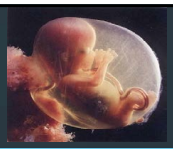


Fine particulate matter (2): effects on reproductive function, risk and risk management

Particules fines (2) : effets sur la function de reproduction, gestion du risque

Rémy Slama

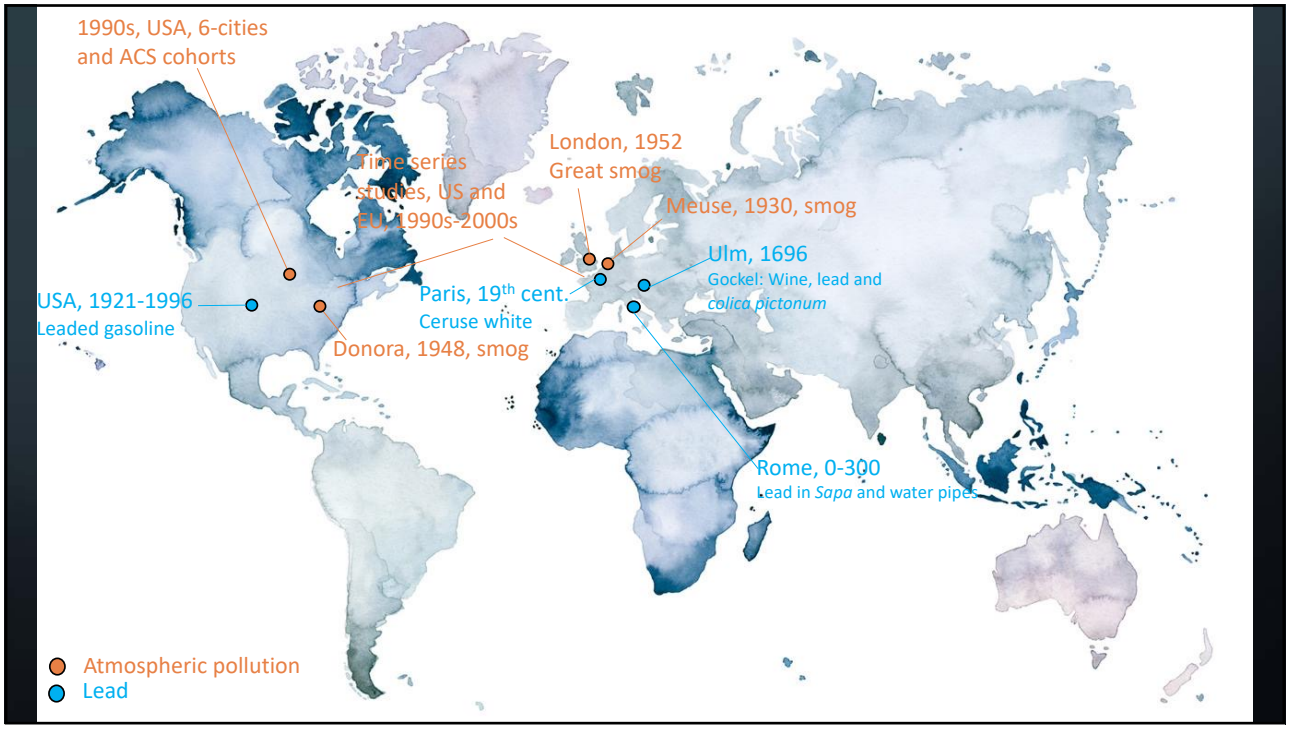
Collège de France & Inserm

The relations between human health and the environment in the Anthropocene

Lecture #4 – 20 April 2022

COLLÈGE DE FRANCE 1530

1



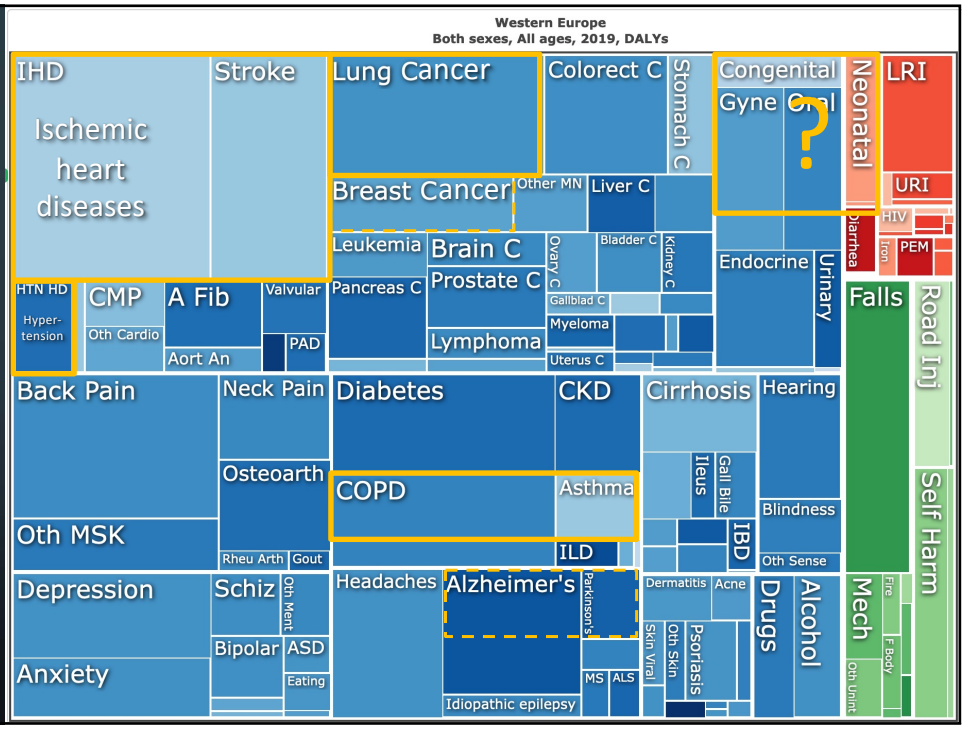
2

Burden of disease

Western Europe, 2019

Source: Institute for Health Metrics and Evaluation (IHME)
https://vizhub.healthdata.org/gbd-compare/

DALYs: Disability-adjusted life year
DALYs equal the sum of years of life lost (YLLs) and years lived with disability (YLDs). One DALY equals one lost year of healthy life.



3

Lecture overview

Lecture #3

A. Nature of atmospheric pollution
B. Effects (1): Peaks and valleys. *Before-after* studies
C. Effects (2): A new microscope - *Time-series* studies
D. Effects (3): Cohorts - making long-term effects visible
E. Effects (4): Overview of cardiovascular and respiratory effects

Effects on the central nervous system *(seminar of Pr. M. Weisskopf)*

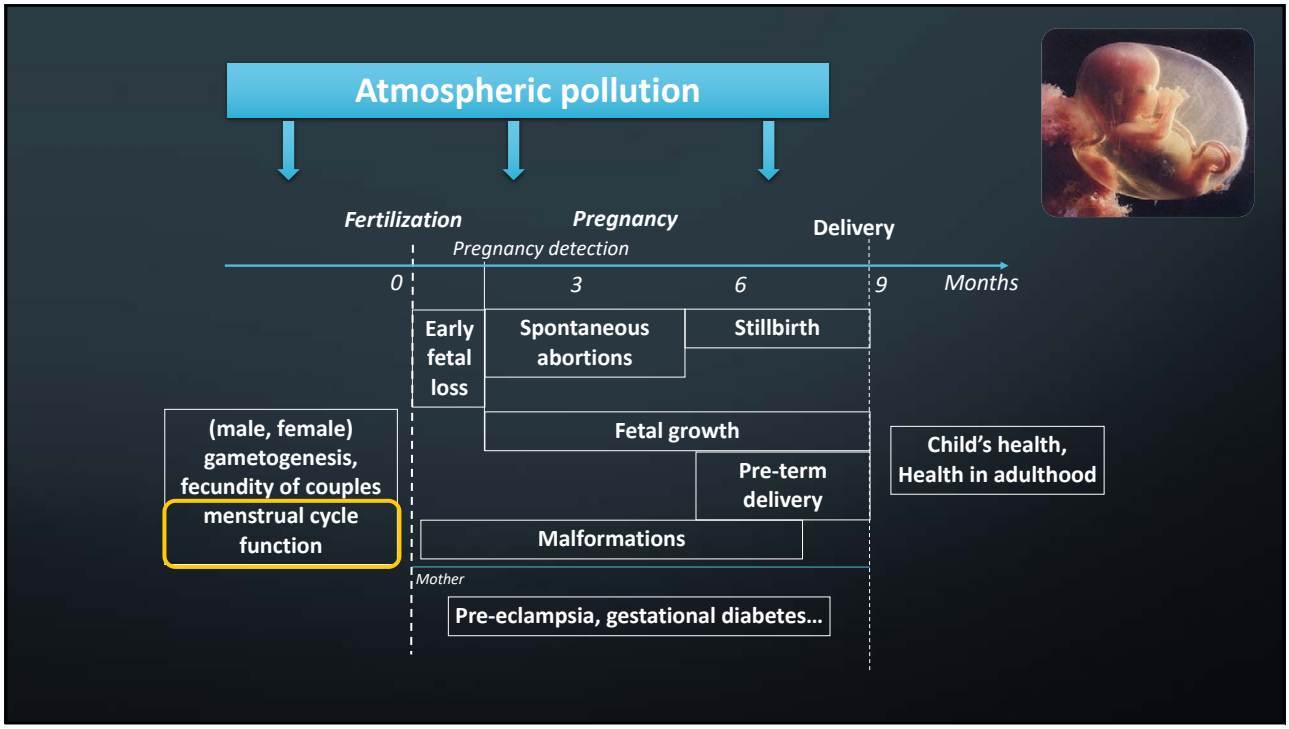
Lecture #4

F. Effects (5): Health targets related to the reproductive function
G. Social inequalities in exposure
H. Health and societal impact
I. Evaluation of risk management options
J. Risk management

4

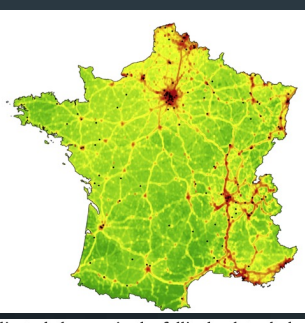
F. Effects of atmospheric pollutants on reproductive function

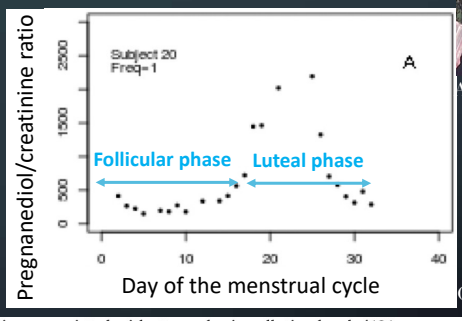
5

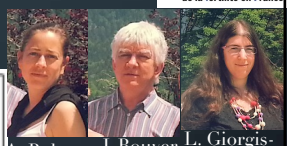


6

Air pollution effects on the duration of the follicular phase of the menstrual cycle





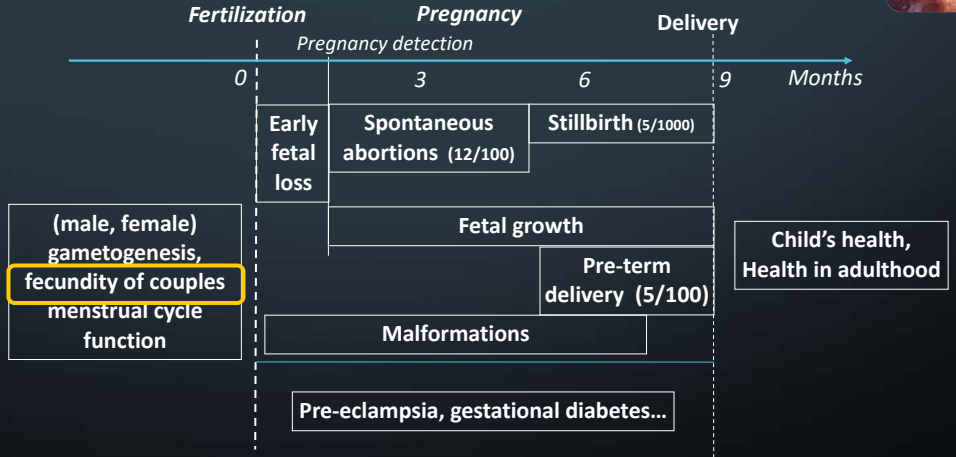


Giorgis-Allemand, *Env Poll*, 2019)

Adjusted changes in the follicular, luteal phases and menstrual cycle durations associated with atmospheric pollution levels (181 women not using hormonal contraception).

