



“Climate change and air quality:
challenges and objectives for the
atmospheric research.”

Epidemiologist point of view

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Mission 4 “Education and Research” - Component 2: “From research to business” - Investment
3.1: “Fund for the realisation of an integrated system of research and innovation infrastructures”



Outline







- 🌐 Environmental epidemiology, an overview
- 🌐 A focus on air pollution
- 🌐 Hints on biological mechanisms
- 🌐 Health effects from long-term and short-term exposures
- 🌐 Long-term exposures: a literature review, the ELAPSE project
- 🌐 Short-term exposure: a literature review
- 🌐 A digression on the health effects of climate change and extreme temperatures

Environmental epidemiology

“A branch of epidemiology concerned with determining how environmental exposures impact human health” (Merrill, Ray M. (2008).

Environmental epidemiology : principles and methods. Sudbury, Mass.: Jones and Bartlett Publishers. pp. 8–9)

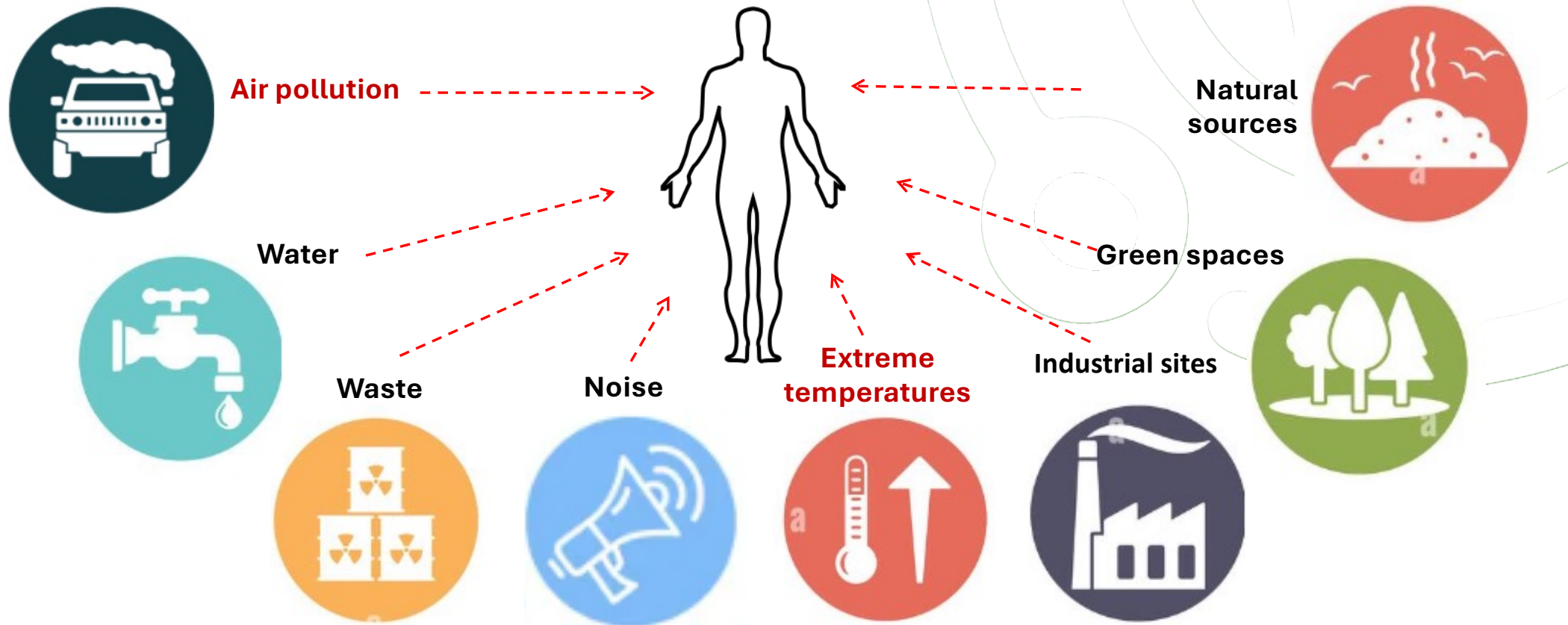
Some examples:

-  How does living in a polluted area increase chances to develop cancer?
-  w many deaths were caused by heat waves on summer 2023?
-  Is living (and accessing) green spaces in a city beneficial for health?
-  Does traffic noise increase depression or anxiety disorders?
-  Does water/soil contamination cause adverse health effects in the population?
-  How do all the above environmental factors interact on human health?

Why is this so important

- ✓ **Etiology:** understand biological mechanisms of disease onset and progression, and identify putative causal relationships
- ✓ **Public health:** protect population health from environmental risks
- ✓ **Policy:** provide evidence on environmental hazards, and evaluate the effectiveness of potential policy interventions
- ✓ **Ecology:** promote environmental sustainability
- ✓ **Equity:** identify disparities in environmental hazards among vulnerable subgroups, and promote remediation strategies
- ✓ ...

Which environmental factors



A focus on air pollution: the GBD study

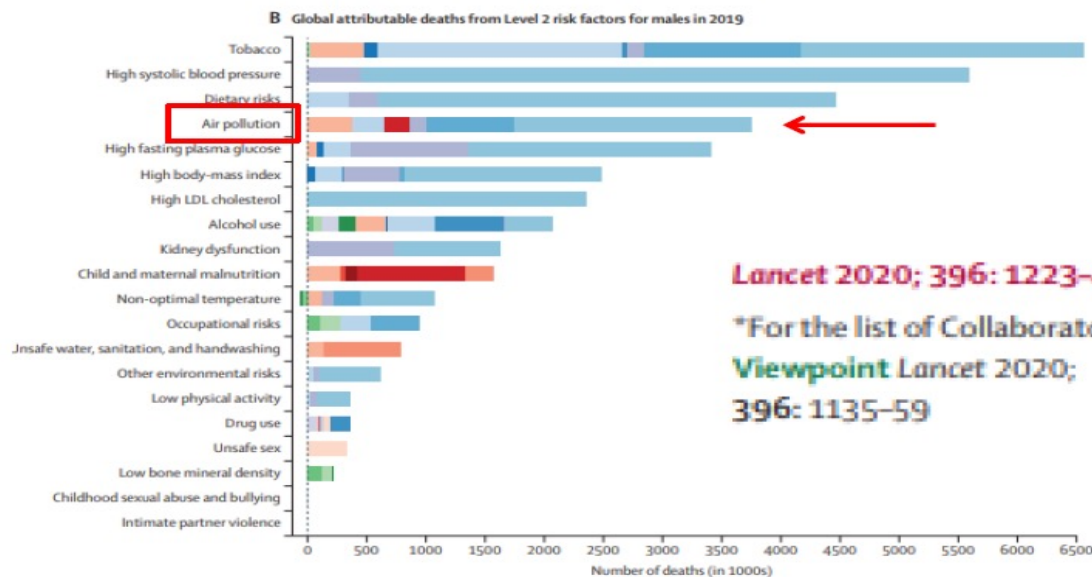
Global burden of 87 risk factors in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019

GBD 2019 Risk Factors Collaborators*



Global Burden of Disease (GBD)

- 87 risk factors
- Air pollution: 4th cause of excess mortality
- It caused approximately 6.7 million deaths on 2019



A focus on air pollution: WHO estimates



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Air pollution

Air pollution – a leading cause of NCD deaths

Most air pollution-related deaths are from noncommunicable diseases (NCDs). In terms of global disease burden, air pollution is the cause of over one-third of deaths from stroke, lung cancer, and chronic respiratory disease, and one-quarter of deaths from ischaemic heart disease.

[↓ Mortality from both ambient and household air pollution for 2016](#)
pdf, 180kb

[↓ Air pollution and NCDs: key figures](#)
pdf, 227kb

THE INVISIBLE KILLER

Air pollution may not always be visible, but it can be deadly.

Organ	Percentage of Deaths
Lung Cancer	29%
Stroke	24%
Heart Disease	25%
Lung Disease	43%

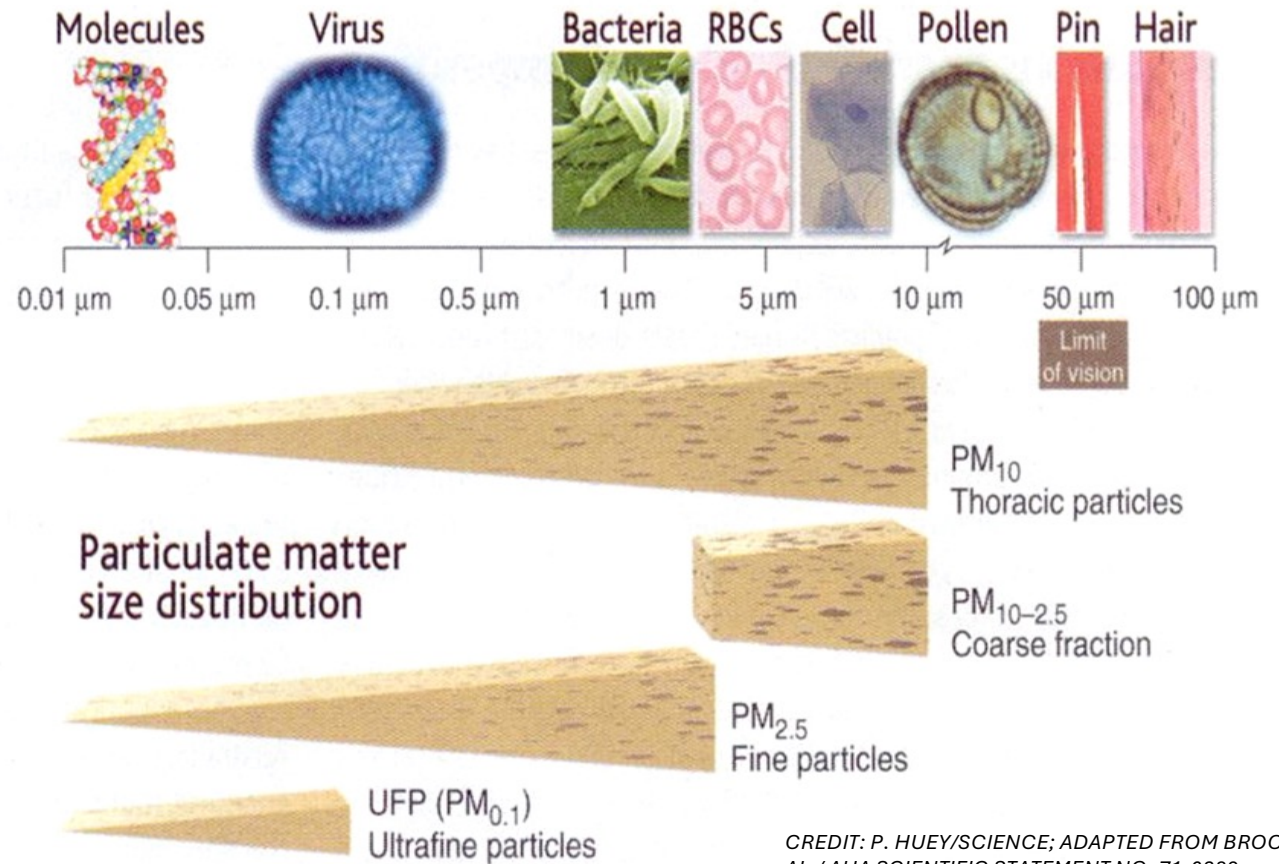
4.2 million deaths every year as a result of exposure to ambient (outdoor) air pollution

3.8 million deaths every year as a result of household exposure to smoke from dirty cookstoves and fuels

91% of the world's population lives in places where air quality exceeds WHO guideline limits

Particulate matter (PM)

- Mix of **liquid and solid** particles
- **Anthropogenic sources** (traffic, heating, industries)...
- ... and **natural sources** (wildfires, desert dust, volcanic ashes, etc.)



