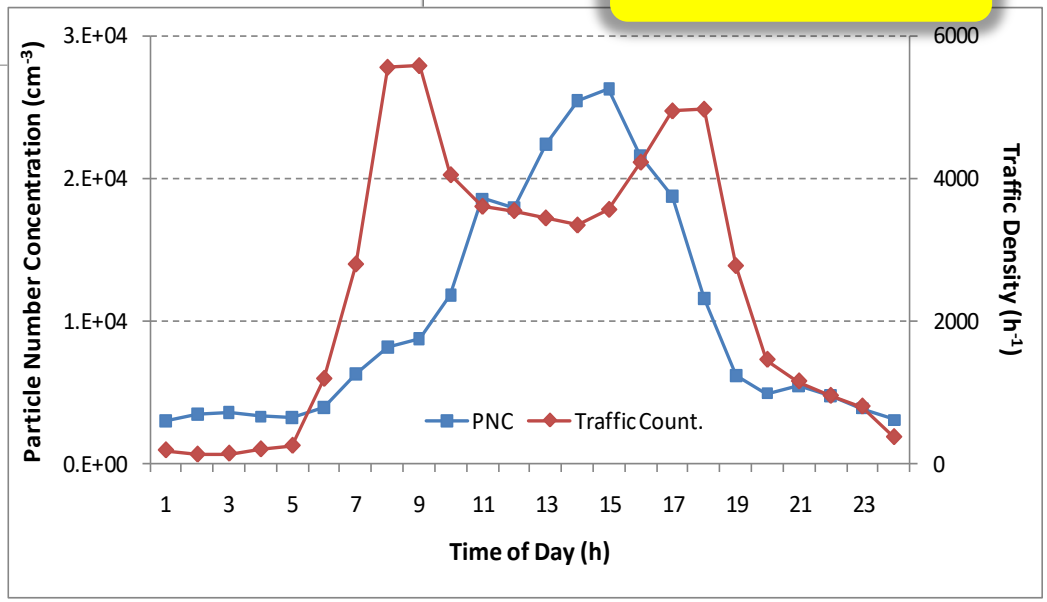
Future studies: modelling or increasing the number of monitors

Temporal variation in PNC: source contribution



traffic

SOA



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Exposure: assessment for epidemiological studies II

Current state of knowledge

The difficulties in obtaining spatially resolved estimates of long-term exposure hamper progress in long-term epi studies on UFP *(high cost of PNC monitors prohibits large-scale monitoring, almost no successful modelling approaches for UFP);*

However, scientific progress on many fronts makes personal exposure assessment possible;

There is a need to develop an optimal way of exposure assessment for epidemiological studies, utilising the emerging science and technology.

Exposure: assessment for epidemiological studies III

Current state of knowledge

Exposure assessment to traffic UFP ➔ simultaneously with other traffic related exposures *(such as to gases, BC or noise)*.

⬇

They are not just co-variables (co-pollutants) ➔ have different pathways in the body, their effects are independent

⬇

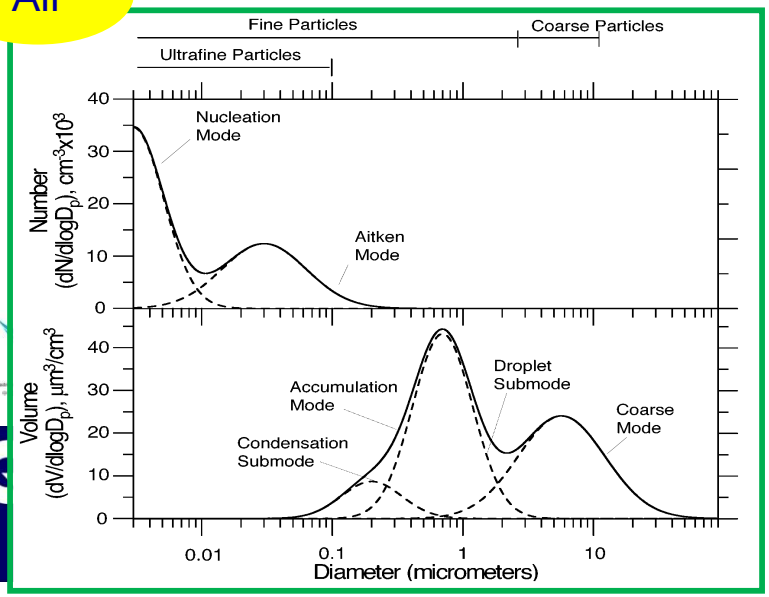
How to do this well, so in the end we are not left without neither evidence for NO_2, nor UFP, nor BC *(because of all the uncertainty, and if mutually adjustments)*?