Pollutant and exposure window [a]	Follicular phase length				Luteal phase length [b]				Total cycle length [c]			
	N	B	95% CI	p-value	N	β	95% CI	p-value	N	β	95% CI	p-value
NO_2-Days 1–30 before cycle start												
Continuous [d]	*159*	*0.74*	*0.15; 1.33*	*0.01*	*144*	*0.28*	*−0.19; 0.75*	*0.24*	*165*	*0.53*	*−0.48; 1.54*	*0.30*
Lowest tertile (6–18 µg/m^3)	38	0	Reference	0.06 [e]	36	0	Reference	0.12 [e]	44	0	reference	0.27 [e]
Medium tertile (18–30 µg/m^3)	51	0.21	−1.47; 1.89		46	0.35	−0.83; 1.53		53	−1.93	−5.18; 1.32	
Highest tertile (30–61 µg/m^3)	70	1.41	−0.16; 2.98		62	1.08	−0.30; 2.45		68	1.14	−1.80; 4.07	

7



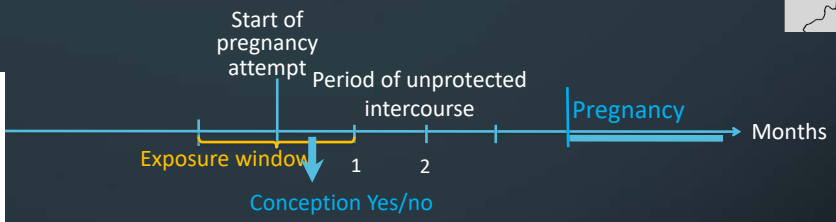
8

Teplice (1989)

Atmospheric pollution and fecundability

A pregnancy cohort in the former Czech Republic

Time Lag Months	Adjusted (M4[d]) FR*	95% CI
$PM_{2.5}$		
Lag 1[e]	0.96	0.86–1.07
Lag 2[e]	0.86	0.77–0.97
Months 1–2[e,f]	0.78	0.65–0.94
Month postoutcome[e,g]	1.04	0.93–1.16
c-PAH		
Lag 1[e]	0.91	0.76–1.08
Lag 2[e]	0.94	0.78–1.13
Months 1–2[e,f]	0.88	0.70–1.10
Month postoutcome[e,g]	0.89	0.74–1.06
O_3		
Lag 1[e]	1.06	0.97–1.15
Lag 2[e]	0.99	0.90–1.09
Months 1–2[e,f]	1.04	0.93–1.17
Month postoutcome[e,g]	1.14	1.04–1.25
NO_2		
Lag 1[e]	0.71	0.57–0.87
Lag 2[e]	1.05	0.83–1.34
Months 1–2[e,f]	0.72	0.53–0.97
Month postoutcome[e,g]	1.08	0.87–1.36



In this former industrial area, in the mid 1990s, fine particulate matter ($PM_{2.5}$) levels during the 2 months before the end of the 1st month of unprotected intercourse were associated with a decrease in fecundability.

Some experimental support to this association (Veras, *Env Res*, 2009)

*FR: Fecundability ratio for an increase by 10µg/m^3 in air pollution concentration, adjusted for maternal age at start of pregnancy attempt, marital status, maternal and paternal smoking, maternal pre-pregnancy BMI, education and seasonal trends (spline smoothing).

(Slama, *Epidemiology*, 2013)

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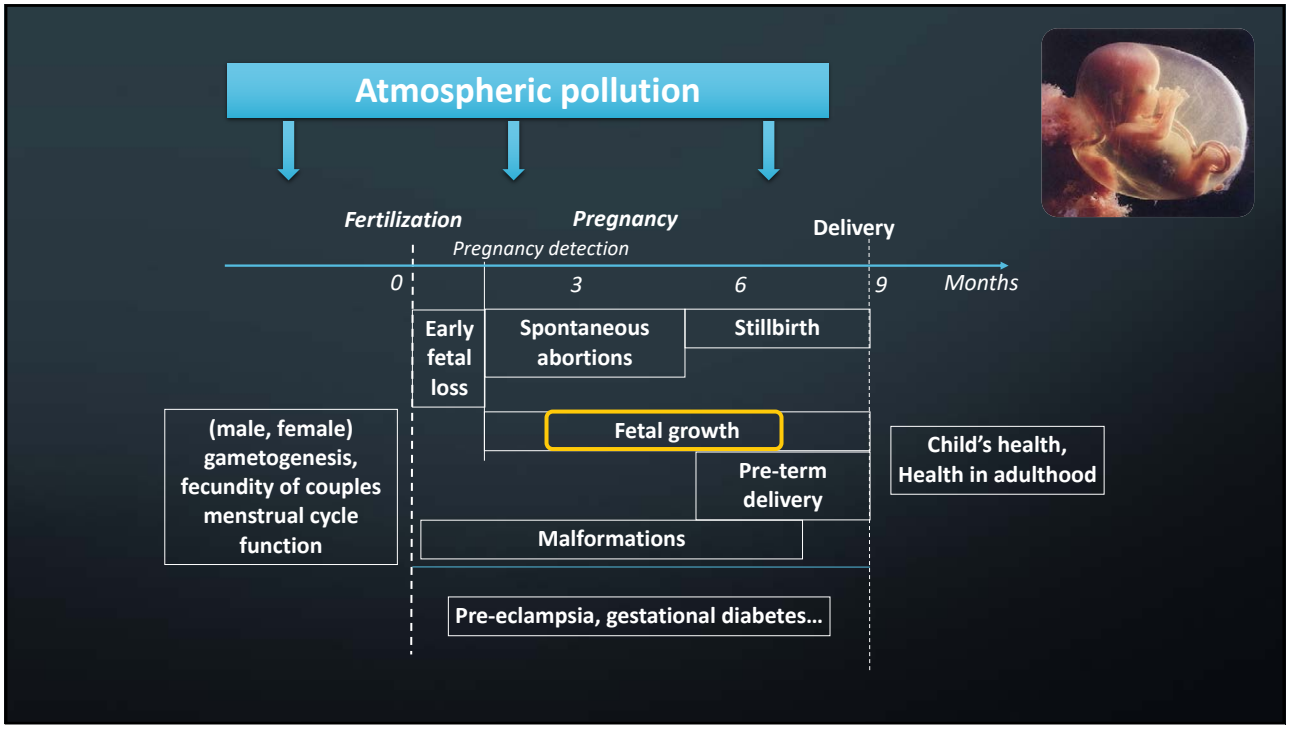


10

London Dec. 1952 smog episode

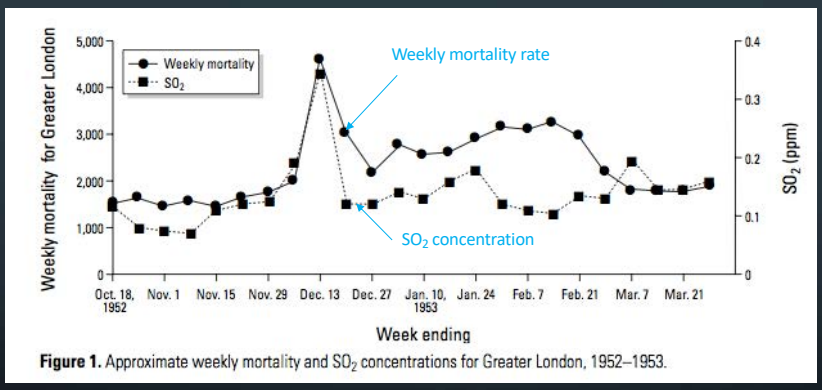
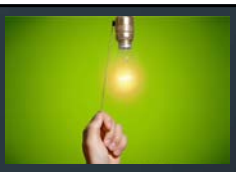


Figure 1. Approximate weekly mortality and SO_2 concentrations for Greater London, 1952–1953.

5000 deaths in excess (London Metropolitan area, Dec. 1952)
Mortality rate multiplied by 2 during the main week of the smog episode

(Bell, *Env Health Perspect*, 2001, 2004)

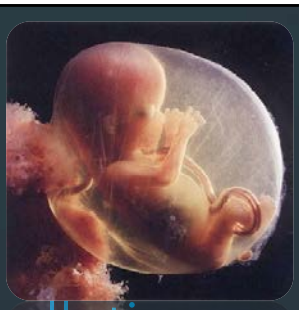


Visible risk factor
No time lag between exposure and effect
Very severe (and accurately monitored) outcome (death)
Rather strong effect at the individual level
Large impact at the population level
No obvious alternative concurrent explanation for the excess death

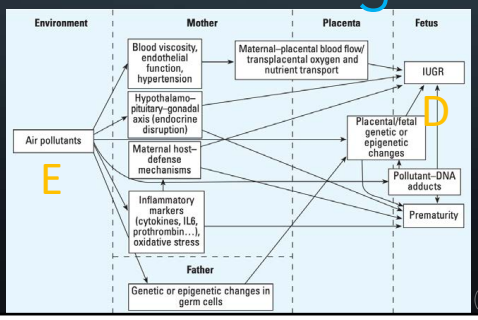
E $\xrightarrow{\Delta t \sim hours}$ D

➔ **Very simple causal model**
➔ No thorough scientific approach required provided **the information is aggregated at the population scale**
➔ Only short-term effects are visible

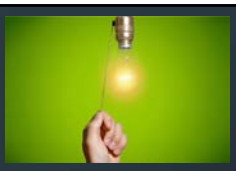
11



Atmospheric pollution effects on foetal growth?