CREDIT: P. HUEY/SCIENCE; ADAPTED FROM BROOK ET AL./AHA SCIENTIFIC STATEMENT NO. 71-0289; IMAGES: EOL BERKELEY NATIONAL LABORATORY, CDC, JUPITER IMAGES

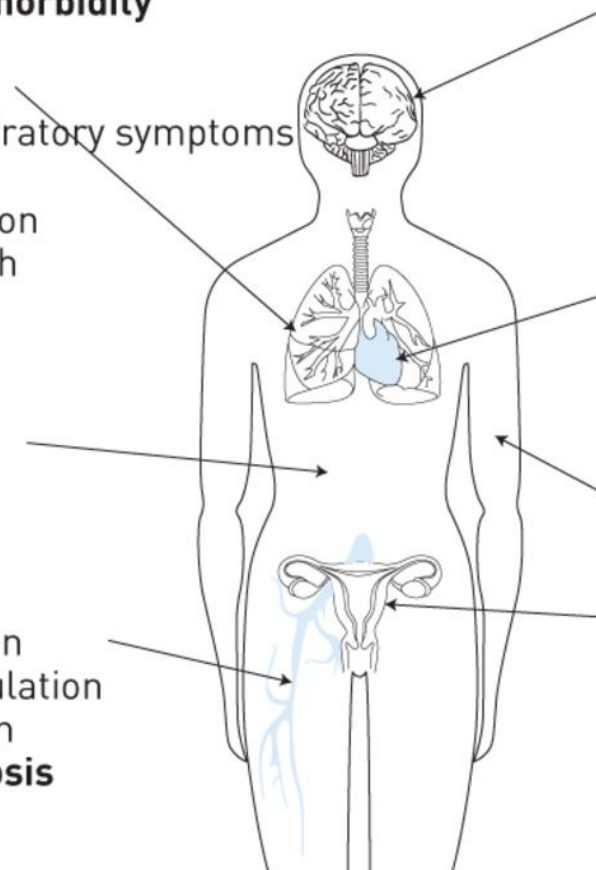
Health effects

Respiratory disease mortality
Respiratory disease morbidity
Lung cancer
Pneumonia

Upper and lower respiratory symptoms
Airway inflammation
Decreased lung function
Decreased lung growth

Insulin resistance
Type 2 diabetes
Type 1 diabetes
Bone metabolism

High blood pressure
Endothelial dysfunction
Increased blood coagulation
Systemic inflammation
Deep venous thrombosis



Stroke
Neurological development
Mental health
Neurodegenerative diseases

Cardiovascular disease mortality
Cardiovascular disease morbidity
Myocardial infarction
Arrhythmia
Congestive heart failure
Changes in heart rate variability
ST-segment depression

Skin ageing

Premature birth
Decreased birthweight
Decreased fetal growth
Intrauterine growth retardation
Decreased sperm quality
Pre-eclampsia

Source: ERS 2017

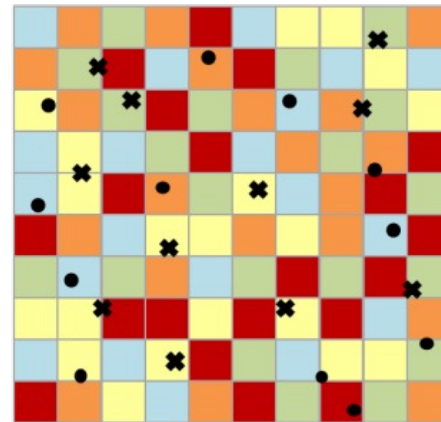
Long-term (or «chronic») effects: a conceptual scheme

Conceptual scheme of the etiological hypothesis and the corresponding statistical question, at the basis of chronic (or «long-term») health effects of air pollution



ETIOLOGICAL HYPOTHESIS

Chronic exposure to air pollution increases the risk of adverse events on the long run

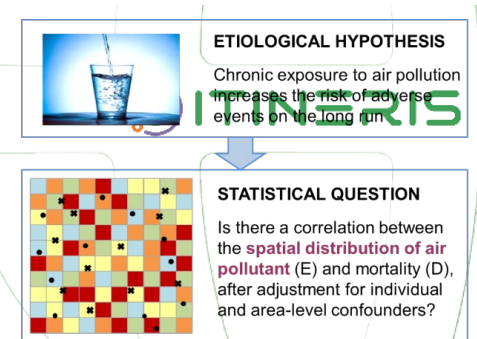


STATISTICAL QUESTION

Is there a correlation between the **spatial distribution of air pollutant** (E) and mortality (D), after adjustment for individual and area-level confounders?

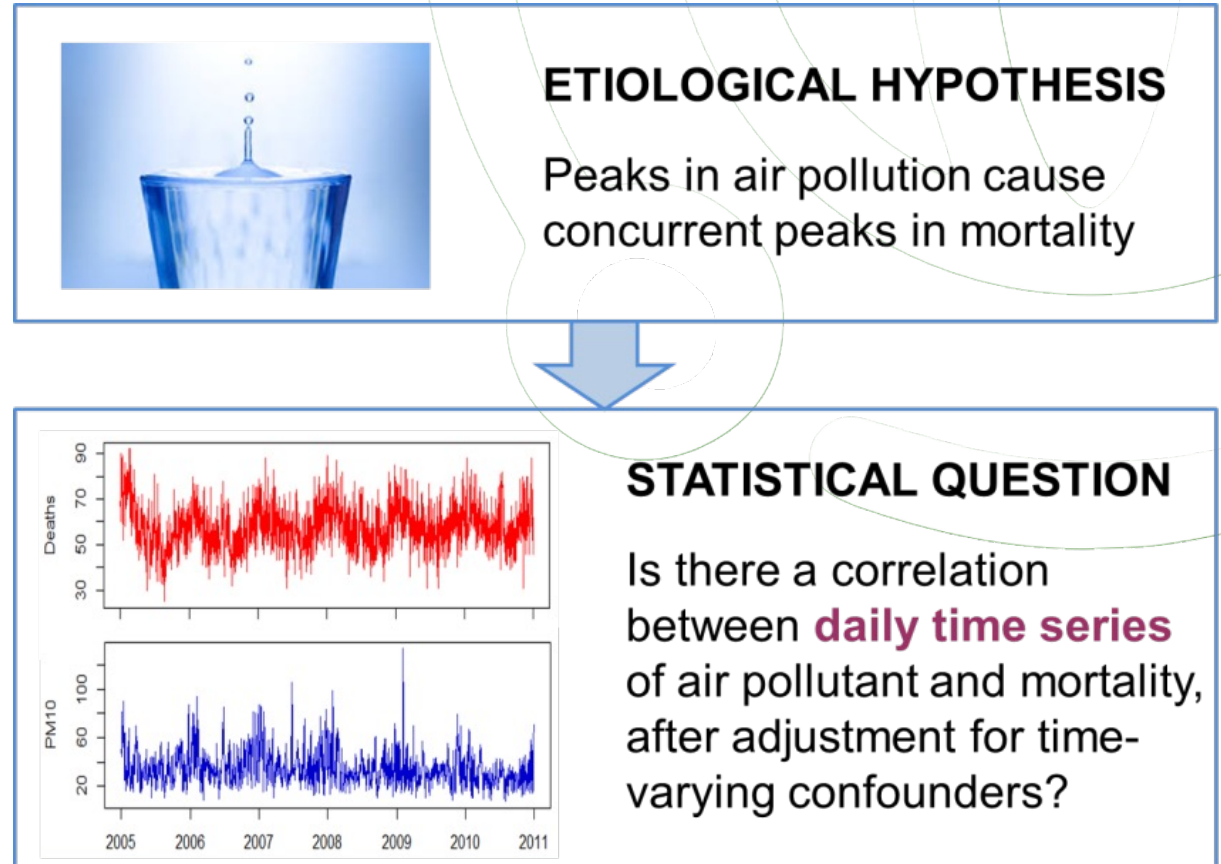
Chronic effects: examples

- Long-term exposure to air pollution and increase in mortality
- Chronic exposure to PM_{2.5} and carotid intima-media thickness (CIMT), a proxy for atherosclerosis
- Prolonged exposure to high temperatures during pregnancy and risk of preterm births
- Beneficial health effects of residing near green spaces
- etc. etc.



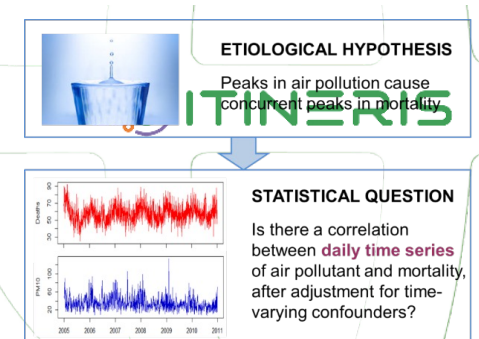
Short-term (or «acute») effects: a conceptual scheme

Conceptual scheme of the etiological hypothesis and the corresponding statistical question, at the basis of acute (or «short-term») health effects of air pollution



Acute effects: examples

- Daily peaks in air pollution increase daily mortality
- Hourly peaks in exposure to diesel exhaust increase heart rate variability
- Daily exposure to air pollutants and asthma hospitalizations among children
- Heat waves and increased mortality
- Acute exposure to high temperatures and risk of preterm births
- etc. etc.



Long-term effects: a tour of the literature and the ELAPSE project

The Framingham Heart Study



- Rates of heart disease and stroke exploded after World War II.
- To find out why, US public health authorities launched the Framingham Heart Study in 1948
- The Framingham Study identified the major risk factors for cardiovascular disease:
 - Cigarette smoking
 - Hypertension
 - High cholesterol
 - Sedentary life style
 - Diabetes

The Study has produced approximately 1,200 articles in leading medical journals

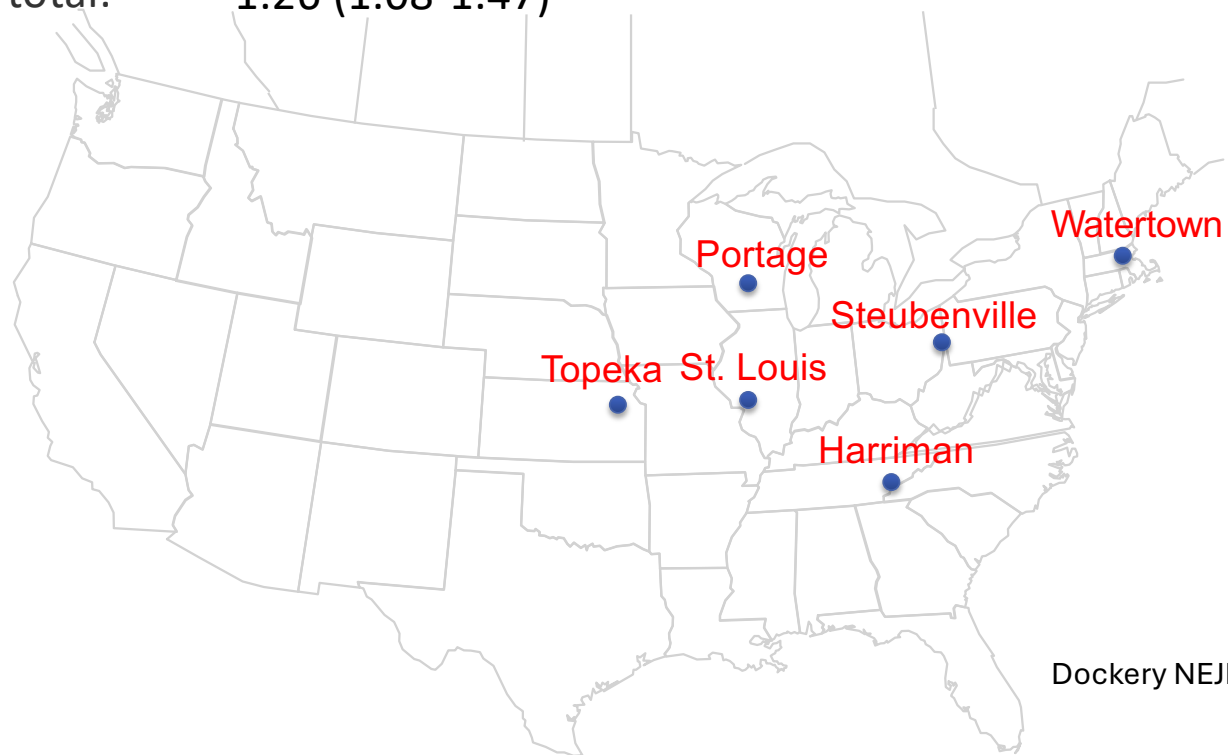
Harvard 6 cities study

Population: 8,111 adults followed 14-16 yrs

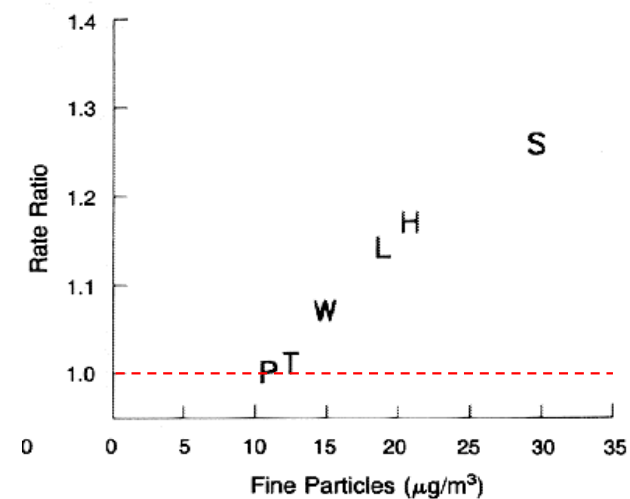
Exposure: Central monitor in each city

Comparison: Most polluted city vs. least

RR total: 1.26 (1.08-1.47)



Dockery NEJM 1993



Modern cohort studies (since the 70's)

1. National Health and Nutrition Examination Survey (NHANES)
2. Nurses' Health Study (NHS)
3. European Prospective study Incidence of Cancer (EPIC)
4. Seveso Cohort
5. Multicenter AIDS Cohort Study
6. American Cancer Society on air pollution (ACS)
7. Newborns cohorts (ALSPAC)
8. ...

Recent administrative cohorts (since 2000's)

- + Based on census data linked to health and pop. archives
- + Population-based
- + Very large (statistical power)
- + Detailed info on area-level vars.
- + Possibility to explore low levels
- Lack of details on individual-level covariates

EXAMPLES

1. Norwegian cohort
2. SIMSAN (Sweden)
3. Danish cohort
4. Dutch cohort
5. English cohort
6. Swiss cohort
7. Rome Longitudinal Study
8. Medicare cohort (USA)
9. CanCHEC (Canada)
10. New Zealand
11. ...