Toxicology: From exposure to internal dose

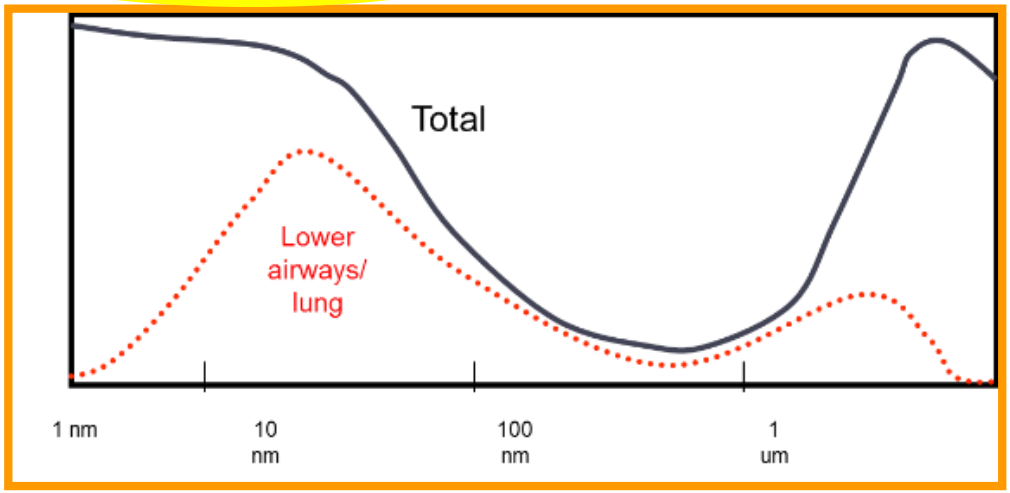
Current state of knowledge

Differences in size/distribution between UFP and larger particles ➔ regional differences in deposited dose, potentially ➔ to different biological responses. Focusing only on $PM_{2.5}$ ➔ overlooking the impact of UFP