(Slama, *EHP*, 2008)



Visible risk factor
No time lag between exposure and effect
Very severe (and accurately monitored) outcome (death)
Rather strong effect at the individual level
Large impact at the population level
No obvious alternative concurrent explanation for the excess death

E $\xrightarrow{\Delta t \sim months}$ D

➔ **More complex causal model**

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Establishing *causality* in environmental health research? *A practical view*

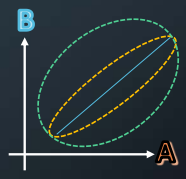
- Epistemologically, causality is a complex and debated concept
- In practice, it is relevant to establish/validate causal models and causal chains, in particular to identify targets for public health interventions
- Whether or not one accepts the concept of causality, documenting the *level of evidence* of environmental health theories is also essential to justify and prioritize public health action.
- Whatever the conceptual framework, some form of *evidence pluralism* is often required to establish causality or increase the level of evidence
  - Evidence pluralism states that, to establish causal claims in medicine, one typically needs evidence of difference-making and evidence of mechanism: Russo-Williamson thesis (Russo & Williamson, 2007)

(cf. seminar by Pr. F Russo, 1 June 22)

13

Establishing *causality* in environmental health research? *A practical view*

A → B



1. Statistical characterization of the association between A and B
   Strength(s) of association (slope, p-level), predictive value, population impact: Human studies
2. Internal validity
   Verify that the association cannot be explained by specific extraneous factors (confounders), measurement error, selection bias: *quantitative bias analysis* (Lash, 2009)
   Experimental studies in models or in humans
3. External validity/generalisability
   Discard random fluctuations as an explanation of the association. Validity in various settings/populations: *replication in other human studies*
4. Explanatory dimension (underlying mechanisms)
   Understanding of the association at a finer scale (i.e., exploration of the causal chain from A to B, identification of the intermediary factors): *reductionist approaches (molecular toxicology, molecular epidemiology)*

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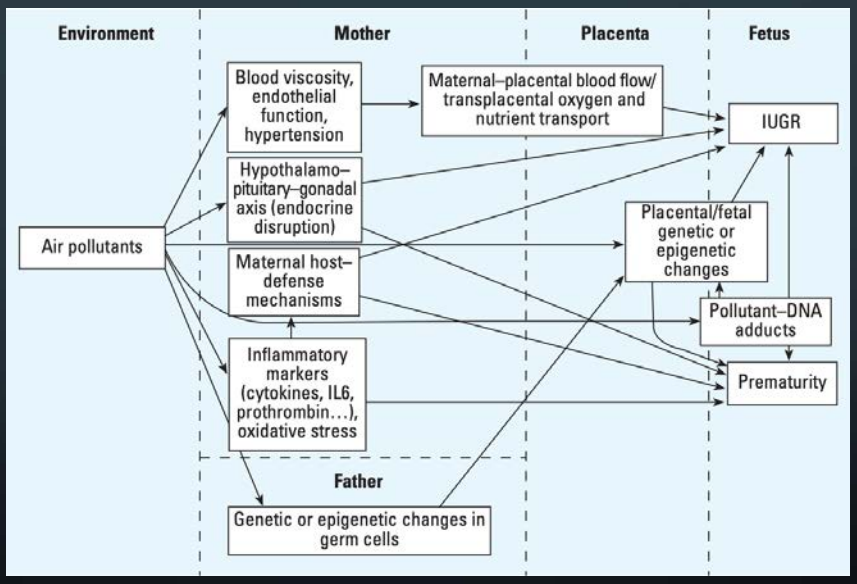

-Improve exposure assessment
-Control for potential confounders (or provide experimental evidence)
-Document possible underlying pathways
-Cohort as an a priori relevant design
-Quantify population impact

IUGR: Intra uterine growth restriction

(Slama et al., *EHP*, 2008)

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Atmospheric pollution and fœtal growth
A retrospective cohort based on Californian birth certificates (n=18,200 term births, year: 2000)

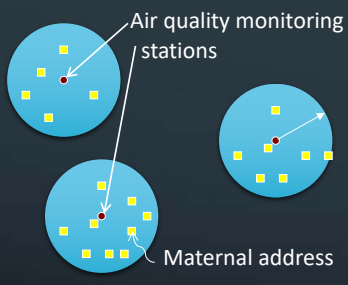

TABLE 3. Associations Between Birth Outcomes and Nine-Month Maternal Exposure to $PM_{2.5}$ and CO

	Birth Weight, mean g		SGA	
	β	95% CI	OR	95% CI
PM 2.5, μ/m³				
Unadjusted				
<11.9	Referent		Referent	
11.9–13.9	16.1	−2.4 to 34.7	0.87	0.75 to 1.02
13.9–18.4	−10.5	−29.0 to 8.1	0.99	0.85 to 1.15
>18.4	−25.4	−44.0 to −6.9	1.09	0.94 to 1.26
Adjusted*				
<11.9	Referent		Referent	
11.9–13.9	8.4	−10.6 to 27.4	0.87	0.75 to 1.02
13.9–18.4	−13.7	−34.2 to 6.9	0.97	0.82 to 1.15
>18.4	−36.1	−55.8 to −16.5	1.12	0.96 to 1.31

* Adjusted for maternal race, education, marital status, age, parity, and season of delivery.
† Adjusted for above variables in * and CO.

(Parker, *Pediatrics*, 2005)

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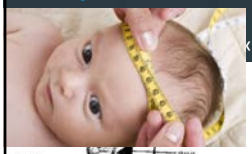
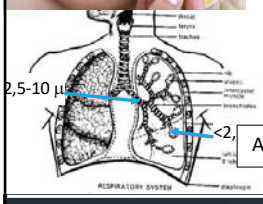
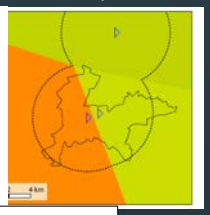
Improving the spatial resolution of exposure models



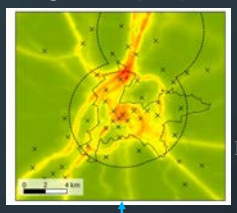
« Station-only model »





(Ritz, *EHP*, 1999; Parker, *Pediatrics*, 2005)

Land Use Regression (LUR) model



(Lepeule, *EHP*, 2010; Sellier, *Env Int*, 2014; Pedersen, *Lancet Resp Med*, 2013)

B. Brunekreef
Utrecht Univ.

ESCAPE

* Odds Ratio (OR) for **Term Low Birth Weight** associated with Pregnancy Mean Exposure

Exposure	N	OR*	95% CI
$PM_{2.5}$ (for an increase by 5 µg/m³)	50,151	1.18	1.06; 1.33

*Effect estimates are from the pooled sample using logistic regression models with random effect of center adjusted for gestational age (weeks and weeks²), sex, parity, maternal height, pre-pregnancy weight (broken stick model with a knot at 60 kg), maternal active smoking during second trimester of pregnancy (cigarettes/day), maternal age, maternal education and season of conception.

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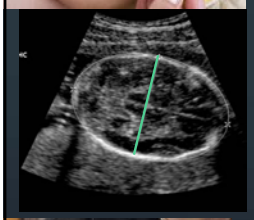
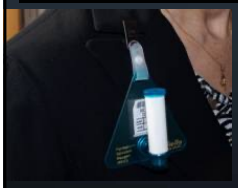
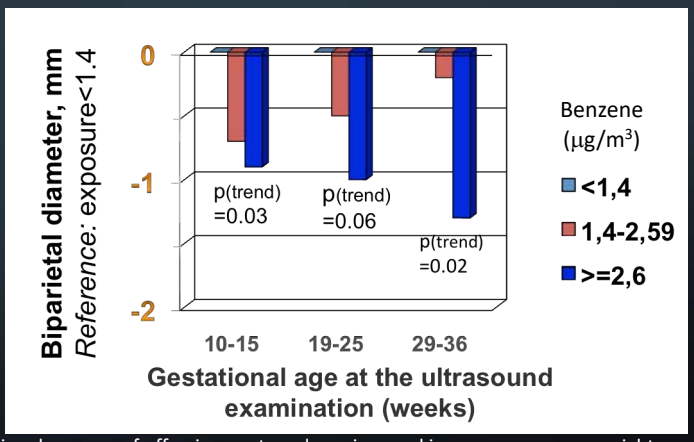
Adjusted variations in biparietal diameter associated to maternal personal benzene exposure

(272 non-smoking women, Eden cohort)







* Adjusted for gestational age, sex of offspring, maternal passive smoking, pre-pregnancy weight, height, parity, education level, month of conception and recruitment centre (3 distinct linear regression models).

(Slama, *EHP*, 2009)

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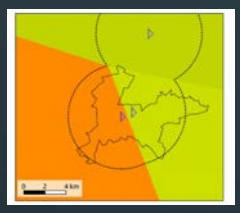
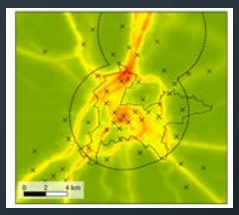
Further improving tools to assess air pollution exposure

Early 2000s: Permanent stations data



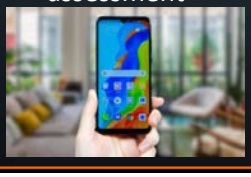
2010s: Fine scale (dispersion-type) environmental models



2020: SEPAGES mother child cohort

(Ouidir, *Env Int*, 2015, Lyon-Caen, *IJERPH*, 2019)

Smartphone-based time-space activity assessment



Fine-scale dispersion model

Personal measurements of air pollution

$PM_{2.5}$

NO_2, benzene…

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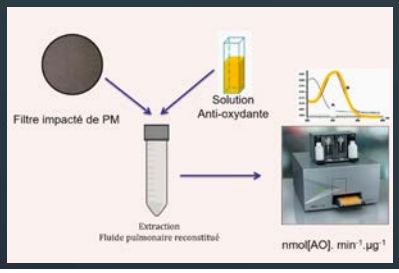
$PM_{2.5}$ oxidative potential as an alternative metric (more toxicologically relevant?) to mass concentration

$PM_{2.5}$

Weighting of filter
Assessment of $PM_{2.5}$ mass concentration

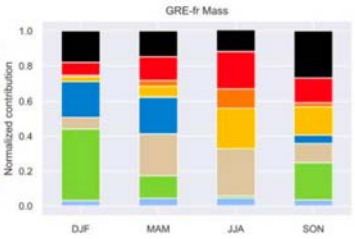
Assessment of $PM_{2.5}$ oxidative potential
(G. Uzu, IRD, IGE Grenoble)



(Weber, *Atmosphere*, 2019)

Contribution of PM sources for each metric

$PM_{2.5}$ mass concentration



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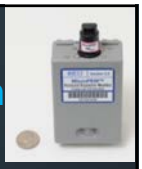
Associations of size at birth with $PM_{2.5}$ oxidative potential (OP^{DTT}, OP^{AA}) and $PM_{2.5}$ mass concentration in *SEPAGES* couple-child cohort



Birth outcome	Exposure		Fully adjusted models*				
			n	Change	p-value	95% Confidence Interval	
Weight (g)	$PM_{2.5}$ mass concentration		333	-53.3	0.02	-98.5	-8.2
	OP_v^{DTT}		333	-63.7	0.02	-115.9	-11.4
	OP_v^{AA}		333	-14.5	0.57	-64.0	35.1
Height (mm)	$PM_{2.5}$ mass concentration		332	-2.3	0.05	-4.5	-0.01
	OP_v^{DTT}		332	-3.5	0.01	-6.0	-0.9
	OP_v^{AA}		332	-2.0	0.11	-4.5	0.4
Head circumference (mm)	$PM_{2.5}$ mass concentration		330	-0.1	0.87	-1.6	1.4
	OP_v^{DTT}		330	-0.2	0.79	-2.0	1.5
	OP_v^{AA}		300	0.9	0.27	-0.7	2.6

* Adjusted for gestational duration (week, weeks²), child sex, parity, maternal characteristics (height, weight before pregnancy, head circumference, age, educational status), marital status, season of conception, maternal smoking anytime during the pregnancy.

(Borlaza et al., *manuscript*)

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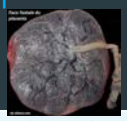
Documenting the mechanisms possibly implied through molecular epidemiology approaches



(Slama, *EHP*, 2008)

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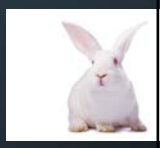
Experimental evidence of air pollution effects on the foetal-placental unit?