HEI CALL

14-3 Assessing Health Effects of Long-term Exposure to Low Levels of Ambient Air Pollution



Average PM_{2.5} levels:
15 µg/m³ (Europe)
11 µg/m³ (U.S.A.)
7 µg/m³ (Canada)

The ELAPSE project

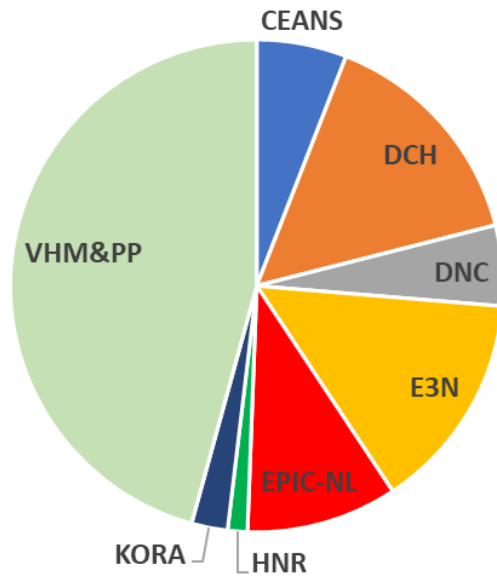


Utrecht University

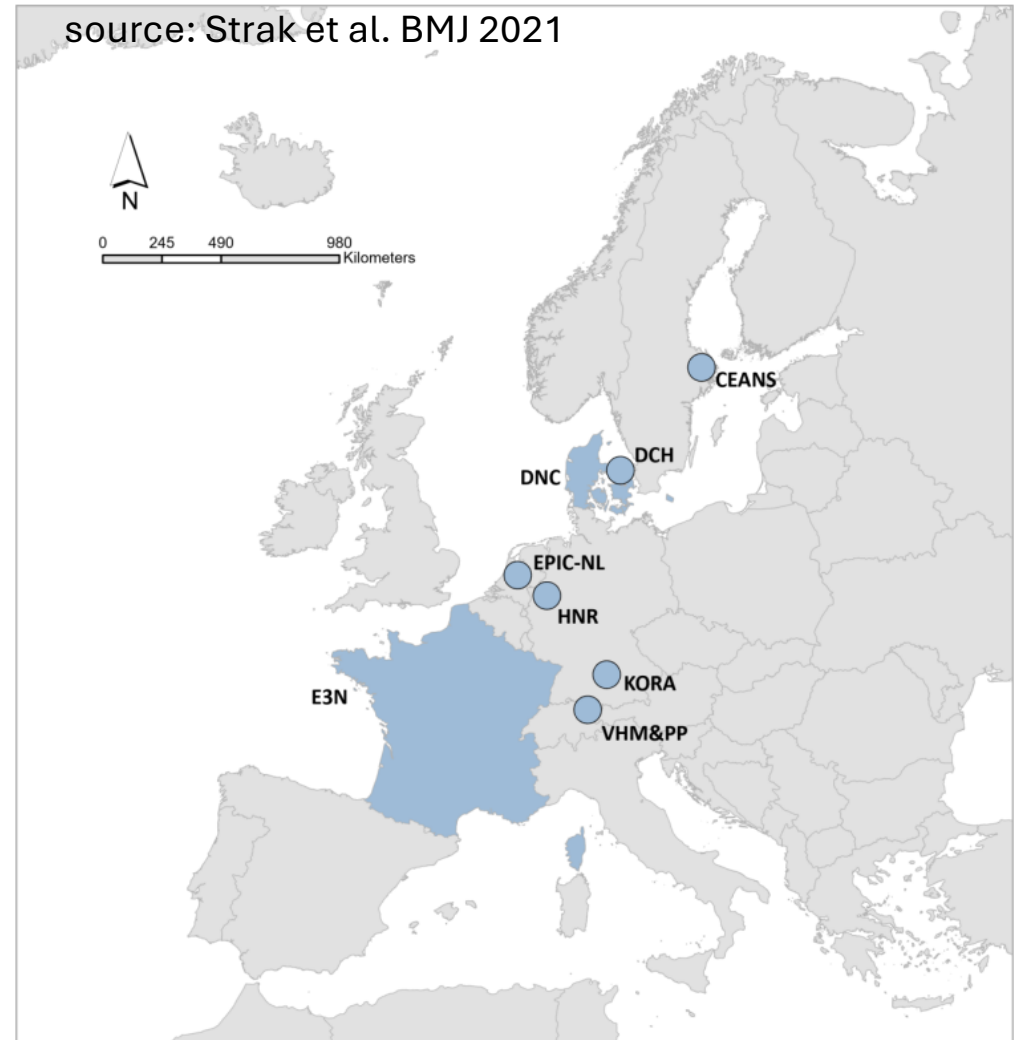
ELAPSE Effects of Low-Level Air Pollution: A Study in Europe

- Background: Associations between air pollution and health have been observed at **low concentrations**
- Objectives: Investigate associations between long-term exposure to PM_{2.5}, NO₂, O₃, BC and:
 - Natural and cause-specific mortality
 - Incidence of lung cancer and cardiovascular events

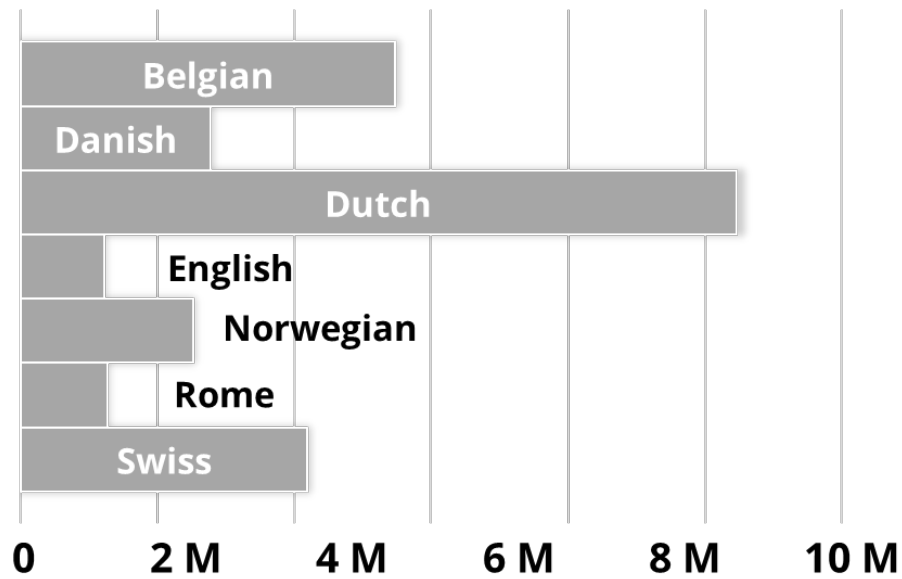
Pooled cohort



- N = 325,367 (complete data),
P-Y = 6,339,553, Deaths = 47,131
- Extensive covariate information: age, sex, smoking, BMI, marital status, employment, area-level income



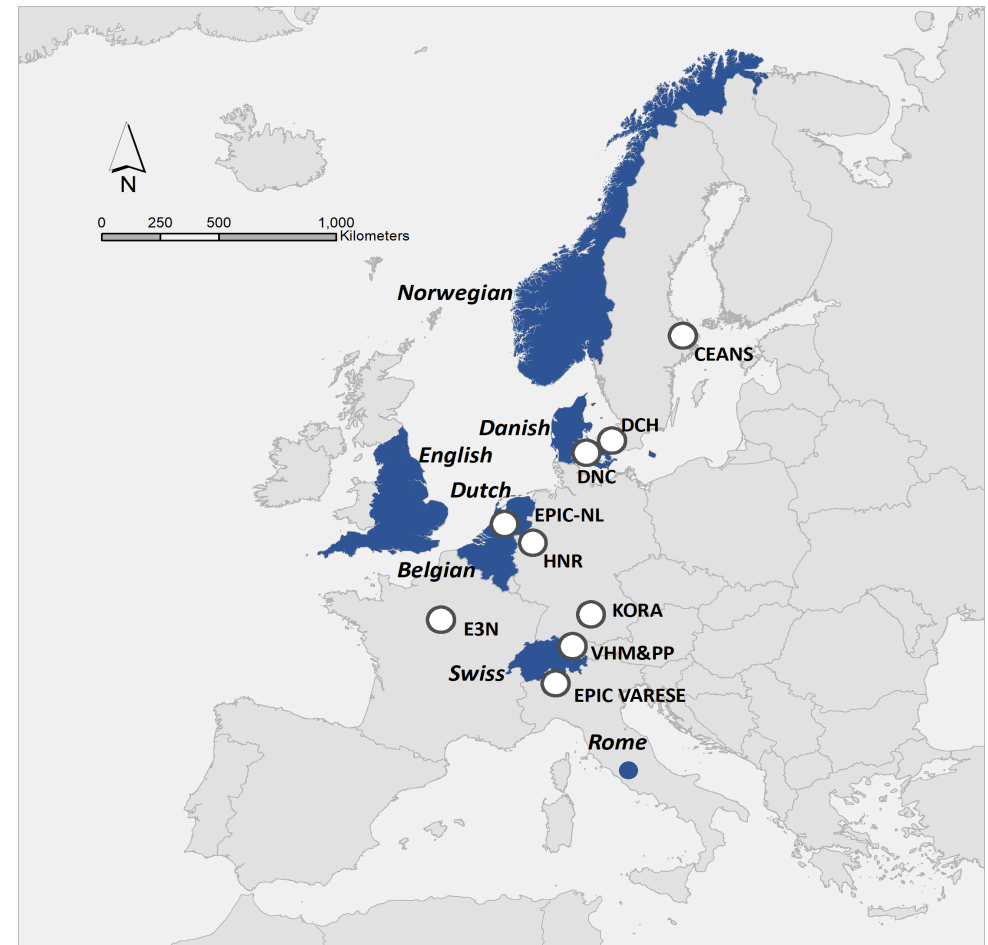
Administrative cohorts



N = 28,153,138 (complete data)

- Limited covariate info (except English)
- Analyzed individually -> Meta-analysis

source: Stafoggia et al. Lancet Planetary Health 2022



Administrative cohorts

Cohort-specific descriptives (source: Stafoggia et al. Lancet Planetary Health 2022)

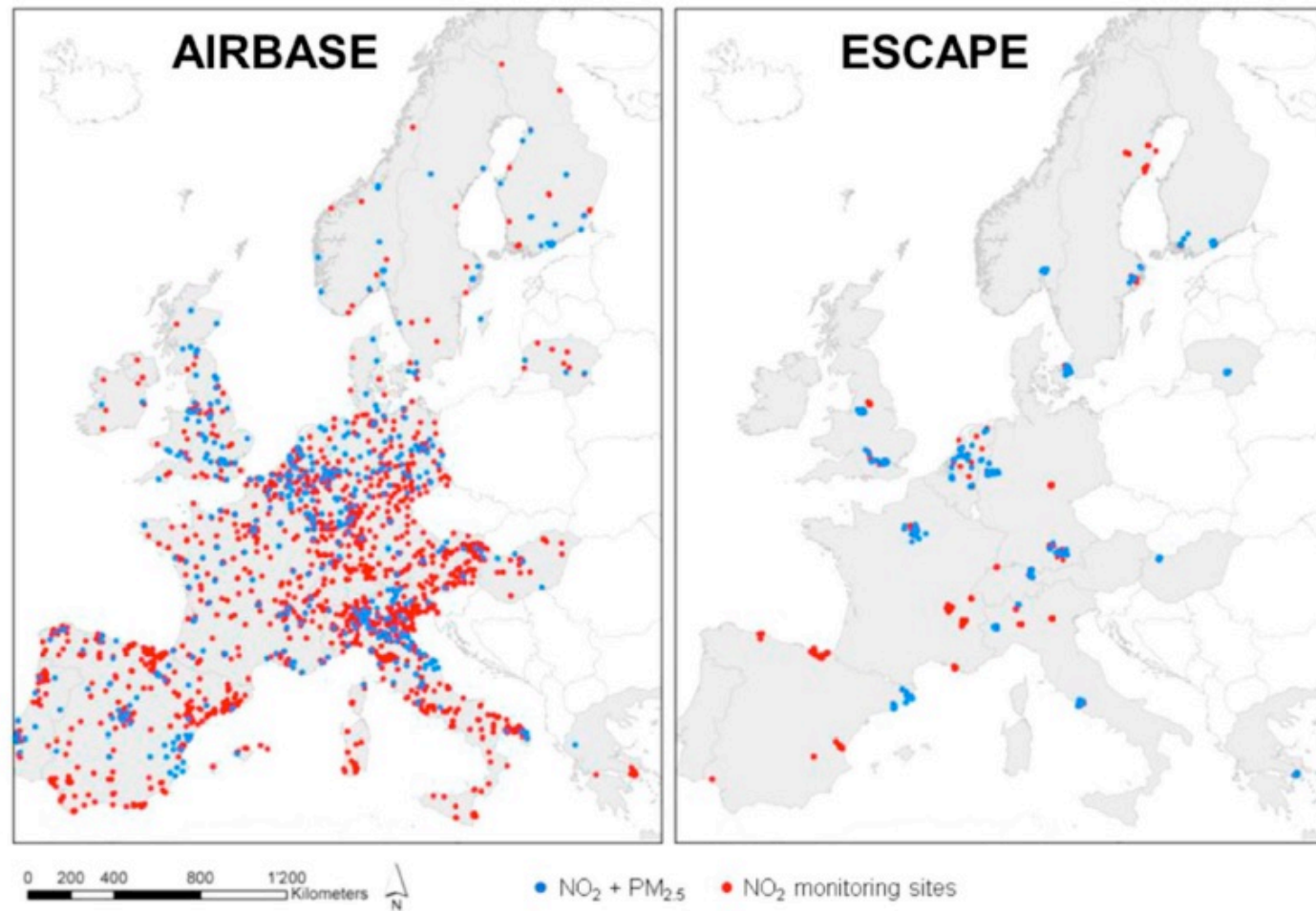
Covariates	Belgian cohort	Danish cohort	Dutch cohort	English cohort	Norwegian cohort	Roman cohort	Swiss cohort
Individual-level							
Age	✓	✓	✓	✓	✓	✓	✓
Sex	✓	✓	✓	✓	✓	✓	✓
Country origin	✓	✓	✓				✓
Mother tongue							✓
Marital status	✓	✓	✓		✓	✓	✓
Education level	✓				✓	✓	✓
Occupation status	✓	✓			✓	✓	✓
Household income		✓	✓		✓		
Smoking status				✓			
BMI				✓			
Area-level							
Income	✓	✓	✓		✓	✓	
Education	✓	✓			✓	✓	✓
Unemployment rate	✓	✓	✓		✓	✓	✓
Non western ethnic	✓		✓				
SES score			✓	✓		✓	✓