Air



Lung deposited

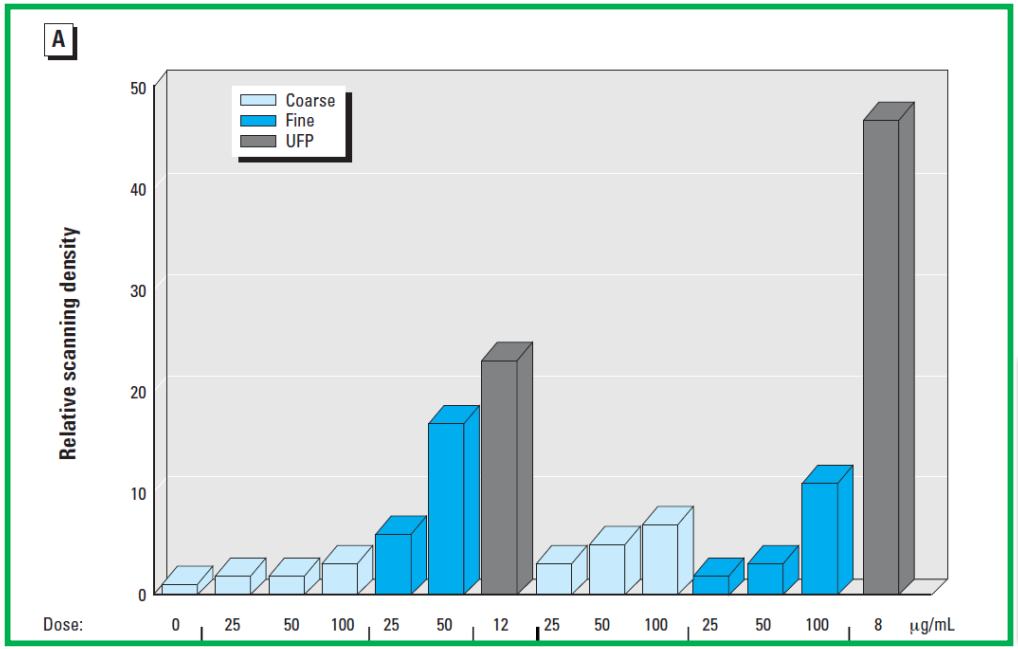


Toxicology I

Current state of knowledge

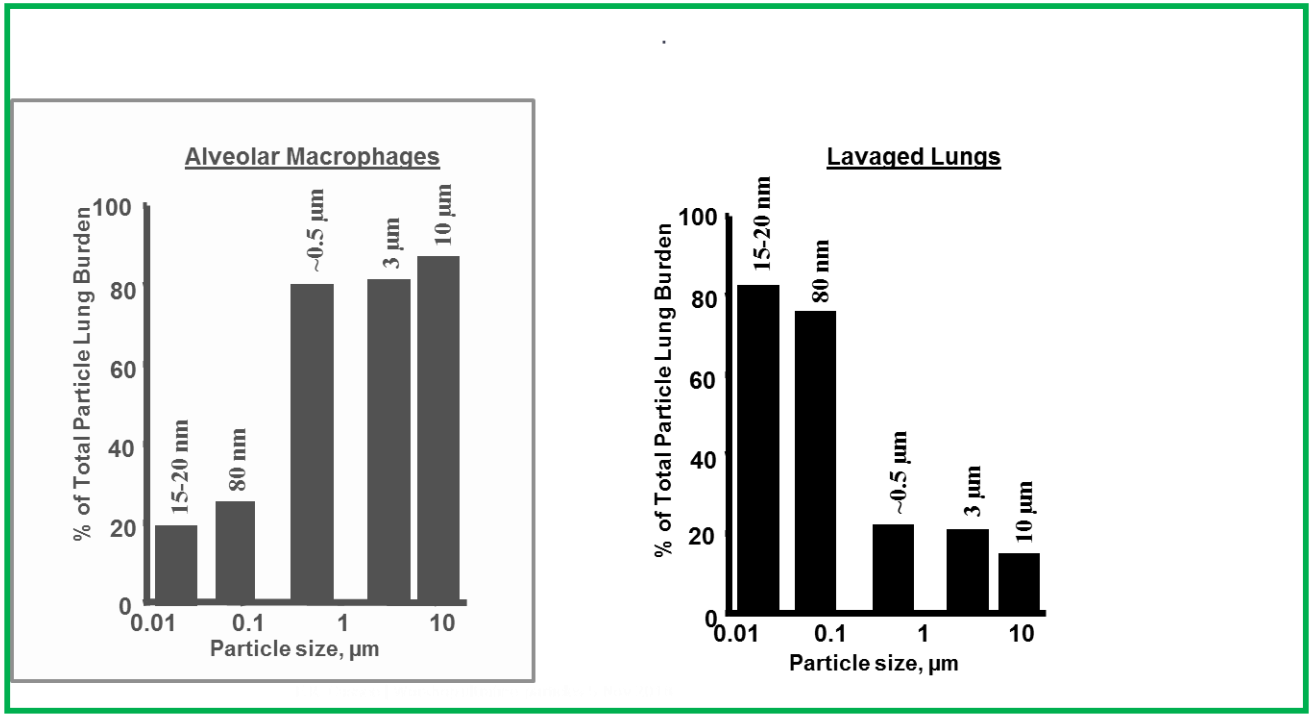
The toxic potency of UFP when using mass as a dose descriptor often (but not always) differs from $PM_{2.5}$, showing that UFP cause > effects.

In the lung ➔ different response to UFP than to larger particles.



Induction of oxidative stress in pulmonary macrophages using different size fraction of the ambient PM mixture from an urban background or urban heavy traffic area (Li et al., 2003)

Toxicology II



The effect of size on clearance and retention of particles in the rat lung *(Oberdörster 2004)*

Toxicology: metric for the UFP concentration-effect relationships?

Current state of knowledge

For practical reasons, using PNC as a predictor may be preferred above mass and surface area.

But, increased understanding of the importance of chemical composition for toxicological effects of UFPs and the use of surface area rather than mass as dose metric may possibly shed more light on the issue.

Toxicology: does the toxicity of UFP depends on source?

Current state of knowledge

There are considerable differences in the toxic potency of UFP released from various sources when using mass as unifying metric.

Toxicology: acute (peak) exposures) versus long term UFP exposures and health impacts?

Current state of knowledge

Shorter averaging times (< 24 h) seem relevant to determine the health impact of UFP ➔ but there is a lack of data from experimental studies.

At present, it is unknown whether (repeated) peak exposures are more relevant than continuous exposures to lower PNC, but with the same mean dose.