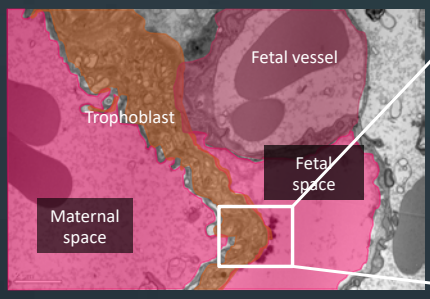
RIVM
National Institute for Public Health and the Environment
Ministry of Health, Welfare and Sport

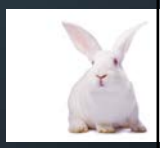
(Valentino, *Part Fibr Tox*, 2016)

23

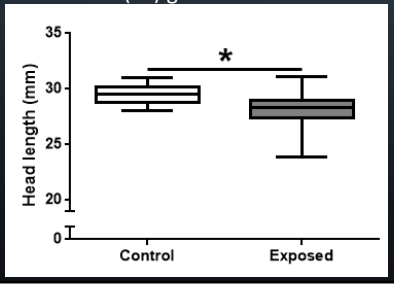
PM translocate to the placenta

Placenta of exposed mother-offspring pairs

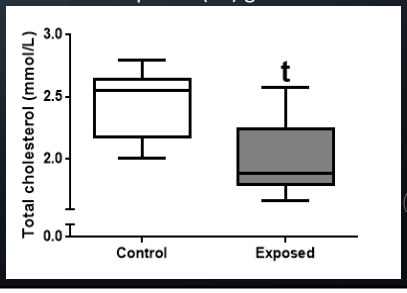




Decreased head length in *in-utero* exposed (F1) generation



Decreased total cholesterol in offspring of *in-utero* exposed (F2) generation



(Valentino, *Part Fibr Tox*, 2016)

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Can we obtain experimental evidence of air pollution effects on birth outcome in humans?

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Impact of Reduced Maternal Exposures to Wood Smoke from an Introduced Chimney Stove on Newborn Birth Weight in Rural Guatemala

Lisa M. Thompson,[1,2] Nigel Bruce,[3] Brenda Eskenazi,[4] Anaite Diaz,[5] Daniel Pope,[3] and Kirk R. Smith[2]

Table 4. Difference in birth weight associated with chimney stove use based on unadjusted and adjusted linear regression models.

		Unadjusted model		Adjusted model[a]	
	Mean birth weight, g (95% CI)	β-Coefficient, g (95% CI)	*p*-Value	β-Coefficient, g (95% CI)	*p*-Value
Stove type					
Open fire ($n = 105$)	2,729 (2,654 to 2,804)	Referent			
Chimney ($n = 69$)	2,797 (2,697 to 2,896)	68 (–56 to 191)	0.28	89 (–27 to 204)	0.13
Timing of stove introduction					
First/second trimester ($n = 17$)	2,732 (2,526 to 2,937)	Referent			
Third trimester ($n = 52$)	2,796 (2,684 to 2,907)	63 (–157 to 285)	0.56	117 (–96 to 331)	0.27

[a]Adjusted for maternal height, gravidity, maternal diastolic blood pressure, and season of birth.

(Thompson, *EHP*, 2011)

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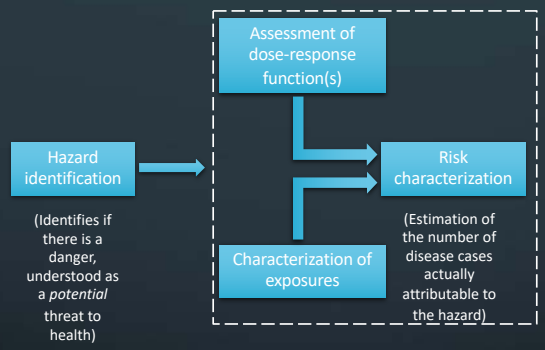
From hazard identification to risk quantification



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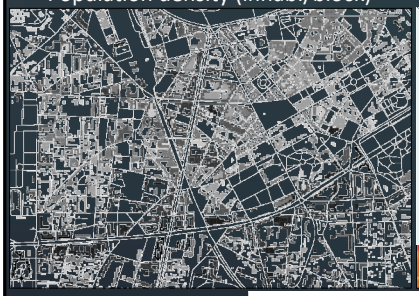
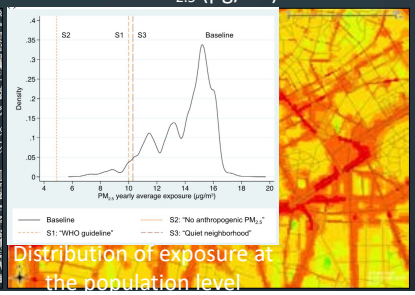
Health impact of $PM_{2.5}$ in Grenoble area (440,000 inhabitants)

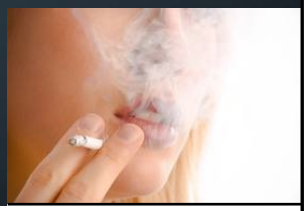
Population density (inhab./block)



$PM_{2.5}$ ($\mu g/m^3$)



Distribution of exposure at the population level



Outcome	Number of attributable cases* (share of the total number of yearly cases)	95% Confidence Interval (share of the total number of yearly cases)	Number of cases attributable to (maternal) smoking
Term low birth weight cases	49 (26%)	19 to 76 (10% to 41%)	(13% to 22%)
Deaths	145 (5.6 %)	90 to 199 (3.5% to 7.7 %)	About 12%
Lung cancer	16 (7.5 %)	8 to 24 (3.5% to 11 %)	About 80%

*Counterfactual scenario: No anthropogenic source of $PM_{2.5}$ (4.9 $\mu g/m^3$) (Morelli, *Env Res*, 2016; *Env Int*, 2019)

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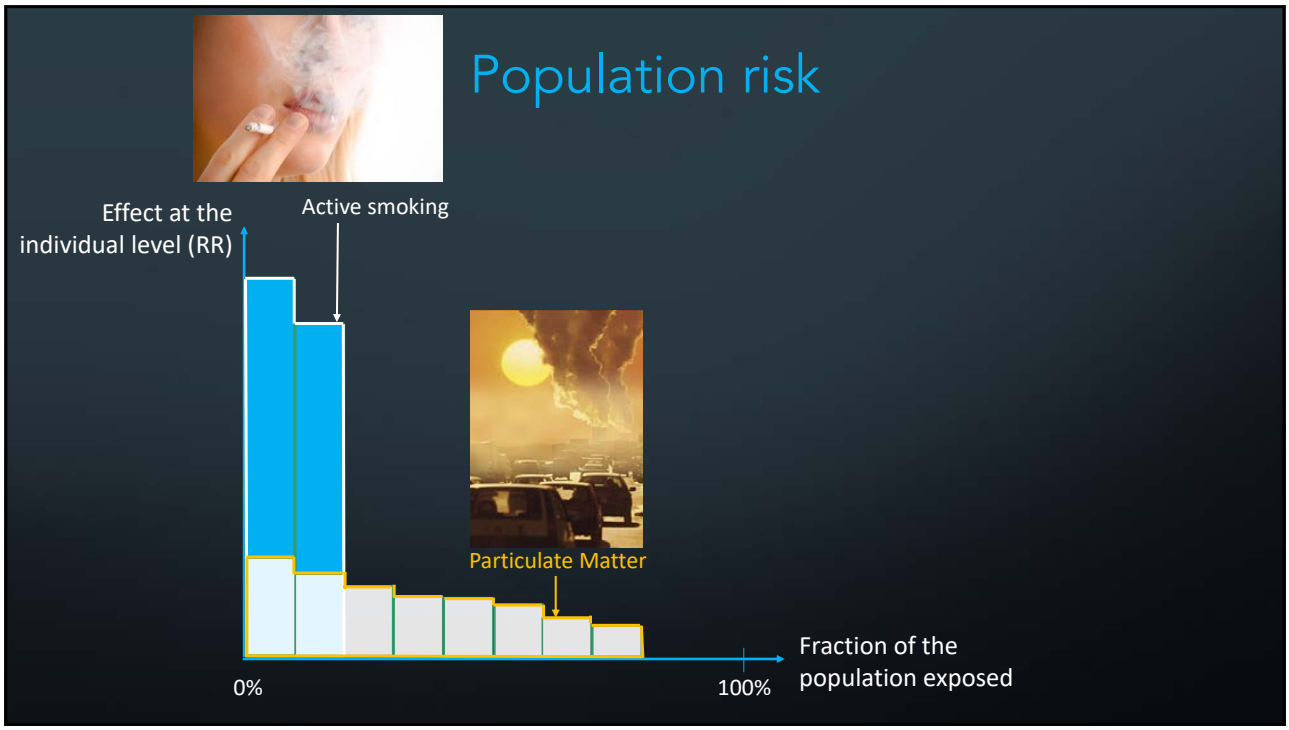
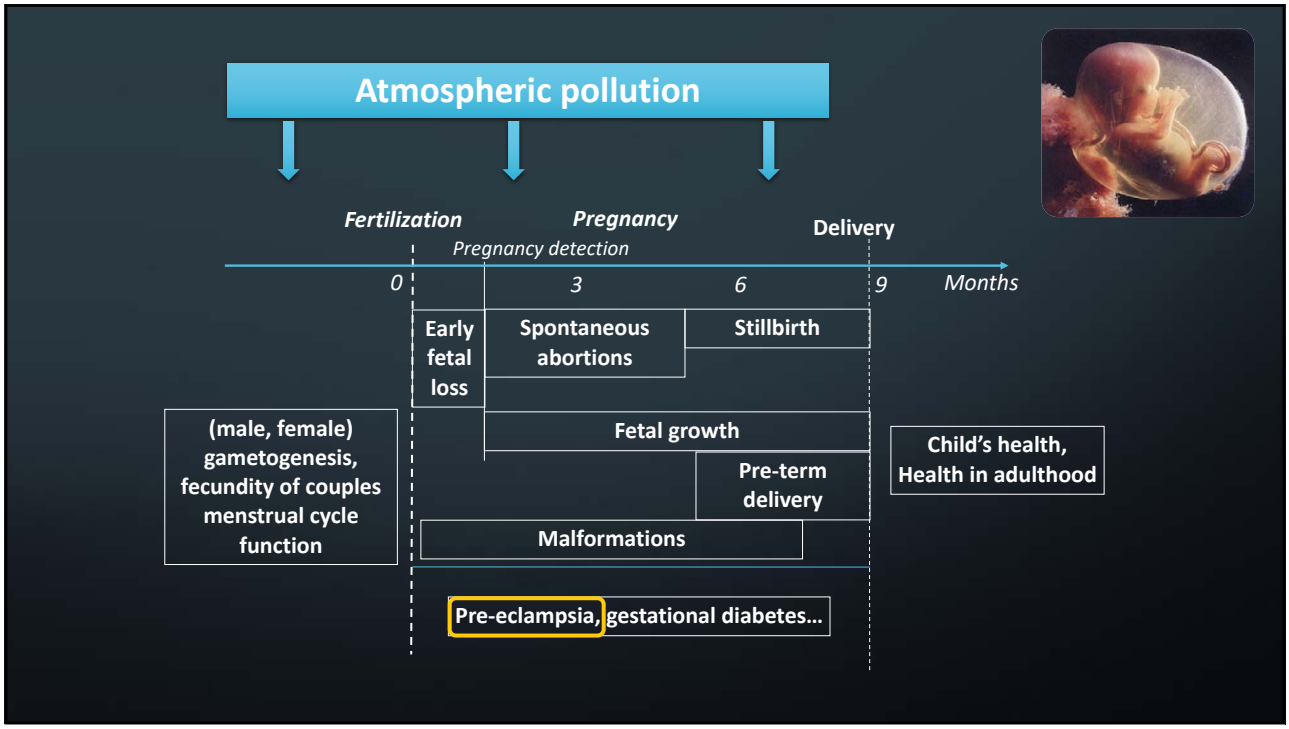
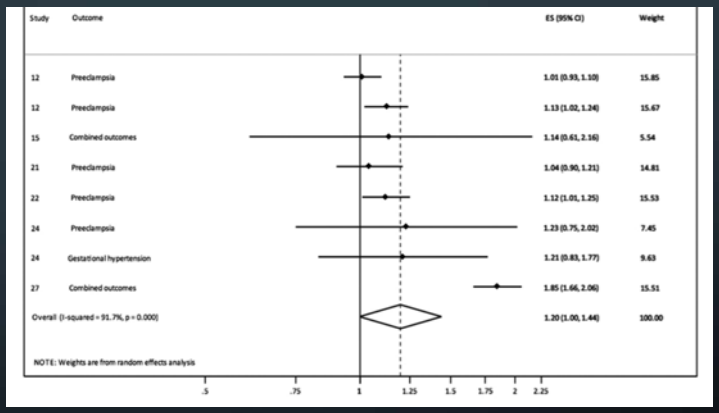