N = 28,153,138

Deaths = 3,593,741

P-years = 257,859,621

Air pollution exposure



Air pollution exposure

source: de Hoogh et al. *EnvInt* 2018

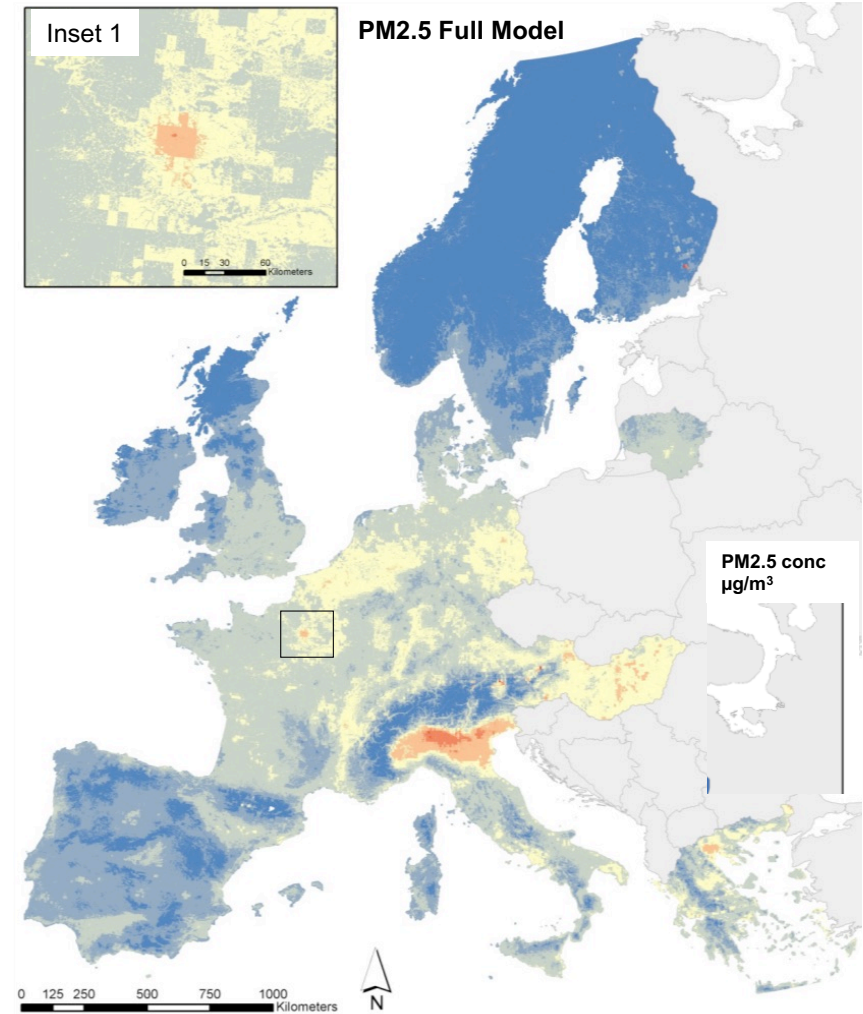
Central exposure assessment

Europe-wide hybrid land use regression models
(100x100 m)

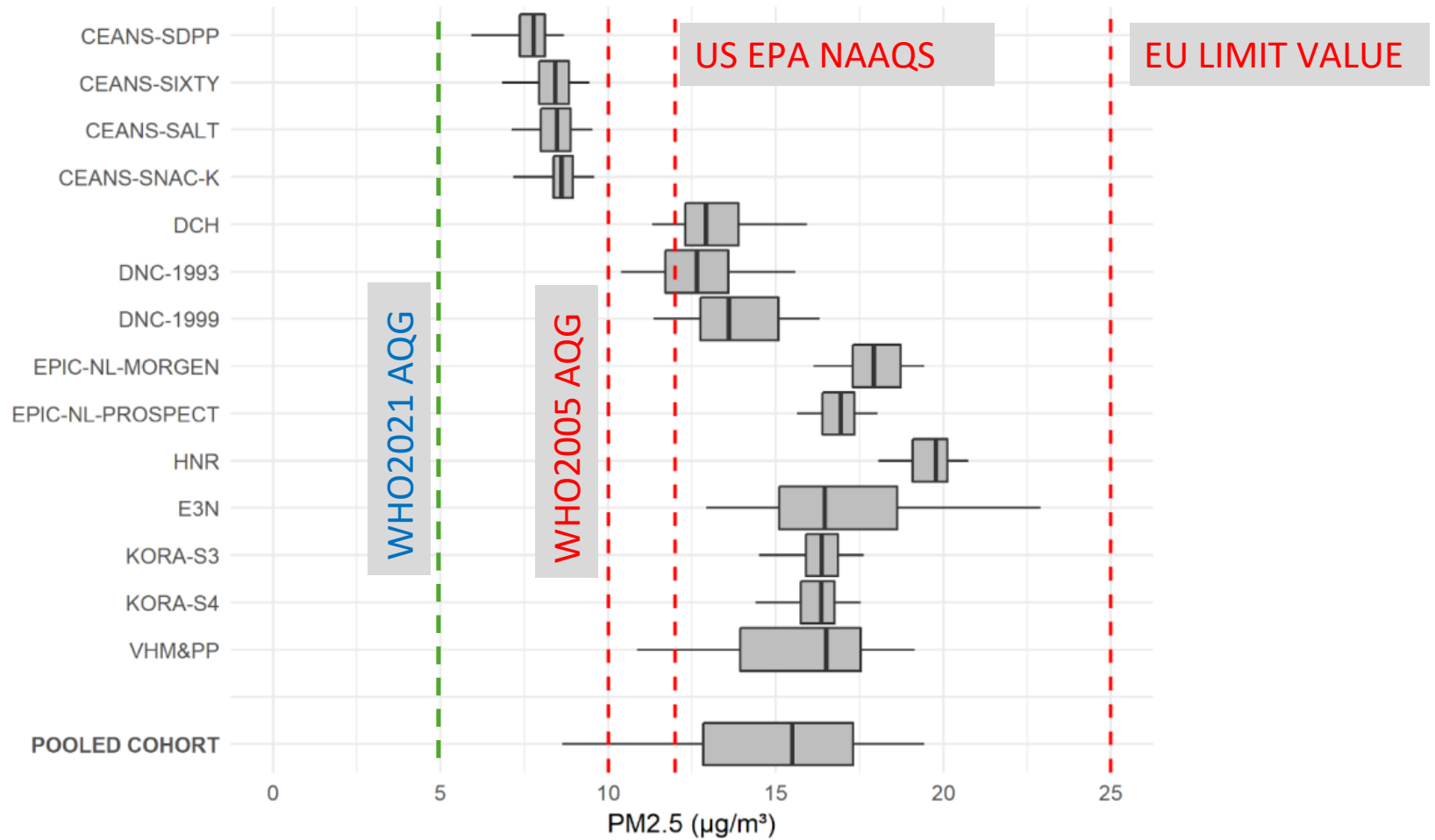
Land use and road data, with satellite observations
and dispersion model estimates as additional
predictors

Local exposure models

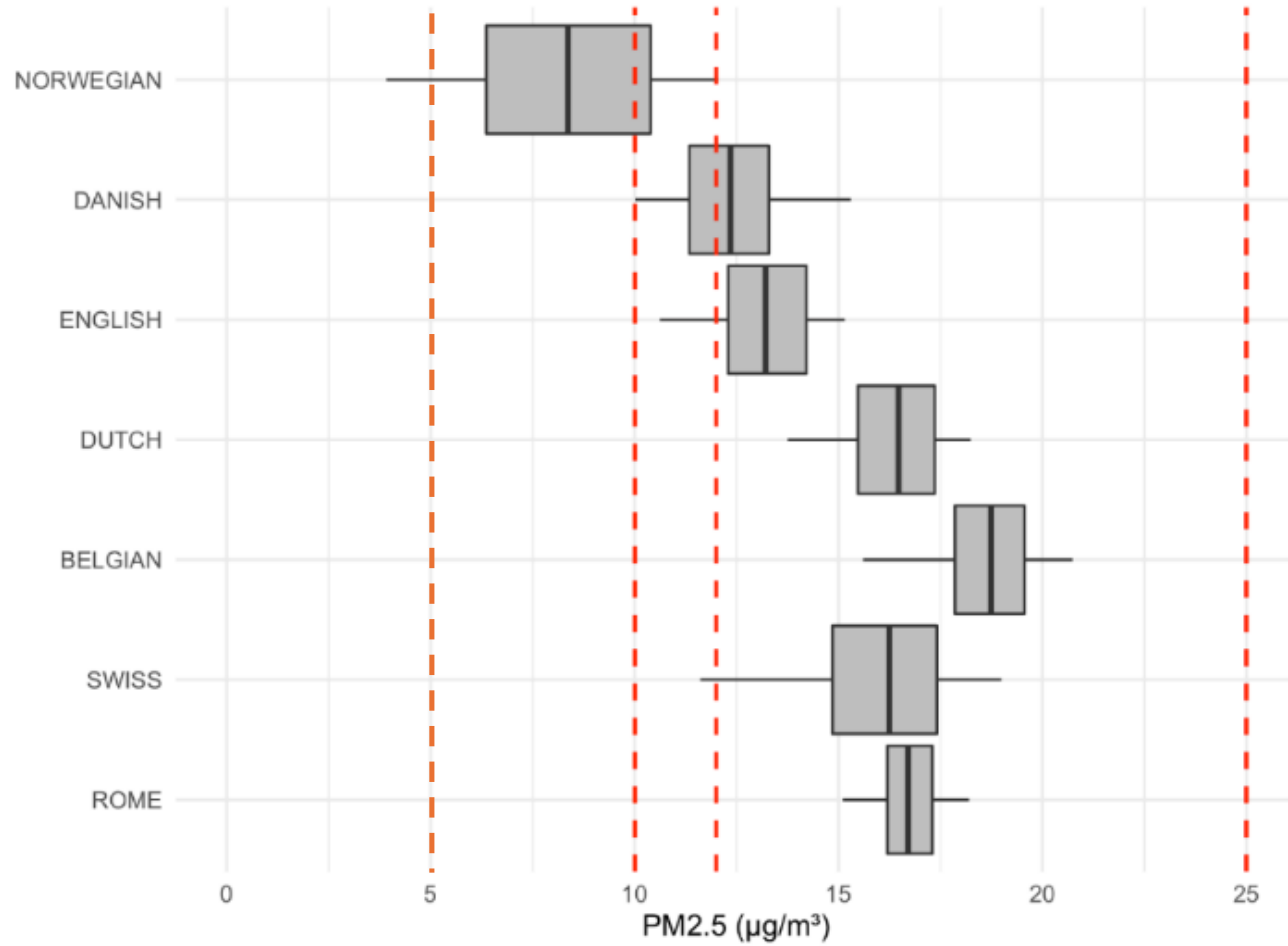
Existing LUR and/or dispersion models



PM_{2.5} in the pooled cohort



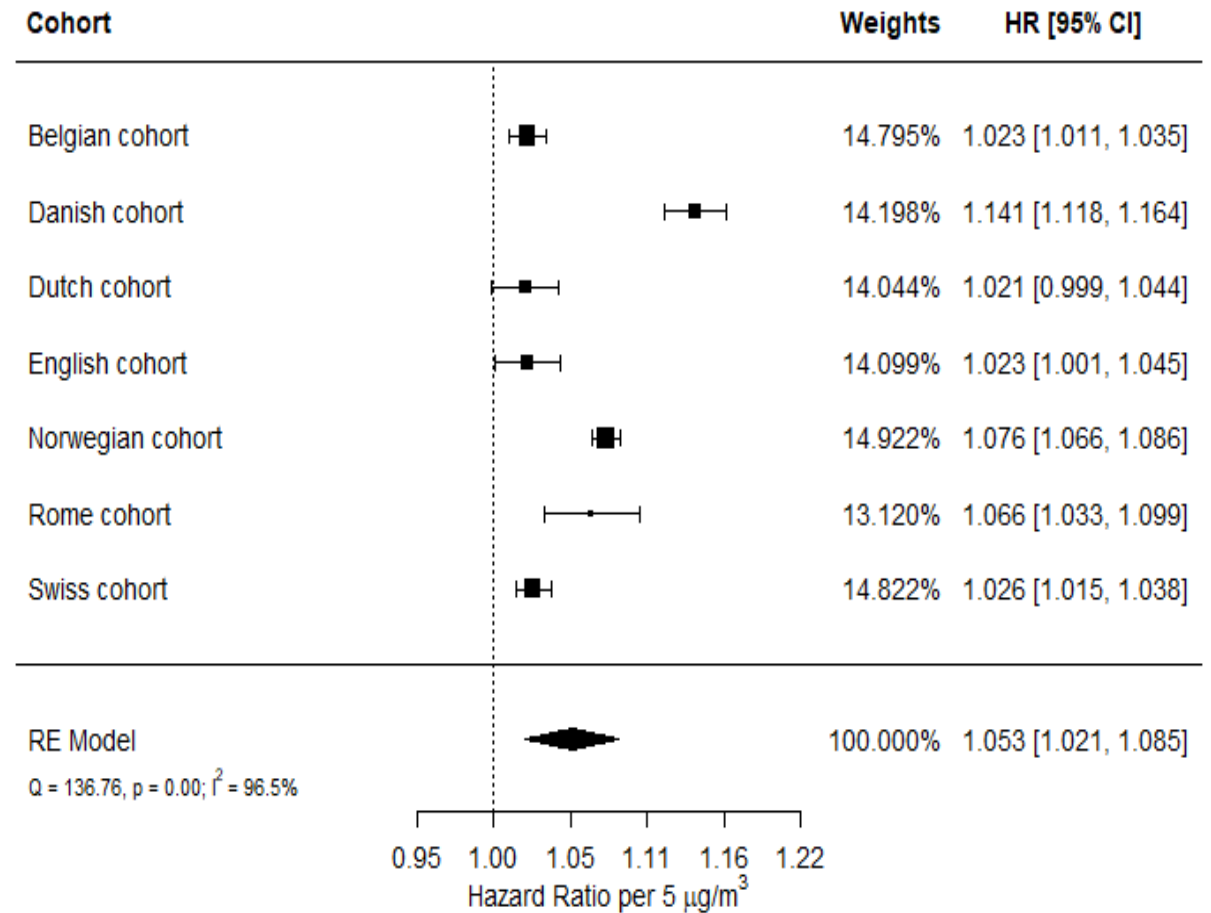
PM_{2.5} in the administrative cohorts



Linear effects

Association between PM_{2.5} and natural-cause mortality:

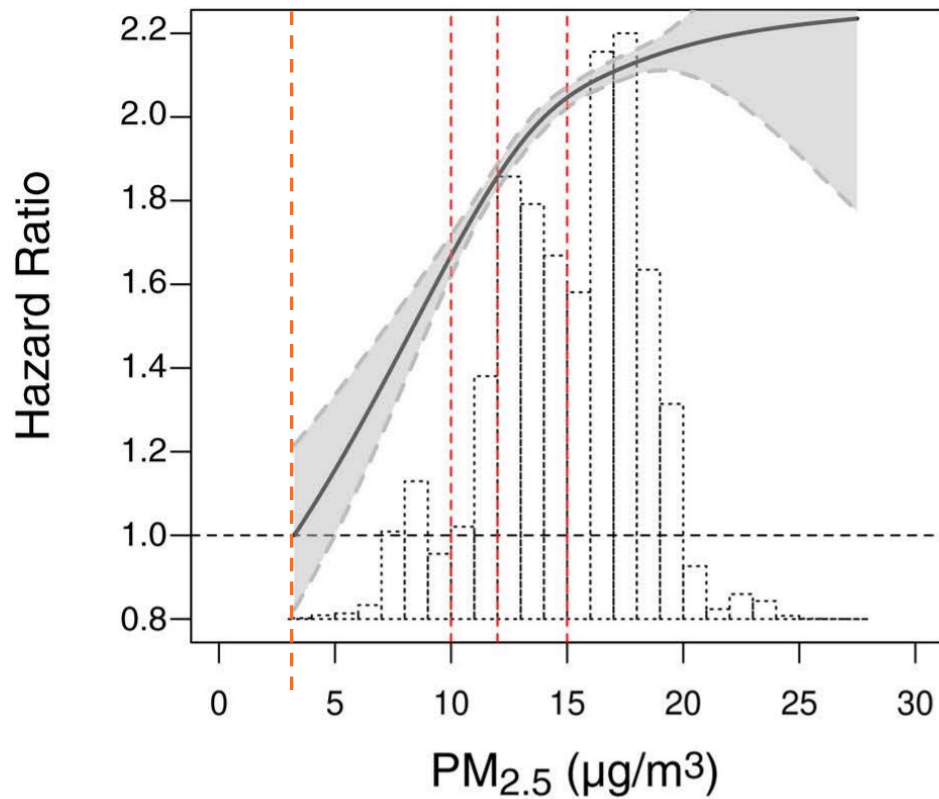
Cohort-specific effects in the administrative cohorts



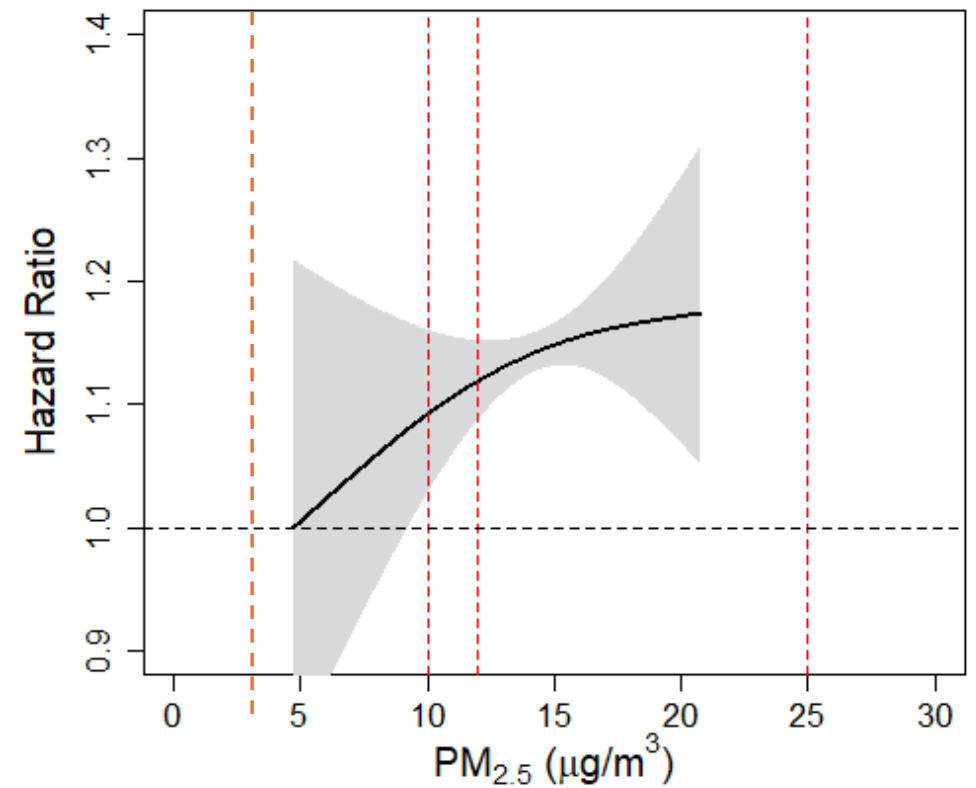
Non-linear effects

PM_{2.5} and natural-cause mortality: HR and 95% CI per increasing PM_{2.5}

Pooled cohort

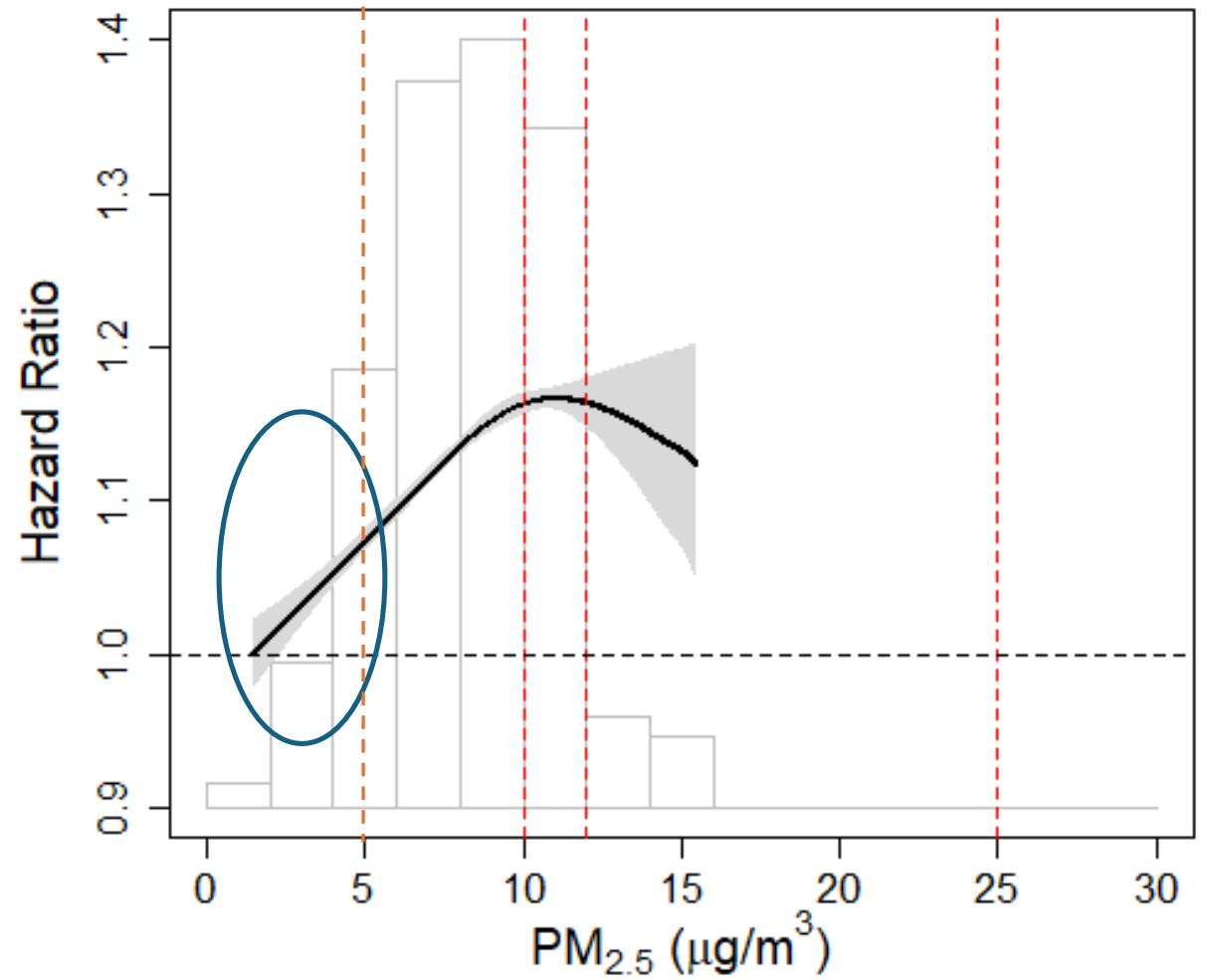


Administrative cohorts



Non-linear effects

Results of the Norwegian cohort



Short-term effects: an historical perspective

An historical overview: first studies on peaks

Meuse Valley ('30s).

1930 Meuse Valley fog

 4 languages ▼

Article Talk

Read Edit View history Tools ▼

From Wikipedia, the free encyclopedia

The **1930 Meuse Valley fog** between December 1st and December 5th, killed 63 people in Belgium owing to a combination of industrial [air pollution](#) and a localized weather inversion.

The River [Meuse](#) flows from [France](#) through [Belgium](#) and the [Netherlands](#) before entering the [North Sea](#). The area in the Meuse Valley where the incident occurred, between the cities of [Huy](#) and [Liege](#) and centered around the town of [Engis](#), was densely populated and had 27 factories. These factories produced zinc, steel, fertilizer, and explosives, amongst many other products. This was added to by large numbers of coal and wood heaters burning due to unseasonably cold weather. There were several thousand cases of illness over the week and the sixty three deaths occurred at the same time, with the first death occurring on December 3rd. Fifty-six of the deaths were to the east of [Engis](#).^[1]

The main symptom was [dyspnea](#) (shortness of breath)^[1] and the average age of those who died was 62, over a range of ages of 20 to 89 years. The youngest, a 20 year old woman named Louise Dammes, died walking home from a party and may have had undiagnosed asthma that contributed to her death. ^[2] Cattle in the area were also affected.^[3] [Kaj Roholm](#), Danish scientist and the world's leading authority on fluorine, determined that it was the [fluorine](#) gas from the nearby factories that was the killer.^[1] The exact date of this disaster is unknown. A statue and plaque commemorating those who died were inaugurated in Engis on 2 December 2000.^[2]

Due to a similar(albeit less severe) incident that occurred in a nearby valley in 1911 that killed off many cattle, many farmers in the Meuse Valley fled to the hillside during the first two days of the smog, reducing livestock casualties and likely saving the lives of several farmers as well.



An historical overview: first studies on peaks

Donora ('40s)...

Donora smog

updated Nov 30, 2010 by Steven Gilbert

TXP-2

Overview

The 1948 Donora smog was a historic air inversion resulting in a wall of smog that killed 20 people and sickened 7,000 more in Donora, Pennsylvania, a mill town on the Monongahela River, 24 miles southeast of Pittsburgh.



Toxicological Perspective

The smog first rolled into Donora on [October 27, 1948](#). By the following day it was causing coughing and other signs of respiratory distress for many residents of the community in the Monongahela River valley. Many of the illnesses and deaths were initially attributed to asthma. The smog continued until it rained on October 31, by which time 20 residents of Donora had died and approximately a third to one half of the town's population of 14,000 residents had been sickened. Sixty years later, the incident was described by [The New York Times](#) as "one of the worst air pollution disasters in the nation's history". Even ten years after the incident, mortality rates in Donora were significantly higher than those in other communities nearby.

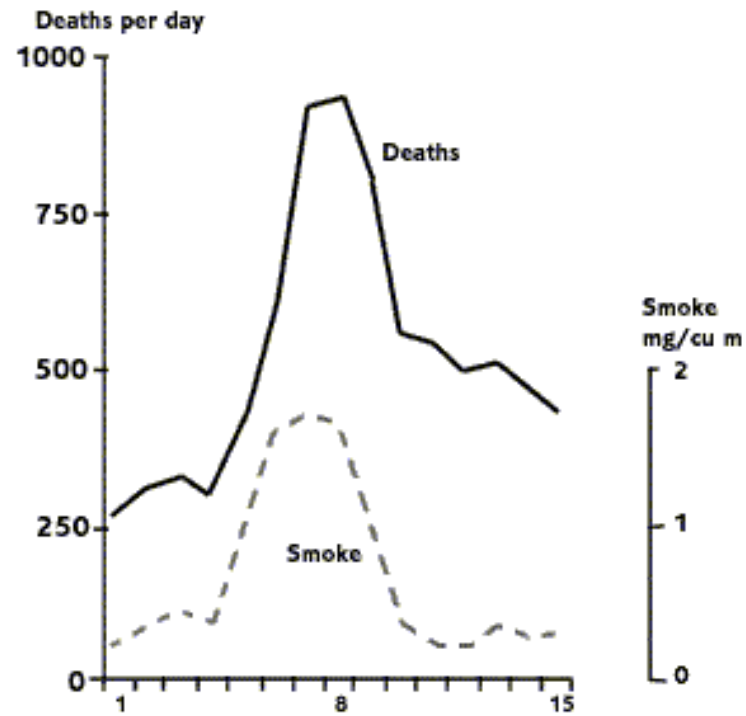
Causes

Sulfur dioxide emissions from U.S. Steel's Donora Zinc Works and its American Steel & Wire plant were frequent occurrences in Donora. What made the 1948 event more severe was a temperature inversion, in which a mass of warm, stagnant air was trapped in the valley, the pollutants in the air mixing with fog to form a thick, yellowish, acrid smog that hung over Donora for five days. The



An historical overview: first studies on peaks

... and London ('50s)



Logan WP. Mortality in the London fog incident, 1952. Lancet. 1953 Feb 14;1(6755):336-8.