Epidemiology I

Summary of the number studies based on two systematic reviews

*HEI Perspective 3. 2013
** Ohlwein et al IJPH 2019

	1997-2011*	2011-2017**	Sum
Long-term			
Mortality	0	1	**1**
Morbidity	0	4	**4**
Emergency/hospital call/admission	0	0	**0**
Subclinical	0	5	**5**
All	0	10	**10**
Short-term			
Mortality	11	7	**18**
Morbidity/ Emergency/hospital call/admission	15	5	**20**
(Respiratory) Symptoms	8	11	**19**
Subclinical	52	55	**107**
All	86	78	**164**
Total	**86**	**88**	**174**

Epidemiology II

Current progress/state of knowledge

Since then, new studies on UFP exposures within hour/days:

- 3 on mortality,
- 6 on lung function,
- 1 on cardiac function
- 8 on blood biomarkers

Advances made in reliably determining the spatial distribution ➔ to allow investigations of long-term health effects ➔ new studies published recently on long-term effects of UFP

The studies indicate:

- associations between PNC and cardiovascular morbidity
- that the impact of UFP is independent of $PM_{2.5}$ and NO_2

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Contents lists available at ScienceDirect

Environment International

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

Short-term effects of ultrafine particles on daily mortality by primary vehicle exhaust versus secondary origin in three Spanish cities

Aurelio Tobías[a,*], Ioar Rivas[b], Cristina Reche[a], Andrés Alastuey[a], Sergio Rodríguez[c], Rocío Fernández-Camacho[d], Ana M. Sánchez de la Campa[d], Jesús de la Rosa[d], Jordi Sunyer[b,e,f,g], Xavier Querol[a]

[a] Institute of Environmental Assessment and Water Research (IDAEA), Spanish Council for Scientific Research (CSIC), Barcelona, Spain
[b] ISGlobal, Centre for Research in Environmental Epidemiology (CREAL), Barcelona, Spain
[c] Joint Research Unit to CSIC "Studies on Atmospheric Pollution", Izaña Atmospheric Research Centre, AEMET, Santa Cruz de Tenerife, Spain
[d] Centre Associate Unit CSIC-UHU "Atmospheric Pollution", Research in Sustainable Chemistry (CIQSO), University of Huelva, Huelva, Spain
[e] Pompeu Fabra University (UPF), Barcelona, Spain
[f] Consortium for Biomedical Research in Epidemiology and Public Health (CIBERESP), Spain
[g] Hospital del Mar Medical Research Institute (IMIM), Barcelona, Spain

ARTICLE INFO

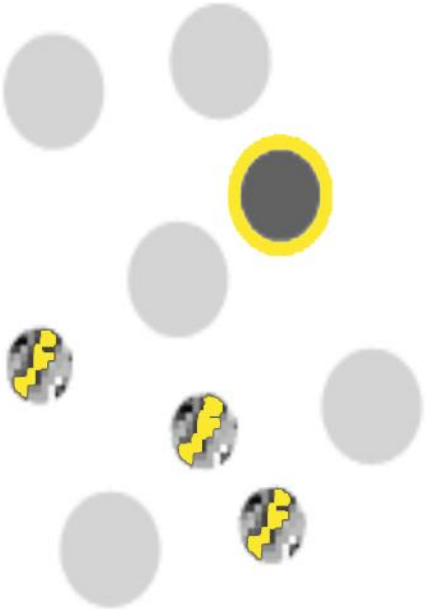
Keywords:
Ultrafine particles
Black carbon
Vehicle exhaust
Secondary emissions
Mortality

ABSTRACT

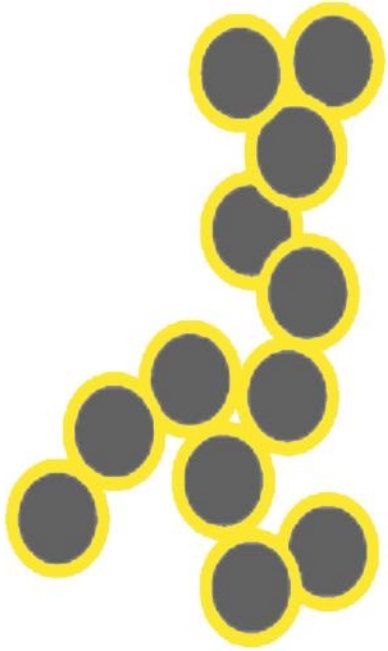
Background: Evidence on the short-term effects of ultrafine particles (with diameter < 100 nm, UFP) on health is still inconsistent. New particles in ambient urban air are the result of direct emissions and also the formation of secondary UFP from gaseous precursors. We segregated UFP into these two components and investigated their impact on daily mortality in three Spanish cities affected by different sources of air pollution.