Population risk
Effect at the individual level (RR)
Active smoking
Particulate Matter
Fraction of the population exposed
0%
100%

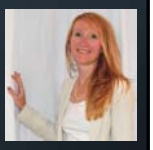
29


Atmospheric pollution
Fertilization
Pregnancy
Pregnancy detection
Delivery
0
3
6
9
Months
Early fetal loss
Spontaneous abortions
Stillbirth
Fetal growth
Pre-term delivery
Malformations
Pre-eclampsia, gestational diabetes…
(male, female) gametogenesis, fecundity of couples menstrual cycle function
Child's health, Health in adulthood

30

Air pollution (NO_2, $PM_{2.5}$) pregnancy exposure is associated with preeclampsia risk





M. Pedersen, Copenhagen Univ.

Exposure to NO_2 → Pre-eclampsia

(Pedersen, *Hypertension*, 2014)

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Air pollution pregnancy level and placental DNA methylation

Contents lists available at ScienceDirect

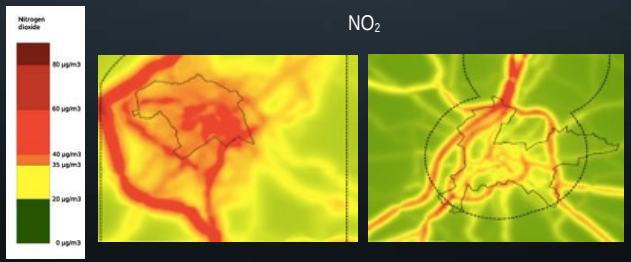
Environment International

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

Pregnancy exposure to atmospheric pollution and meteorological conditions and placental DNA methylation

Emilie Abraham[a], Sophie Rousseaux[a], Lydiane Agier[a], Lise Giorgis-Allemand[a], Jörg Tost[b], Julien Galineau[c], Agnès Hulin[d], Valérie Siroux[a], Daniel Vaiman[e], Marie-Aline Charles[f], Barbara Heude[f], Anne Forhan[f], Joel Schwartz[g], Florent Chuffart[a], Ekaterina Bourova-Flin[a], Saadi Khochbin[a], Rémy Slama[a], Johanna Lepeule[a,*], on behalf of the EDEN mother-child cohort study group

Assessment of exposure to air pollutants



(Abraham, *Env Int*, 2018)

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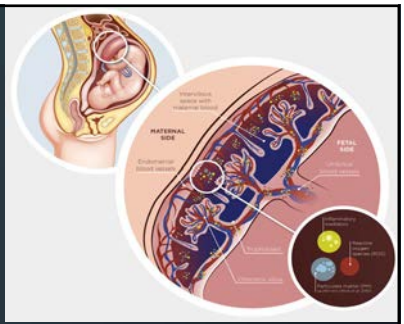
Relevance of placenta to assess DNA methylation



(Luyten, *Env Res*, 2018)

- The placenta plays a key role in fetal programming
  - support foetal development
  - conveys nutrients and oxygen to the fetus, regulates gas and waste exchanges, hormone interactions (Murphy, 2006)
- Air pollutants and tobacco smoke
  - can cross the placenta and expose the developing fetus (Valentino, *Part Fib Tox*, 2016; Wick, 2010)
- The placenta may provide a memory of exposures occurring during pregnancy (an epigenetic memory?)
- Heterogeneous tissue, variable across time

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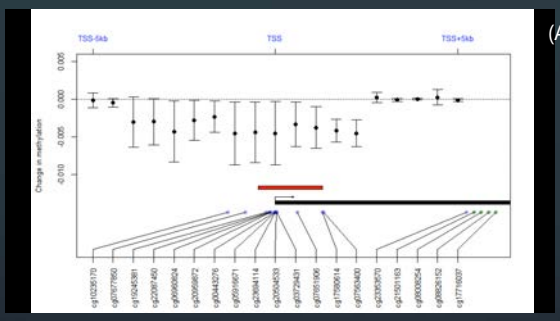
NO_2 exposure was associated with lower methylation levels of *ADORA2B* gene



(Adenosine receptor)

(Pedersen, 2014)

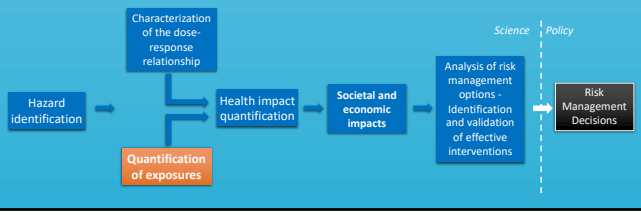
Exposure to NO_2 → *ADORA2B* methylation → ? → ADORA2B signalling → Pre-eclampsia

(Abraham, 2018)

(Huang, 2017)

34

G. « We all breath the same air… »? Social inequalities in air pollution exposure



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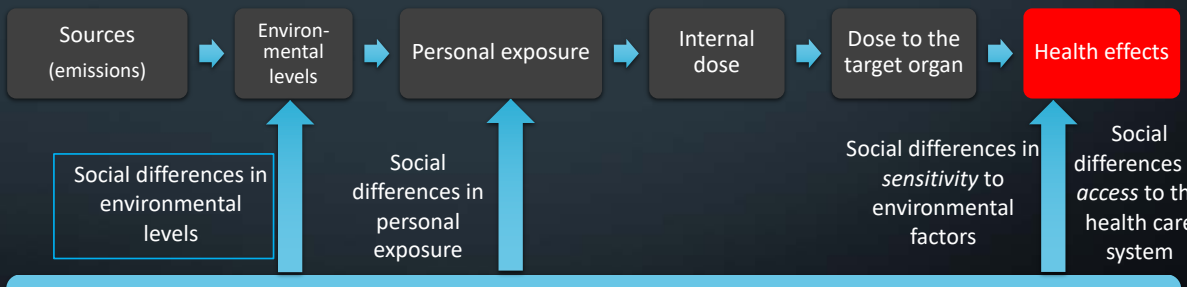
Social factors can come into play at various levels of the exposure-health continuum…



Each of these interactions can contribute to social inequalities in health

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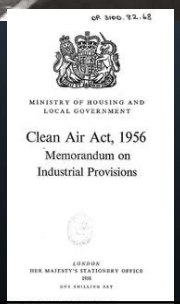
Solving problems or relocating them?

London smog (ca. 1820s-1960s)



New-Delhi smog (2020)

Yearly $PM_{2.5}$ concentration (2020): 84 µg/m^3

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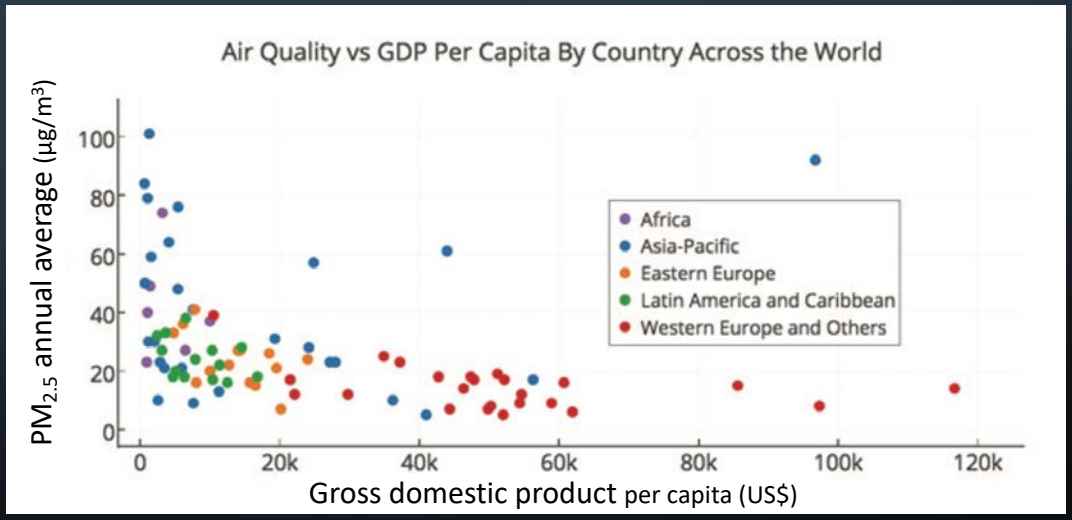
Contrasts in air pollution levels *across* countries



(Hasenkopf, *Clean Air J*, 2016)

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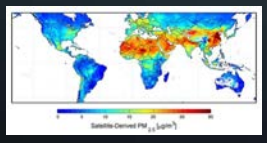
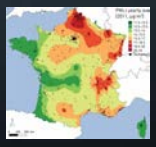
Is the pattern of associations between atmospheric pollution and social classes similar at all scales?



Between-country



Within country (*between*-city)

Within-city

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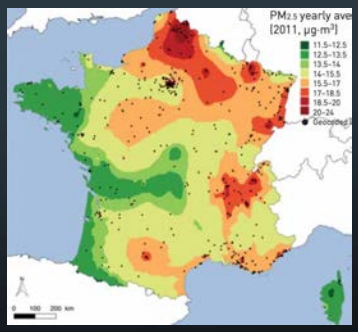
Social inequalities in air pollution exposure at the *country* level



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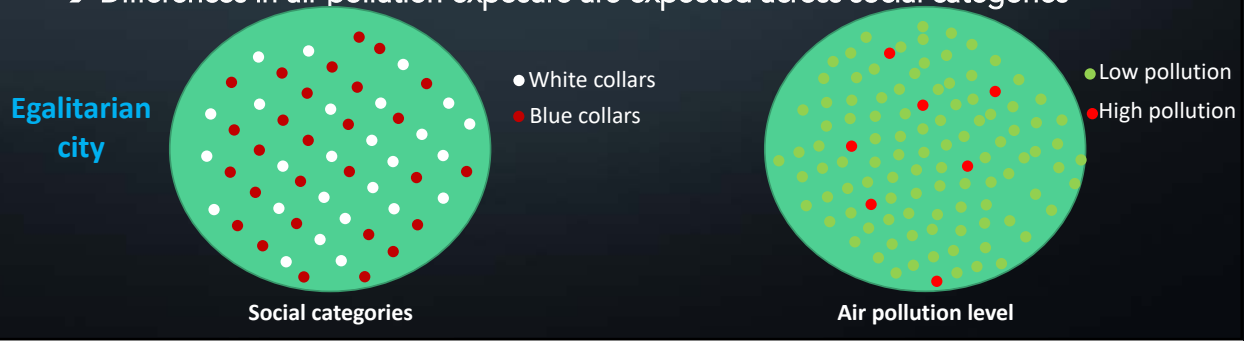
Environmental justice and air pollution exposure

- Social categories are not distributed randomly on a territory
- Neither are air pollution sources
- Factors associated with air pollution exposure also vary across social categories (e.g., time spent in traffic)

➔ Differences in air pollution exposure are expected across social categories



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Environmental justice and air pollution exposure