End 70's: still doubts on the effects at low levels

Am J Epidemiol. 1979 Nov;110(5):527-659.

Health effects of particulate pollution: reappraising the evidence.

Holland WW, Bennett AE, Cameron IR, Florey CV, Leeder SR, Schilling RS, Swan AV, Waller RE.

concluded that «there was not compelling evidence of substantive health effects at low-to-moderate particulate pollution levels»

ACKNOWLEDGMENTS

This work has been supported by a grant from the American Iron and Steel Institute. The full report of *Health Effects of Particulate Pollution. Reappraising the Evidence* includes a chapter on Toxicological Studies, a Commentary on Major Reviews on Health Effects of Pollution, and a full alphabetical bibliography of all work referred to.

80's: first study on the effects at low concentrations

A Search for a Threshold in the Relationship of Air Pollution to Mortality: A Reanalysis of Data on London Winters

by **Bart Ostro***

To control for the influence of weather factors and test for the existence of a threshold level, a regression of the form (1) is used:

$$DM_t = a_0 + a_1B_{1t} + a_2B_{2t} + a_3T_t + a_4H_t \quad (1)$$

where DM = deviations in daily mortality from a 15-day moving average; B^* = hypothesized NOEL; B_1 = British Smoke (BS) for $BS \leq B^*$, and = B^* for $BS > B^*$; B_2 = $BS - B^*$ for $BS > B^*$, and = 0 otherwise; T = daily average temperature; H = relative humidity; t = day of the winter. A NOEL level of BS-150 $\mu\text{g}/\text{m}^3$ was hypothesized. Particular attention was given to the London winters of 1965-66 through 1971-72, to eliminate the possibility of an extreme episode ($BS > 500 \mu\text{g}/\text{m}^3$) affecting the results.

The results of this analysis for the nonepisodic winters of 1965-66 through 1971-72 indicate that **the statistically significant relationship between BS and deviations in daily mortality is not due to the high end values of an atypical winter** (1958-59).

Rather, this analysis of the data suggests that the **lower values of BS are associated significantly with deviations in mortality** in years when there are no BS values above 500 $\mu\text{g}/\text{m}^3$.

Further, for the data set as a whole, there is no evidence to support a no-observed-effects level at $BS = 150 \mu\text{g}/\text{m}^3$.

1990: first time-series study

Am J Epidemiol. 1990 Jan;131(1):185-94.

Mortality and air pollution in London: a time series analysis.

Schwartz J, Marcus A.

Environmental Protection Agency, Washington, DC 20460.

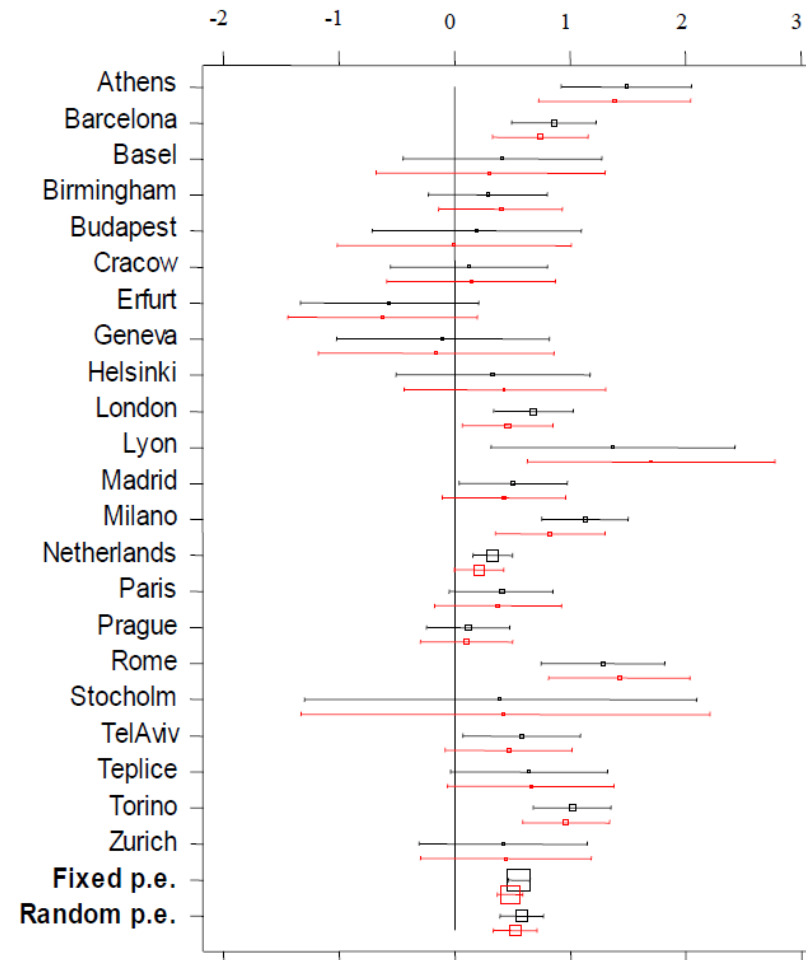
Abstract

The relation between air pollution and mortality in London was examined for the winters of 1958–1972. The data exhibited a high degree of autocorrelation, requiring analyses using autoregressive models. **There was a highly significant relation between mortality and either particulate matter or sulfur dioxide (after controlling for temperature and humidity), both overall and in each individual year. Graphic analysis revealed a nonlinear relation with no threshold, and a steeper exposure–response curve at lower air pollution levels.** In models with both pollutants, particulate matter remained a significant predictor with about a 10% reduction in its estimated coefficients, while sulfur dioxide was insignificant, with a large drop in its estimated coefficient. **The authors conclude that particulates are strongly associated with mortality rates in London, and the relation is likely causal**

End 90's: first multi-center studies: APHEA...

Percent increase in total mortality and 95% CIs associated with an increase of $10\mu\text{g}/\text{m}^3$ in PM10 using loess (upper) and p-splines (lower)

Katsouyanni K, et al. Short-term effects of air pollution on health: a European approach using epidemiologic time series data. The APHEA Project. Air Pollution Health Effects--A European Approach. Public Health Rev. 1997;25(1):7-18; discussion 19-28



... and NMMAPPS (2000)

The New England Journal of Medicine

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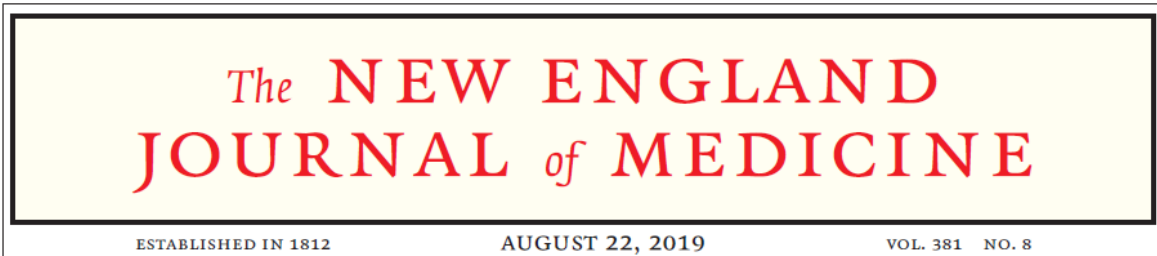
NUMBER 24



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

JONATHAN M. SAMET, M.D., FRANCESCA DOMINICI, PH.D., FRANK C. CURRIERO, PH.D., IVAN COURSAK, M.S.,
AND SCOTT L. ZEGER, PH.D.

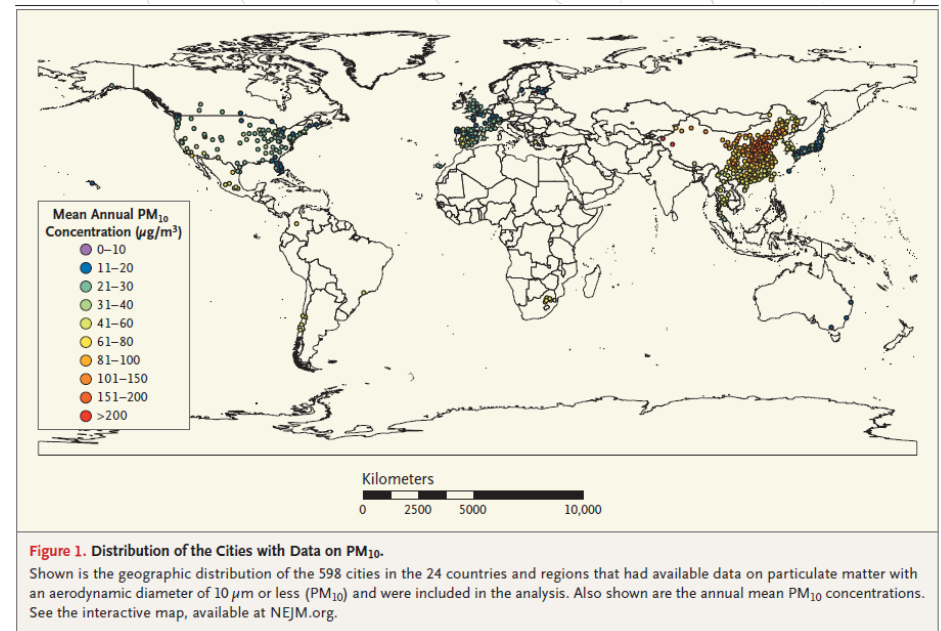
Recently, the MCC network



Ambient Particulate Air Pollution and Daily Mortality in 652 Cities

C. Liu, R. Chen, F. Sera, A.M. Vicedo-Cabrera, Y. Guo, S. Tong, M.S.Z.S. Coelho, P.H.N. Saldiva, E. Lavigne, P. Matus, N. Valdes Ortega, S. Osorio Garcia, M. Pascal, M. Stafoggia, M. Scortichini, M. Hashizume, Y. Honda, M. Hurtado-Díaz, J. Cruz, B. Nunes, J.P. Teixeira, H. Kim, A. Tobias, C. Íñiguez, B. Forsberg, C. Åström, M.S. Ragettli, Y.-L. Guo, B.-Y. Chen, M.L. Bell, C.Y. Wright, N. Scovronick, R.M. Garland, A. Milojevic, J. Kyselý, A. Urban, H. Orru, E. Indermitte, J.J.K. Jaakkola, N.R.I. Rytí, K. Katsouyanni, A. Analitis, A. Zanobetti, J. Schwartz, J. Chen, T. Wu, A. Cohen, A. Gasparini, and H. Kan

ABSTRACT



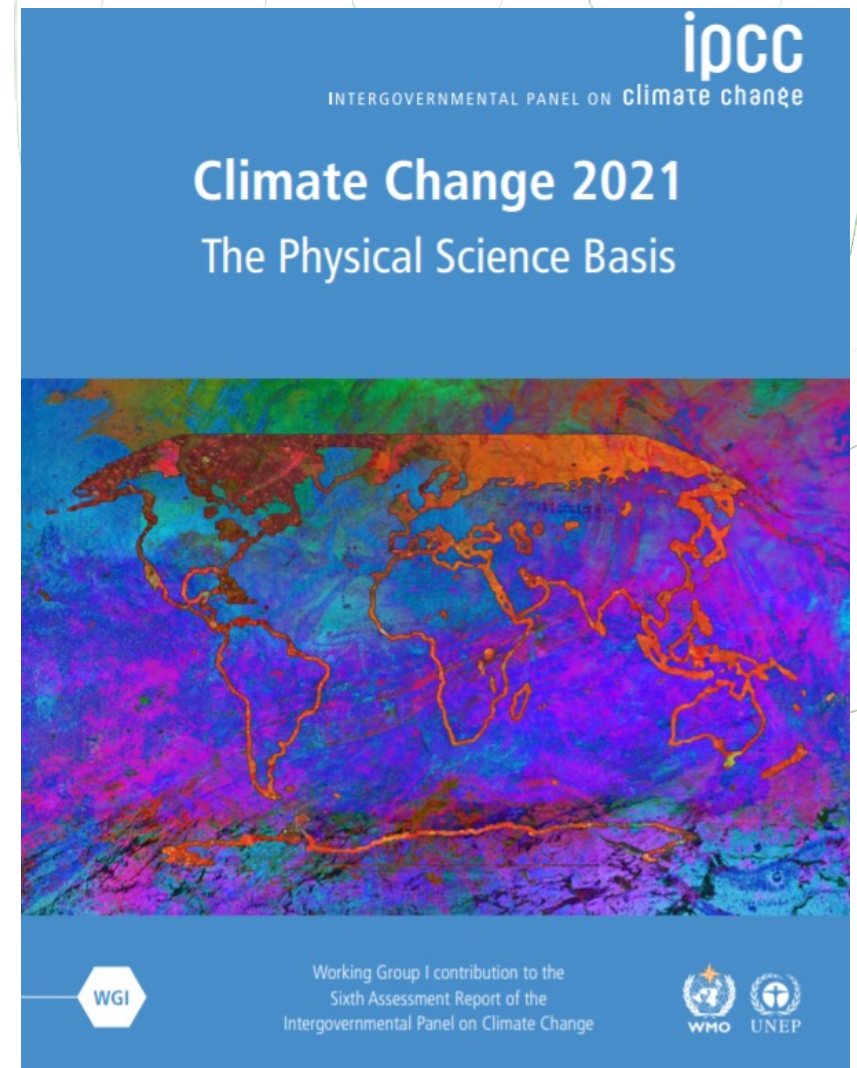
Short-term effects of extreme temperatures: an overview

Climate change

“It is unequivocal that human influence has warmed the atmosphere, ocean and land. Widespread and rapid changes in the atmosphere, ocean, cryosphere and biosphere have occurred.