Methods: We separated the UFP using a method based on the high correlation between black carbon (BC) and

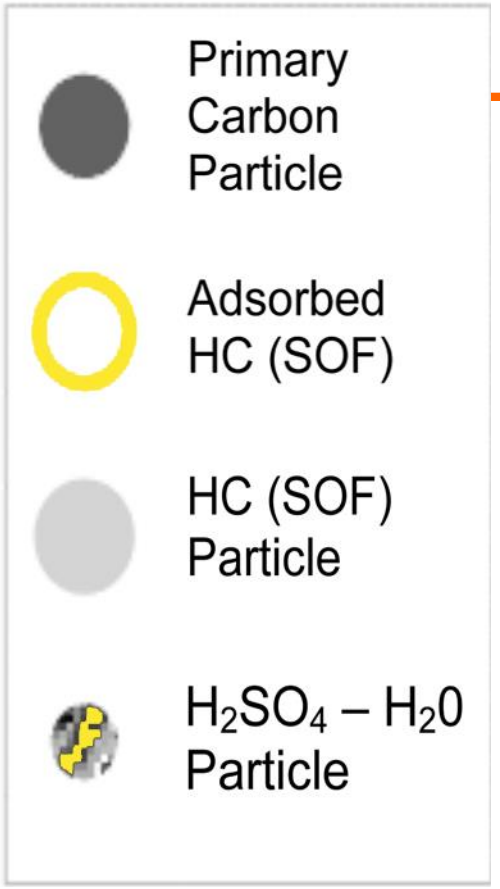
Composition of diesel particles



Nuclei Mode Particles



Accumulation Mode Particle



New method

$$N = N1 + N2$$

N – total particles

N1 – primary UFP + nucleating immediately after emission — correlated with BC

N2 – secondary UFP — low BC bearing particles

Fig. 1. Geographical location of the three study areas (Barcelona, Huelva, and Santa Cruz de Tenerife).

- Mean UFP concentration similar in all 3 cities
- BC higher in Barcelona and Tenerife
- Association with daily mortality:
  - In Barcelona and Tenerife with N1
  - In Huelva with N2

  (none of the associations were significant)

Environment International 114 (2018) 167–180

Contents lists available at ScienceDirect

Environment International

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

Effects of exposure to ambient ultrafine particles on respiratory health and systemic inflammation in children

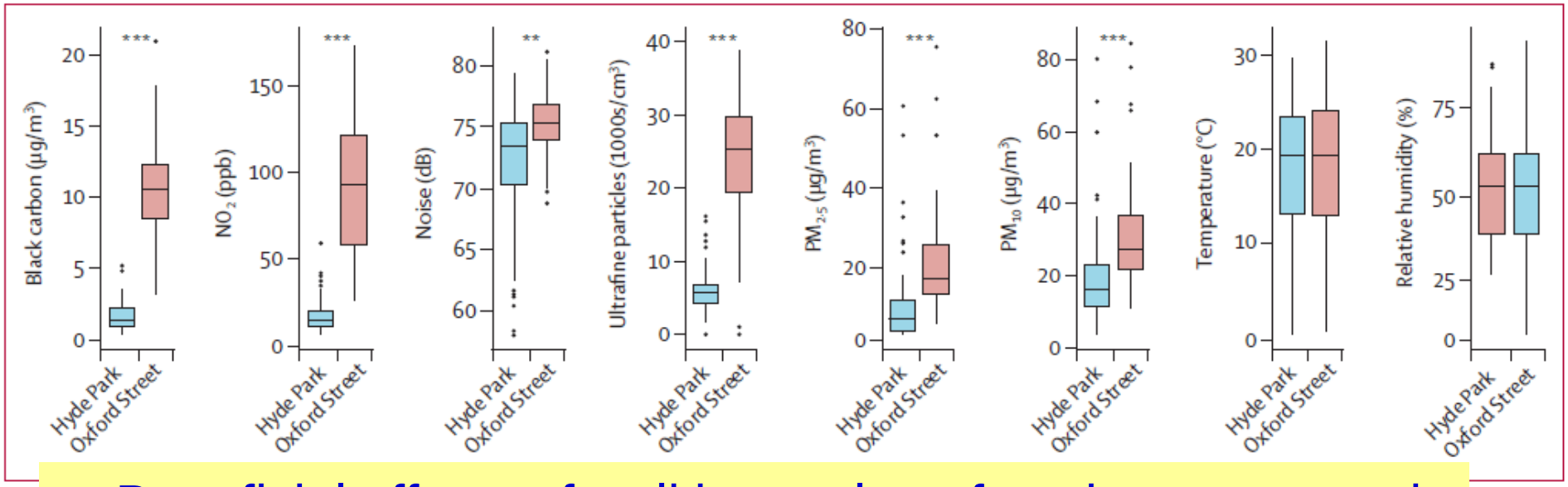
Sam Clifford[a,b,c], Mandana Mazaheri[a], Farhad Salimi[d,e,f], Wafaa Nabil Ezz[g], Bijan Yeganeh[a,f], Samantha Low-Choy[h], Katy Walker[i], Kerrie Mengersen[b,c], Guy B. Marks[f,g,j], Lidia Morawska[a,*]