- Social categories are not distributed randomly on a territory
- Neither are air pollution sources
- Factors associated with air pollution exposure also vary across social categories (e.g., time spent in traffic)

➔ Differences in air pollution exposure are expected across social categories

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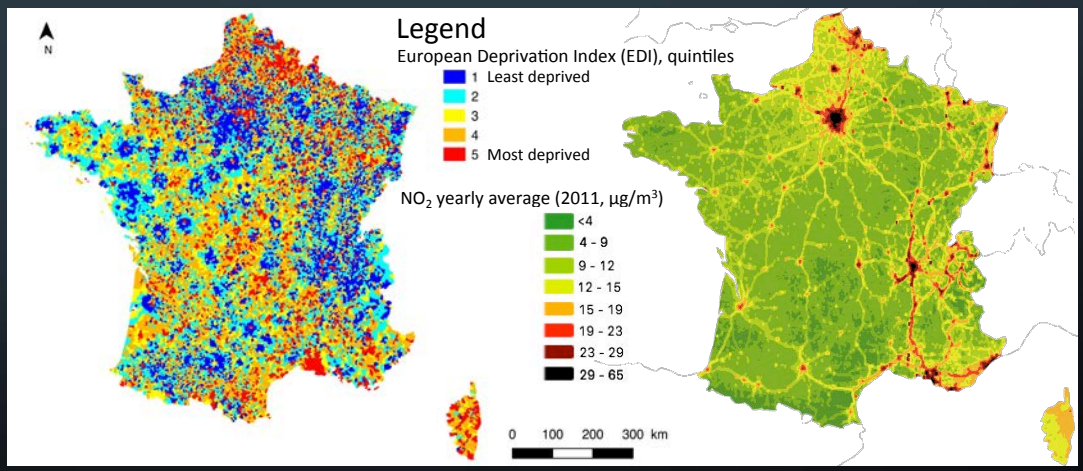
Social deprivation (EDI)
(European Deprivation Index)

Atmospheric pollution
(NO_2)



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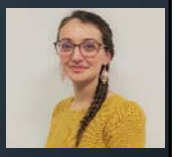
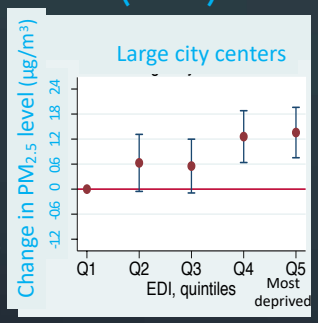
Association between $PM_{2.5}$ exposure and social deprivation (EDI)



M. Ouidir

France

(Ouidir, *J Epid Commun Health*, 2017)



EDI: European Deprivation Index

Q1: most *favoured* areas socially, Q5: most *deprived* areas

Linear regression model adjusted for maternal age, parity, body mass index, marital status, tobacco smoking, education level.

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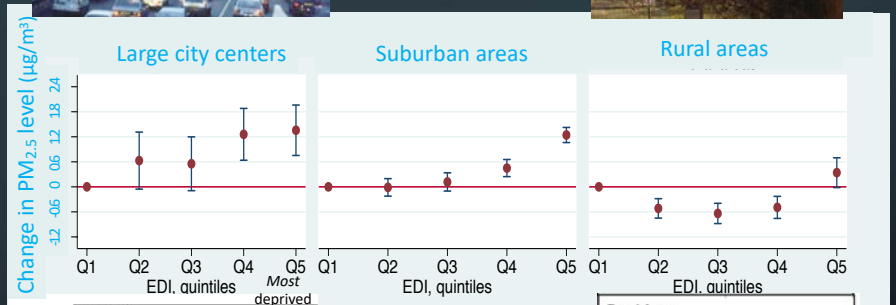
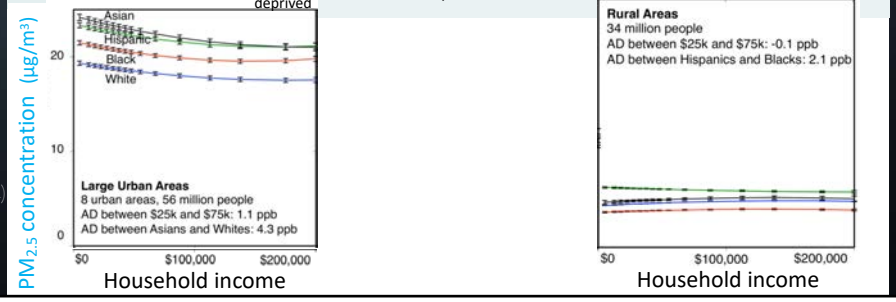
France

(Ouidir, *J Epid Commun Health*, 2017)



USA

(Clark, *PLoSOne*, 2014)



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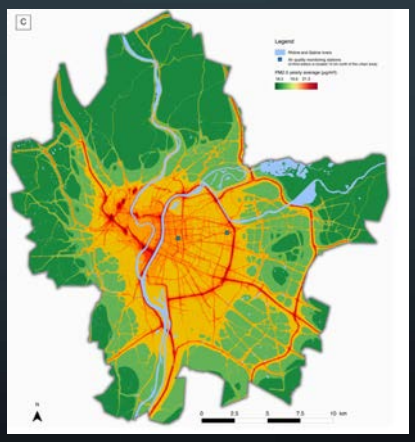
Social inequalities in air pollution exposure at the *city* level



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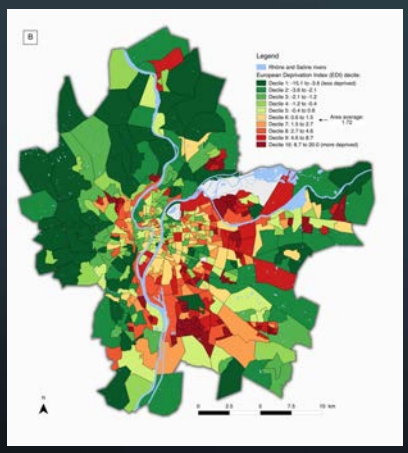
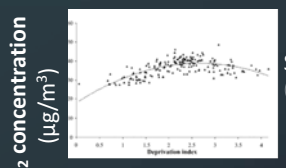
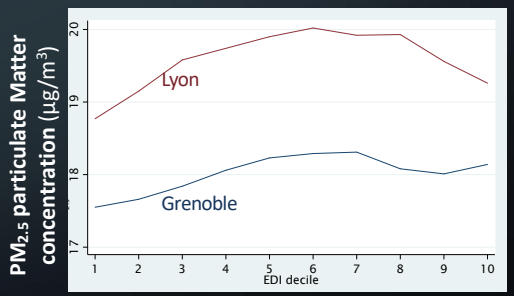
Air pollution levels ($PM_{2.5}$) and social deprivation



Lyon - Défaveur sociale de l'IRIS
(*Red*: most deprived areas socially)



Strasbourg
(Havard, *Epidemiology*, 2009)



Deprivation Index (IRIS scale)
(10: most deprived areas socially)

(Morelli, *Atmosph Env*, 2016)

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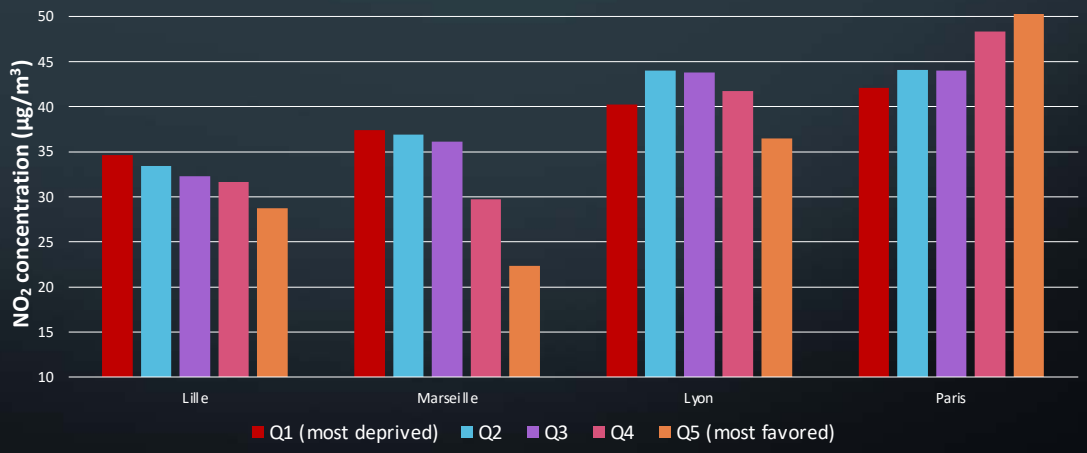
Patterns of association differ across French cities
(Equit'Area project)



(Padilla, *Env Res*, 2014)

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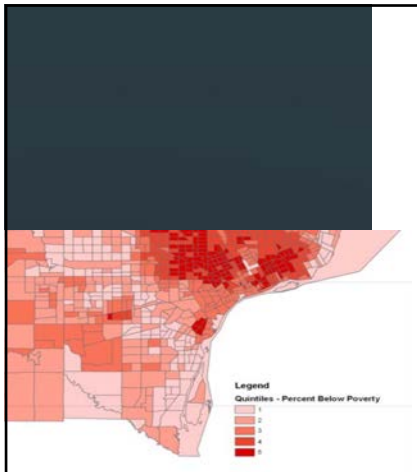

Detroit (USA)

(Padilla, *Env Res*, 2014)

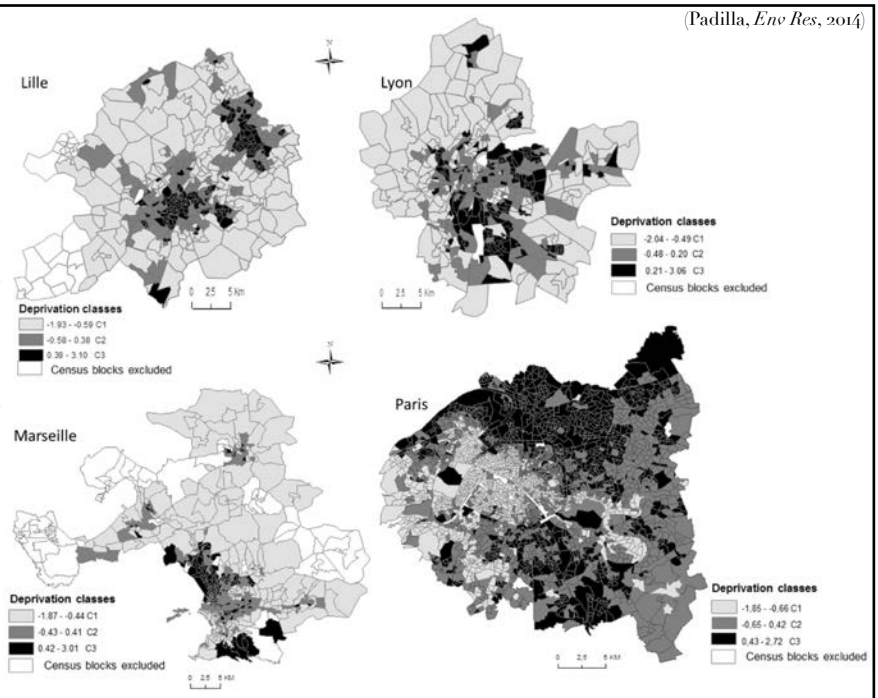

Fig. 2. Spatial distribution of the deprivation index of 2006 in tertiles: Lille, Lyon, Marseille and Paris metropolitan areas.