Evidence of observed changes in extremes such as heatwaves, heavy precipitation, droughts, and tropical cyclones, and, in particular, **their attribution to human influence, has strengthened since the Fifth Assessment Report**”

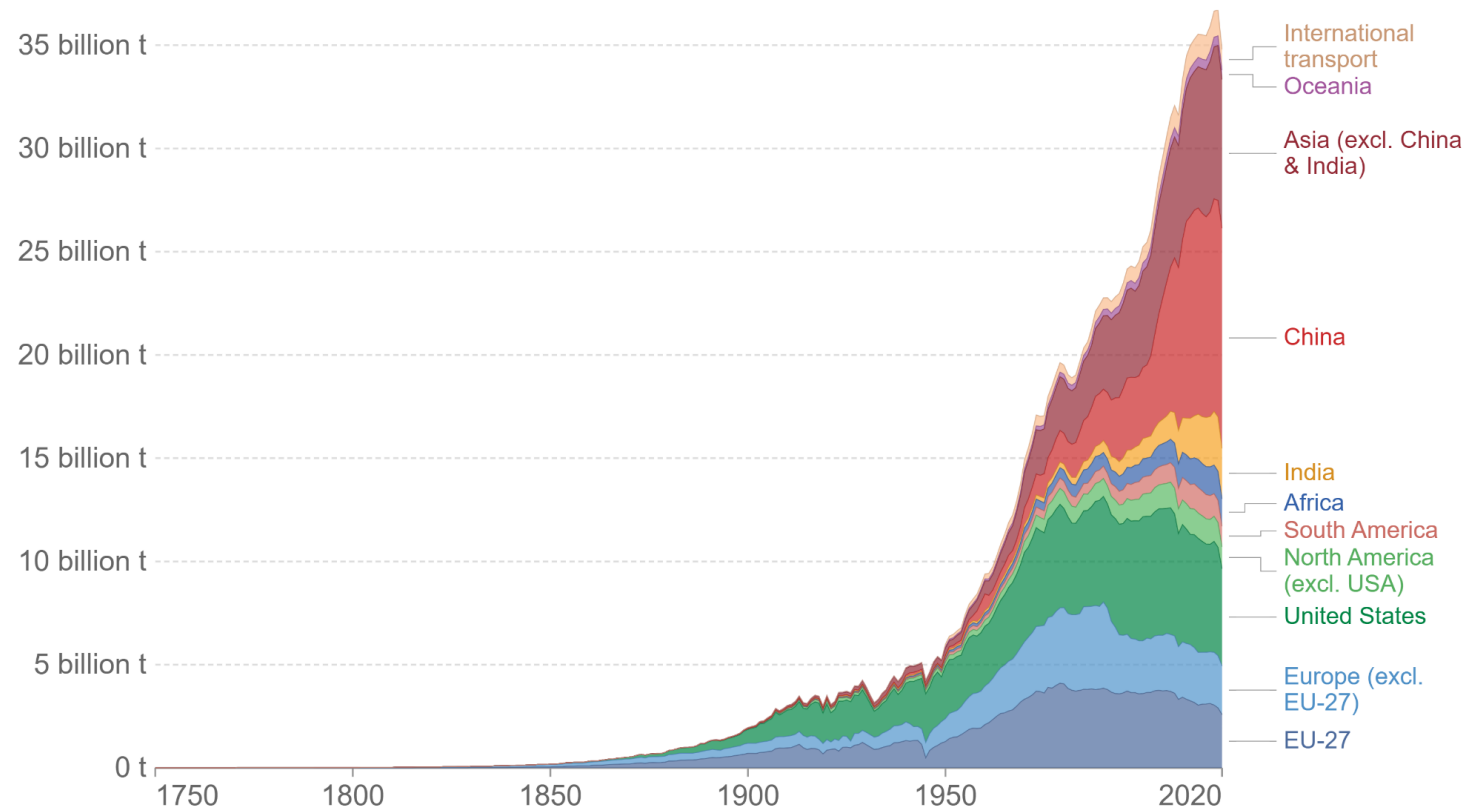
IPCC WG1 6th Report, 2021



Global emissions

Annual CO₂ emissions from fossil fuels, by world region

Our World
in Data



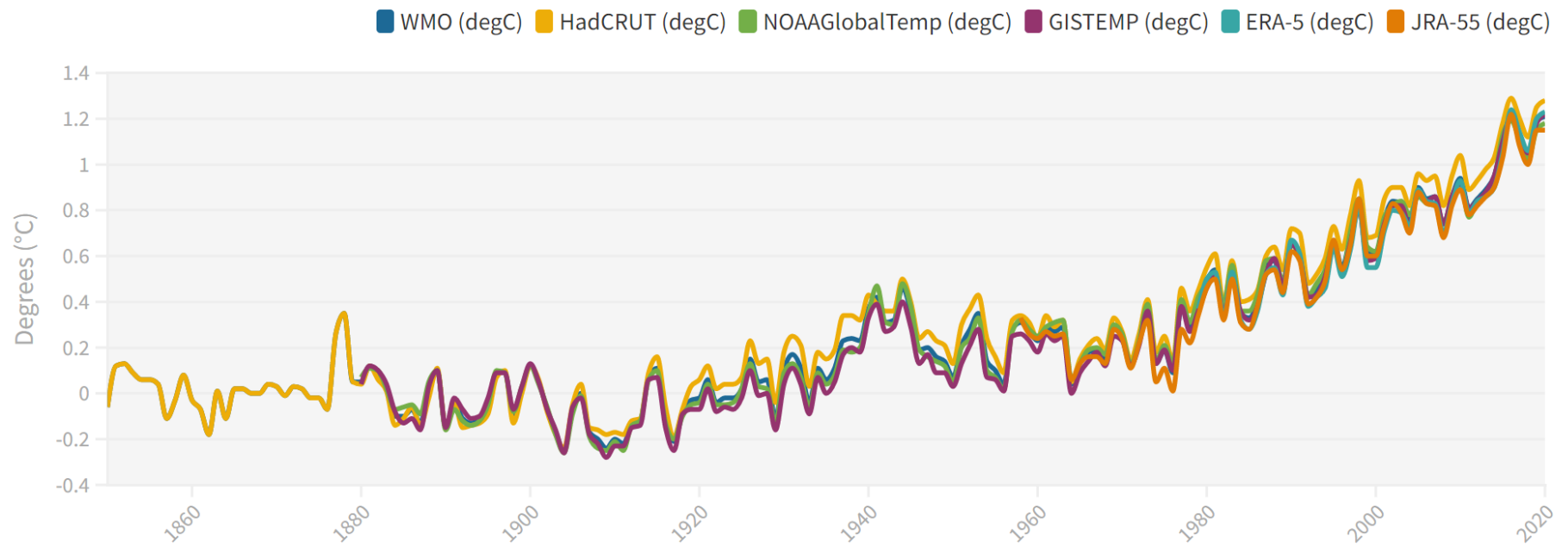
Source: Global Carbon Project

OurWorldInData.org/co2-and-other-greenhouse-gas-emissions • CC BY

Note: This measures CO₂ emissions from fossil fuels and cement production only – land use change is not included. 'Statistical differences' (included in the GCP dataset) are not included here.

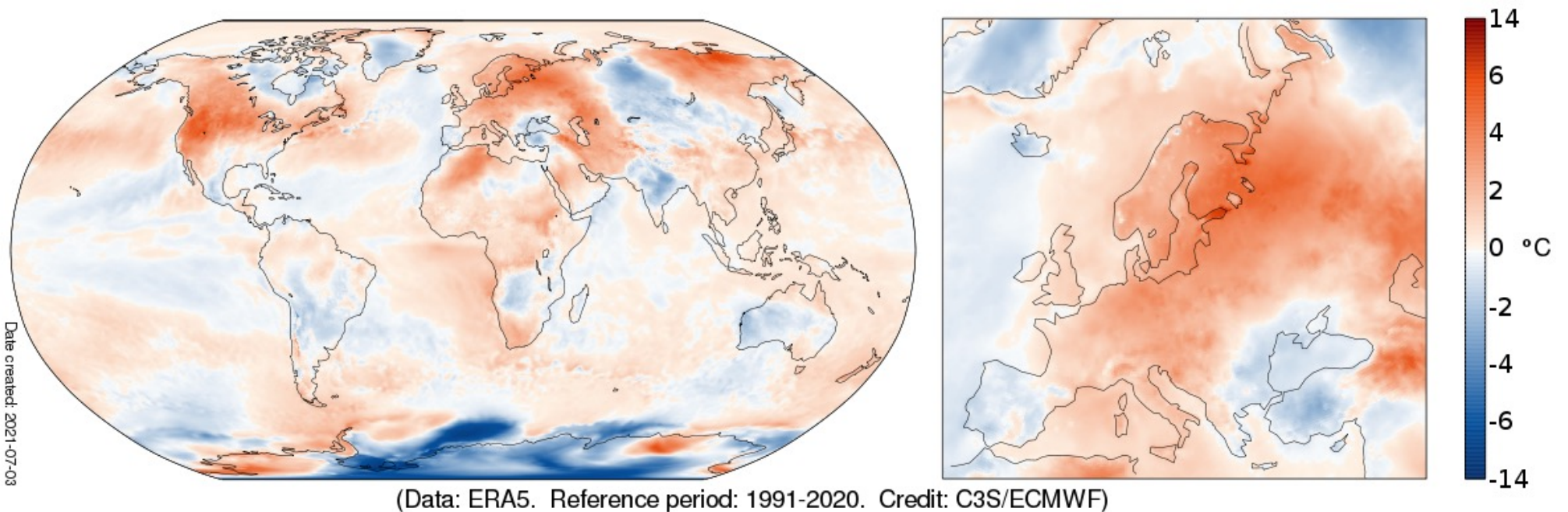
Global temperature anomalies

Temperature Difference from Pre-industrial Conditions
1850-2020

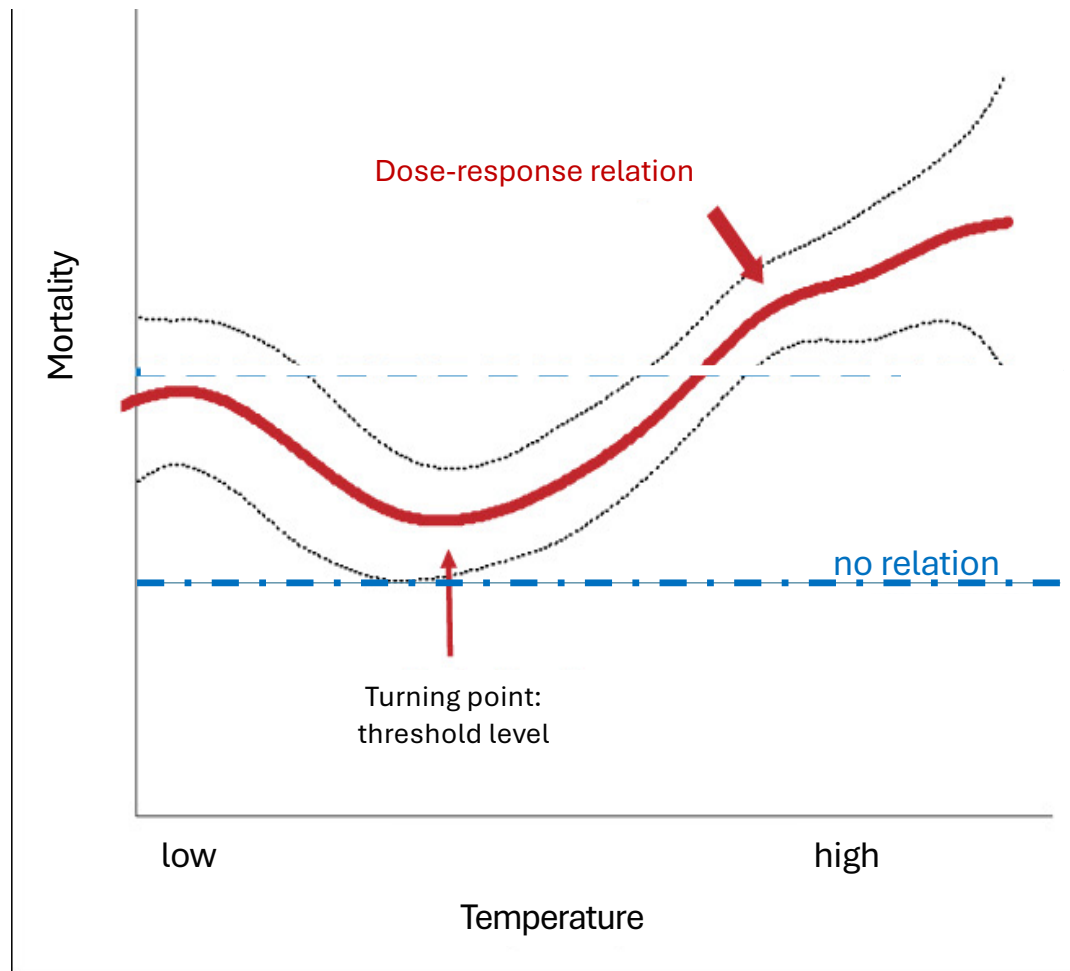


Geographical differences. Observed change in surface temperature June 2021 compared to reference period