- UFPs do not affect respiratory health outcomes in children but do have systemic effects, detected in the form of a positive association with a biomarker for systemic inflammation.
- This is consistent with the known propensity of UFPs to deposit deep into the lung and penetrate to the circulatory

PNC: positively associated with an increase in CRP (1.188-fold change per 1000 UFP cm^{-3} day/day (95% credible interval 1.077 to 1.299)) and an increase in FeNO among atopic participants (1.054 fold change per 1000 UFP cm^{-3} day/day (95% CrI 1.005 to 1.106)).

www.thelancet.com Published online December 5, 2017 http://dx.doi.org/10.1016/ S0140-6736(17)32643-0

Respiratory and cardiovascular responses to walking down a traffic-polluted road compared with walking in a traffic-free area in participants aged 60 years and older with chronic lung or heart disease and age-matched healthy controls:



- Beneficial effects of walking on lung function attenuated by air pollution
- Augmentation was associated UFP, NO_2, BC and $PM_{2.5}$

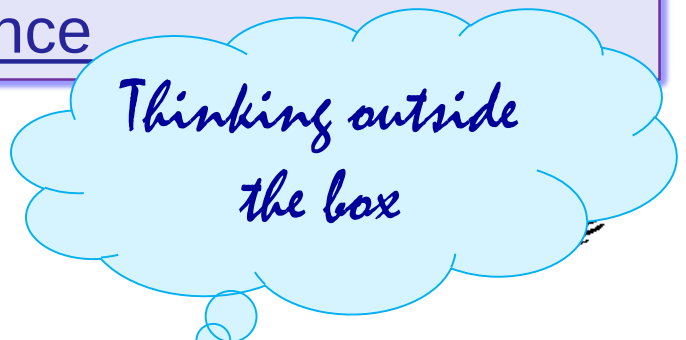
Epidemiology III

Current state of knowledge

Still ➔ an absence of quantitative meta-analyses

An underlying reason ➔ both exposure assessments and the study designs are very heterogeneous across studies

Therefore ➔ timely to reevaluate the overall evidence and consider different designs *(time-series analyses, case-crossover studies, panel studies and quasi-experiments)* using a systematic approach and input from exposure science



Epidemiology IV

These analyses will consider:

- the heterogeneity of populations or patient groups studied
- the differences in UFP measurements
- the differences in exposure-response times (typically operationalized by lag-periods),
- different years of investigation and related underlying time-trends altering the sources and composition of UFP

These (challenging) quantitative meta-analyses will:

- ✓ provide novel insights
- ✓ **impact on regulatory evaluations**
- ✓ generate hypotheses to be tested in epidemiological studies, controlled human exposure and toxicological studies.

The Parachute

RESEARCH

OPEN ACCESS

Check for updates

Parachute use to prevent death and major trauma when jumping from aircraft: randomized controlled trial

Robert W Yeh,[1] Linda R Valsdottir,[1] Michael W Yeh,[2] Changyu Shen,[1] Daniel B Kramer,[1] Jordan B Strom,[1] Eric A Secemsky,[1] Joanne L Healy,[1] Robert M Domeier,[3] Dhruv S Kazi,[1] Brahmajee K Nallamothu[4] On behalf of the PARACHUTE Investigators

BMJ: first published a

Yeh et all, BMJ 2018;363:k5094

CONCLUSIONS

Parachute use did not reduce death or major traumatic injury when jumping from aircraft in the first randomized evaluation of this intervention. However,

Not outside of the box yet, but on the way!

Thank you!

We hope that the outcome of this work will come in time to inform the WHO process