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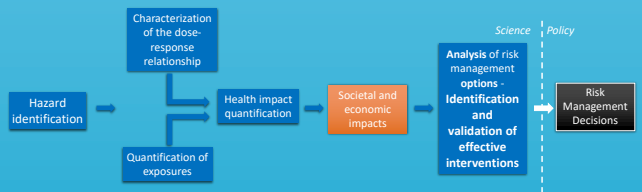
H. Health and societal impacts



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Estimated *impact* of $PM_{2.5}$ exposure (France and world)

Health endpoint	Human evidence	Mechanistic evidence	Attributable fraction or nb of cases*	Reference
Mortality	Certain	Certain	40,000 deaths/year (France), about 6.5% of deaths	(Medina/Santé publique France, 2021)
			4.2 M deaths/year (world)	(Landrigan, *Lancet*, 2018)
Lung cancer	Certain	Certain	3000 cases, 7.6% of all cases (France)	(Kulhanova, *Env Int*, 2018)
Breast cancer	Very likely	Moderate	3% (France)	(Gabet, *EHP*, 2021)

Overall cost of $PM_{2.5}$ exposure in France (2010s): 100 billion €/year (Aïchi, *Sénat*, 2015)

*Fraction of all disease cases attributable to atmospheric pollution exposure, considering a specific counterfactual situation (typically, a mean $PM_{2.5}$ level of 5 µg/m^3)

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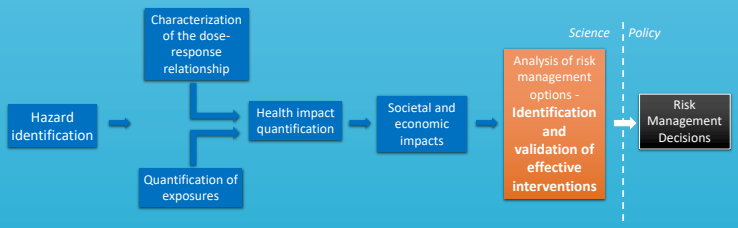
I. Identification of efficient interventions



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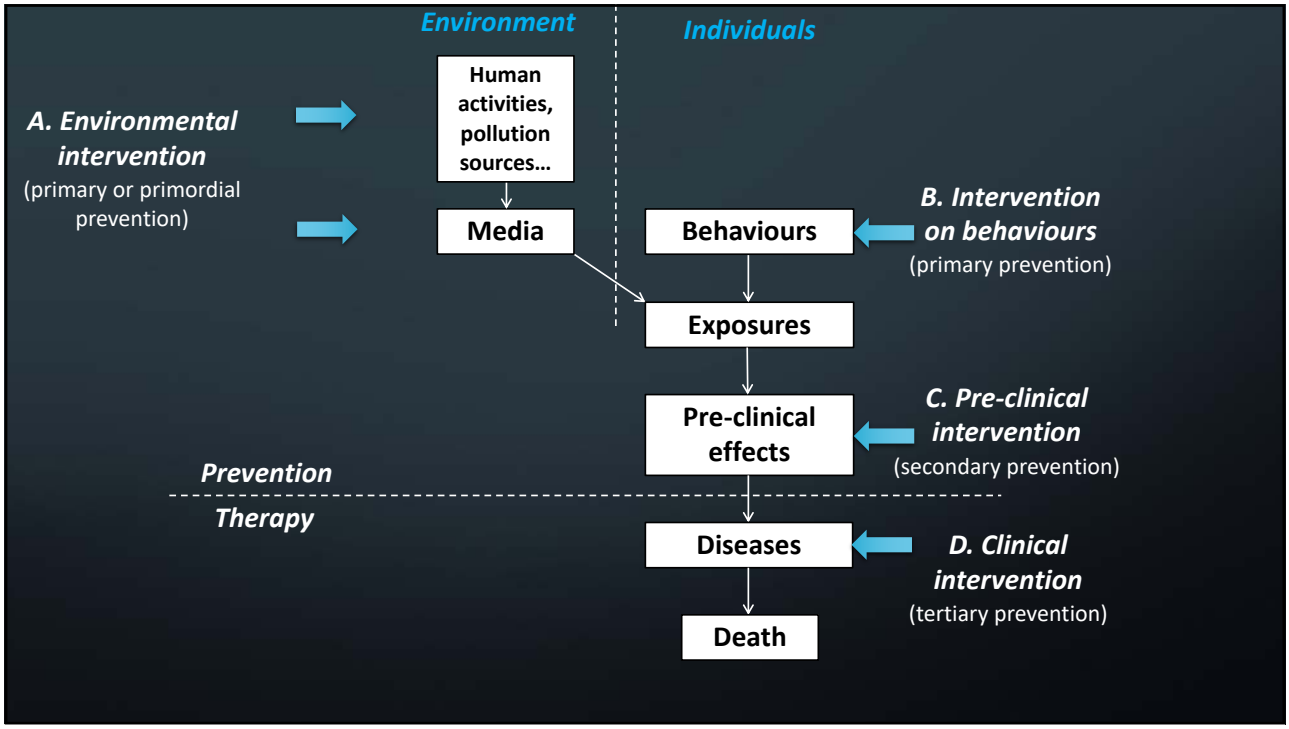

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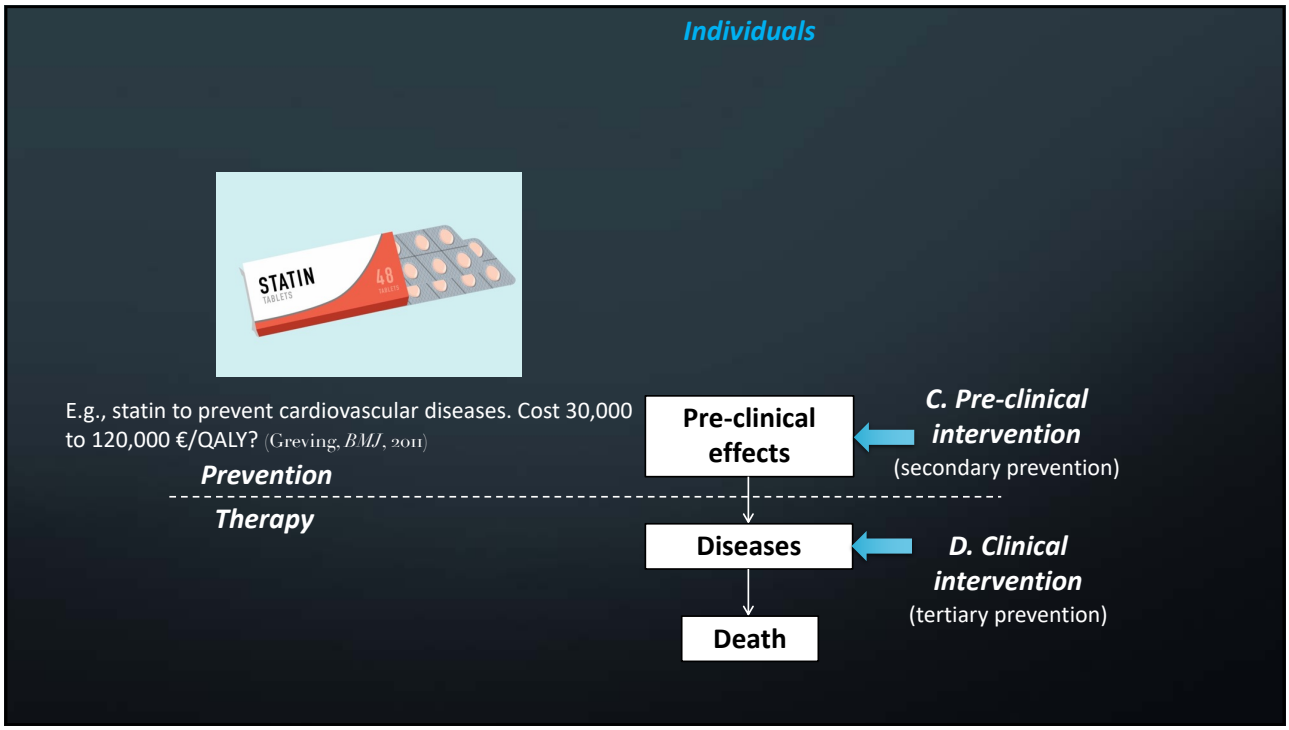
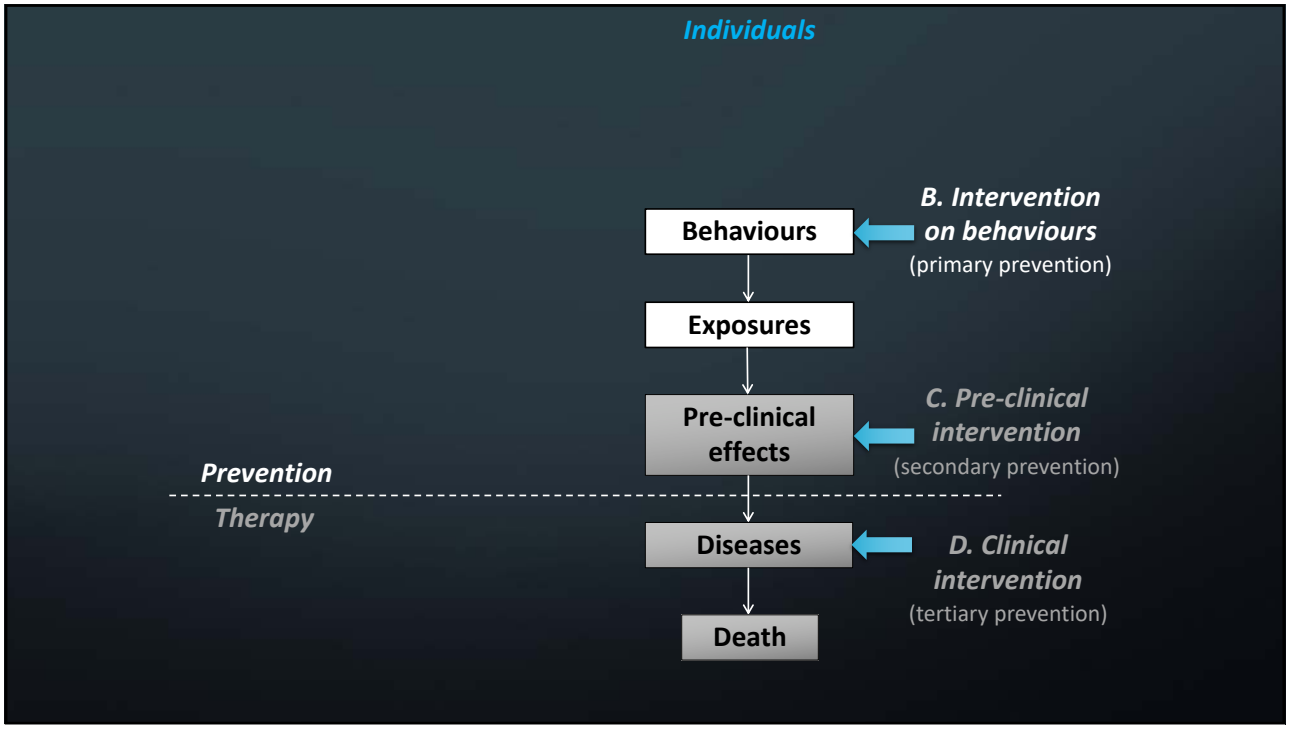

Individuals
STATIN
E.g., statin to prevent cardiovascular diseases. Cost 30,000 to 120,000 €/QALY? (Greving, BMJ, 2011)
Prevention
Therapy
Pre-clinical effects
C. Pre-clinical intervention
(secondary prevention)
Diseases
D. Clinical intervention
(tertiary prevention)
Death

60


Individuals
Behaviours
B. Intervention on behaviours
(primary prevention)
Exposures
Pre-clinical effects
C. Pre-clinical intervention
(secondary prevention)
Prevention
Therapy
Diseases
D. Clinical intervention
(tertiary prevention)
Death

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Impact of a bicycle sharing scheme – The example of Barcelona « *Bicing* » initiative

- Compared to care users, the 182,000 users of *Bicing* shared bikes system had
  - A slightly increased risk of death by road accident (+0.03 death/year)
  - A slightly increased risk of death due to an increased exposure to air pollution (+0.03 death/year) - in the context of the little developed bike lanes in the late 2000s
  - A more strongly decreased risk of death, due to an increase in physical activity (-12.5 deaths/year)

➔ Overall, *12.3 deaths were avoided each year in this population*

Bicing system also allowed to avoid the emission of 9,000 t CO_2.