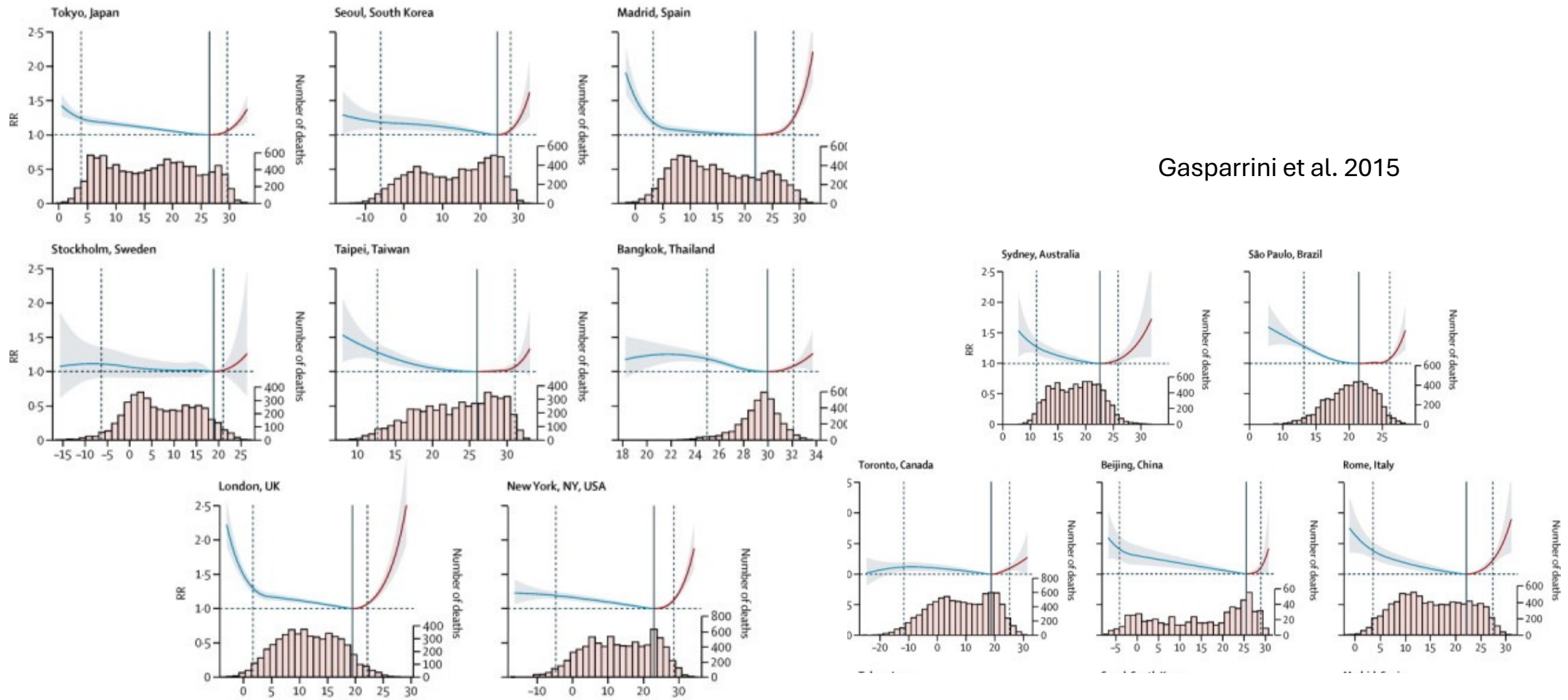
Surface air temperature anomaly for June 2021



Dose-response curve for temperature and mortality

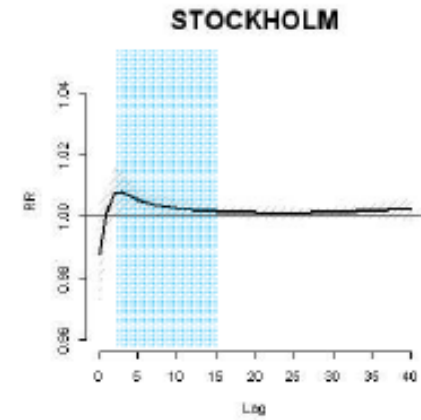
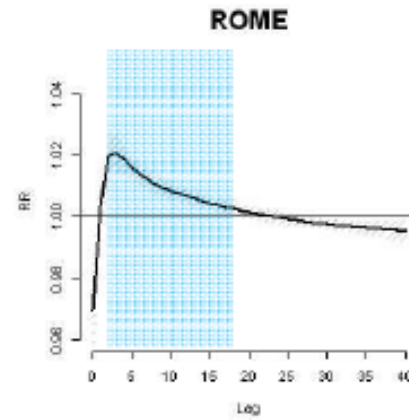
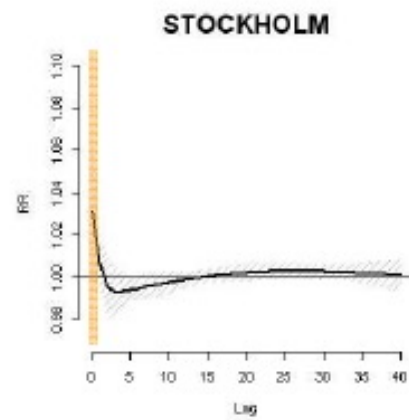
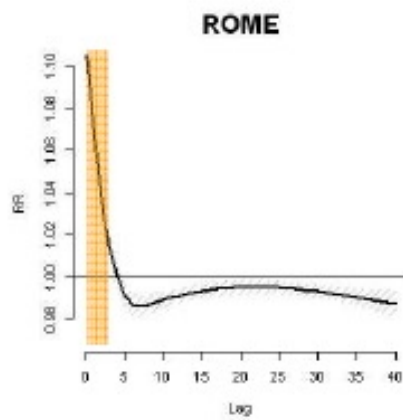
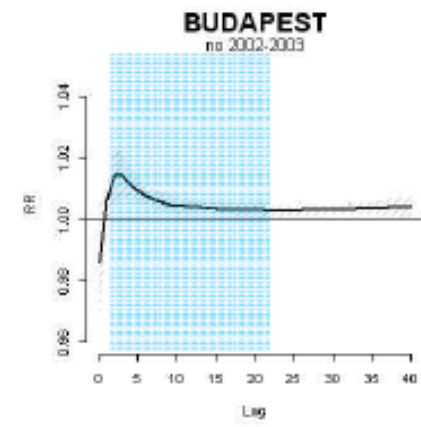
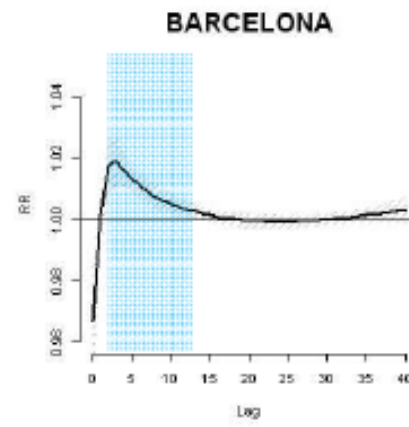
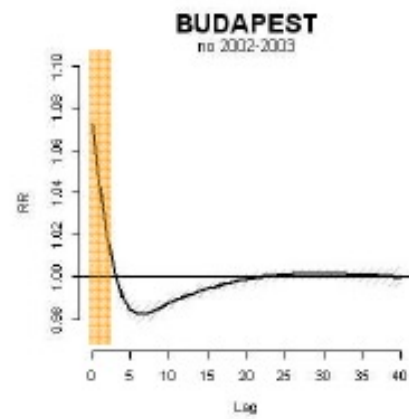
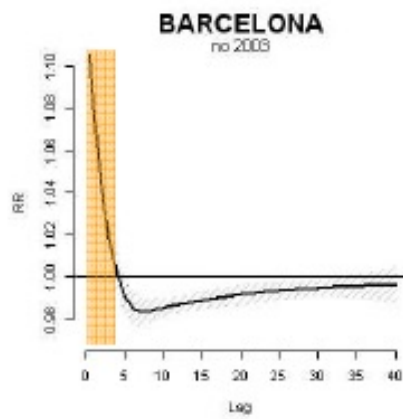


Non-linear effects

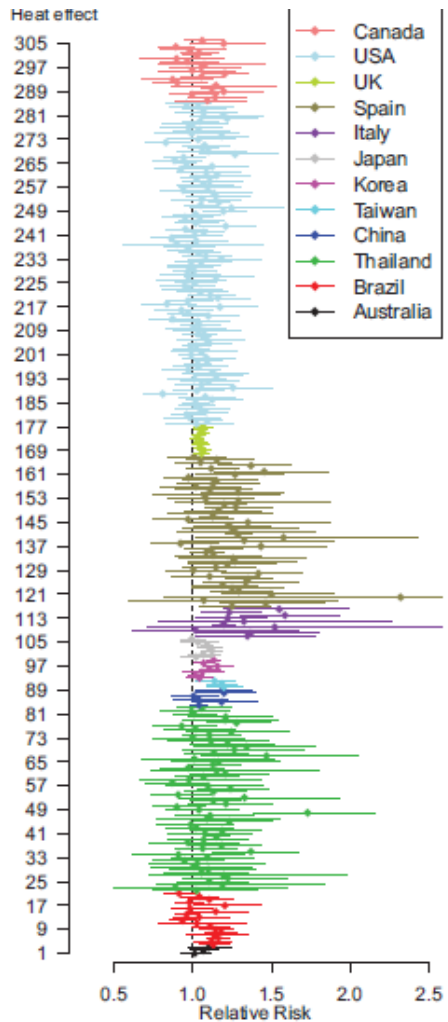


Gasparrini et al. 2015

Delayed effects



Spatially heterogeneous effects



Global Variation in the Effects of Ambient Temperature on Mortality A Systematic Evaluation

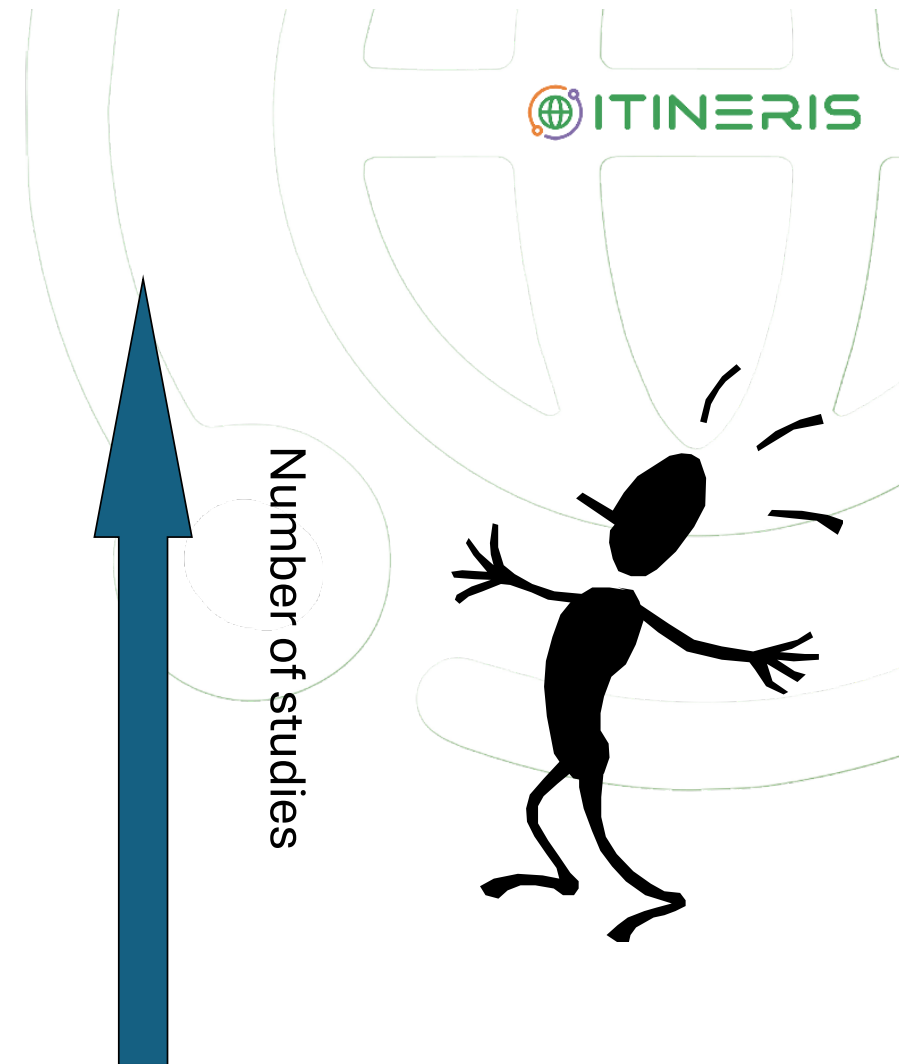
Yuming Guo,^a Antonio Gasparrini,^b Ben Armstrong,^c Shanshan Li,^a Benjawan Tawatsupa,^d Aurelio Tobias,^e Eric Lavigne,^{f,g} Micheline de Sousa Zanotti Stagliorio Coelho,^h Michela Leone,ⁱ Xiaochuan Pan,^j Shilu Tong,^k Linwei Tian,^l Ho Kim,^m Masahiro Hashizume,ⁿ Yasushi Honda,^o Yue-Liang Leon Guo,^p Chang-Fu Wu,^q Kornwipa Punnasiri,^d Seung-Muk Yi,^m Paola Michelozzi,ⁱ Paulo Hilario Nascimento Saldiva,^h and Gail Williams^a

Communities in Italy, Taiwan, and Spain had higher temperature-related (cold and heat) mortality risks than those in other countries.

(Epidemiology 2014;25: 781–789)

Vulnerable population subgroups

- **Age:** elderly, young children
- **Gender:** female
- **Chronic illness:** cardio-respiratory, diabetes, mental health disorders, etc.
- **Social conditions:** low socio-economic status, living alone, socially isolated
- **Urban heat island:** hotter vs cooler areas, presence of green spaces
- **Preventive measures:** air conditioning, changes in behaviour





THANKS!

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Mission 4 “Education and Research” - Component 2: “From research to business” - Investment
3.1: “Fund for the realisation of an integrated system of research and innovation infrastructures”