(Rojas-Rueda, *BMJ*, 2011)

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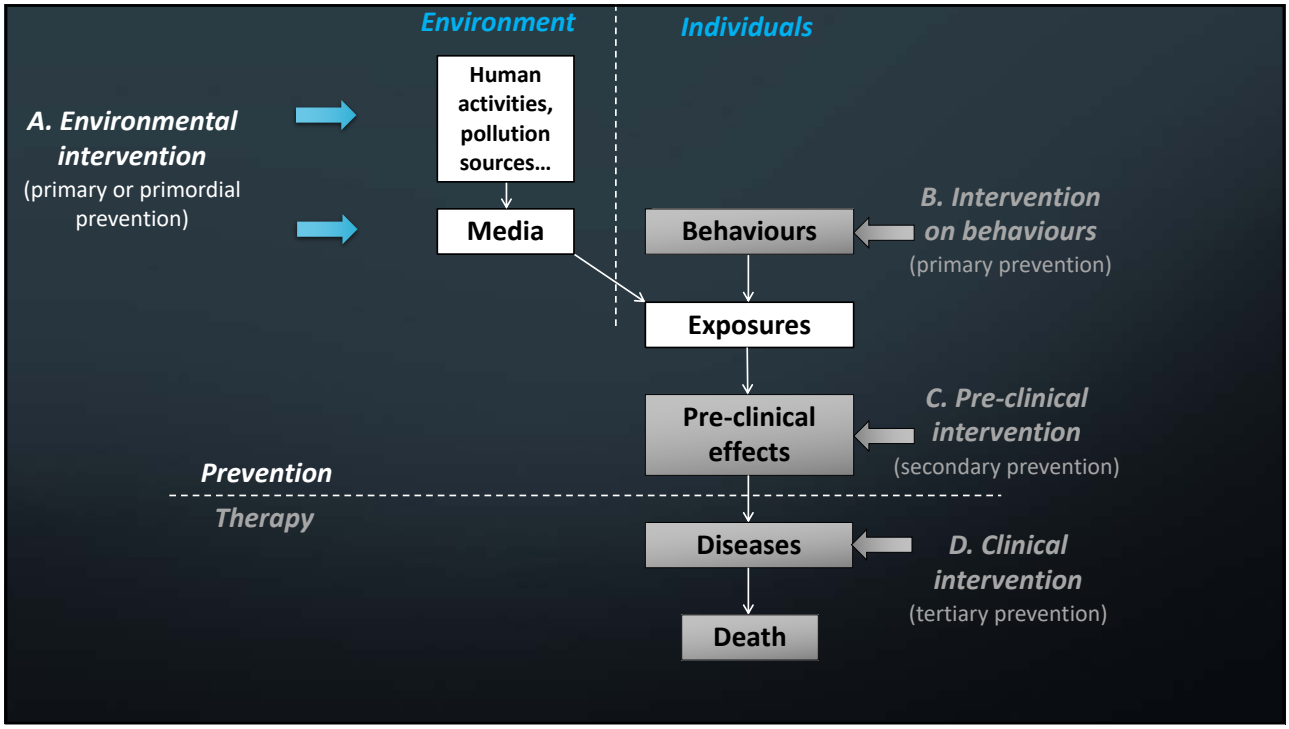

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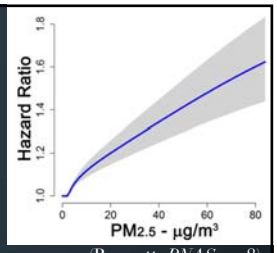
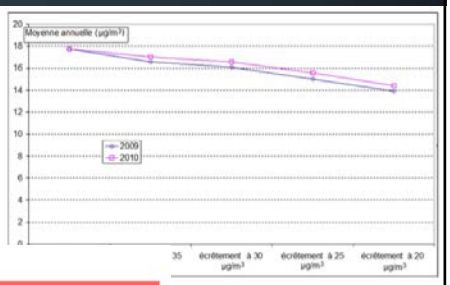
Regulating *extremes* or *mean values*?

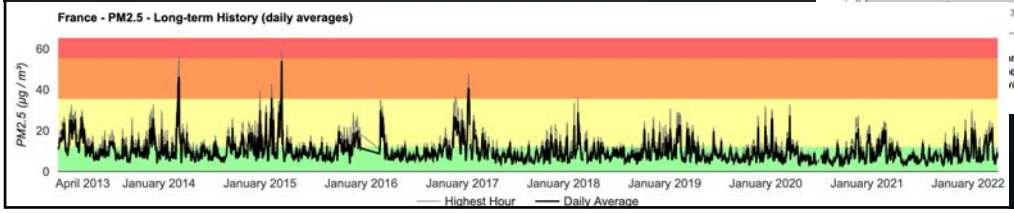
« Haut Comité de Santé Publique underlines that a policy focused on managing "peaks" has little impact on the long-term exposure of the population and that priority should be given to reducing chronic exposure. »

(HCSP, 2012) www.hcsp.fr/explore.cgi/avisrapportsdomaine?clefr=265



(Burnett, *PNAS* 2018)





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Which decrease in air pollution levels should be targeted?

$PM_{2.5}$ exposure reduction scenarios	Population $PM_{2.5}$ exposure		Health benefits concerning all-cause non-accidental mortality									
	Yearly average ($\mu g/m^3$)	5th–50th–95th percentiles ($\mu g/m^3$)	Δ_{NAC}[a,f]	95% CI	% of S2[b]	% of baseline cases[c]	95% CI	Mortality rate gain[d,f]	95% CI	Gain in life expectancy months[e]	95% CI
Grenoble conurbation (444,000 inhabitants)	13.9	10.2–14.6–16.2									
S1: "WHO guideline"	10.0	10.0–10.0–10.0	65	40–90	45%	2.5%	1.5–3.5%	25	15–34	4.5	2.8–6.3
S2: "No anthropogenic $PM_{2.5}$"	4.9	4.9–4.9–4.9	145	90–199	Ref.	5.6%	3.5–7.7%	55	34–76	10.0	6.1–13.9
S3: "Quiet neighborhood"	10.3	10.2–10.3–10.3	61	38–84	42%	2.3%	1.5–3.2%	23	14–32	4.3	2.6–5.9
S4: "-1 $\mu g/m^3$"	12.9	9.2–13.6–15.2	16	10–23	11%	0.6%	0.4–0.9%	6	4–9	1.1	0.6–1.5
S5: "-2 $\mu g/m^3$"	11.9	8.2–12.6–14.2	33	20–45	23%	1.3%	0.8–1.7%	12	8–17	2.1	1.3–2.9

(Morelli, *Env Int*, 2019)

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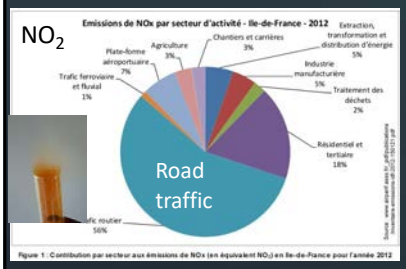
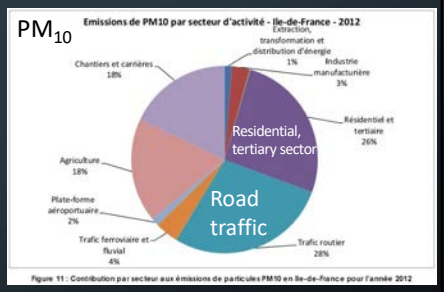
Sources of some primary air pollutants
(Ile de France, 2012)

NO_2



PM_{10}



(Airparif, 2016)

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Acting on urban heating: Dublin bituminous coal ban (1990)

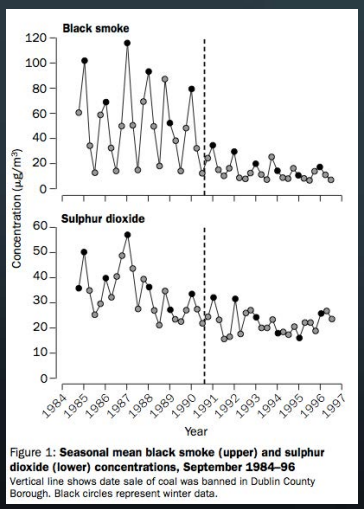
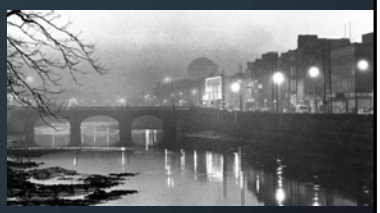


Figure 1: **Seasonal mean black smoke (upper) and sulphur dioxide (lower) concentrations, September 1984–96**
Vertical line shows date sale of coal was banned in Dublin County Borough. Black circles represent winter data.



	Variation *(after-before*)*
B*lack smoke concentration*	-70%
Respiratory mortality	-15.5%
Cardiovascular mortality	-10.3
Total non accidental mortality	-5.7%

*Change between the 7 year average *after* and the 7 year *before* the intervention

(Clancy, *Lancet*, 2002)

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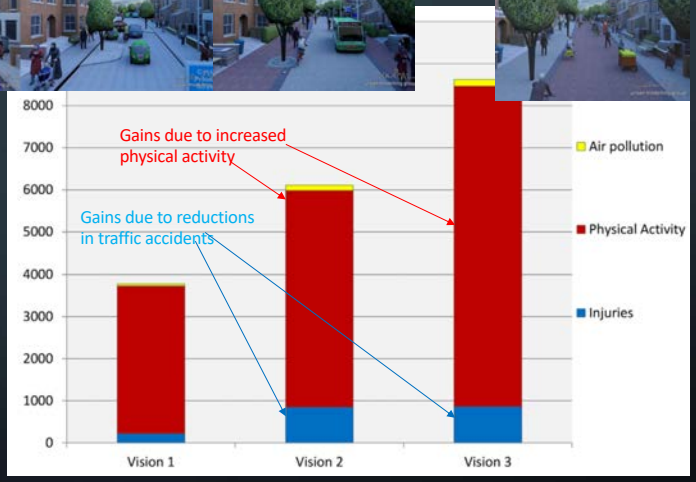
Expected impact of measures on road traffic (UK)

Health gain in DALYs (Disability-Adjusted life years gained)



(Woodcock, *PLoS One*, 2013)

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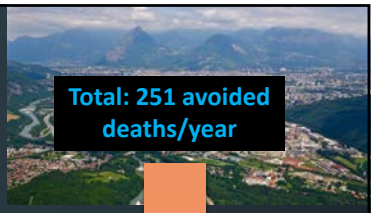
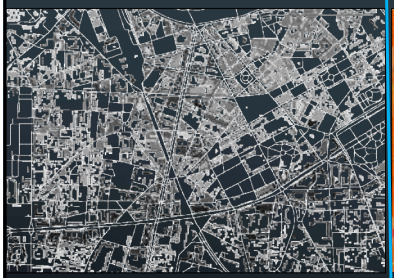
Current impact of fine PM exposure and expected impact of interventions on wood heating and road traffic (Grenoble urban area)



Initial situation (2016)

Population density (inhabitants/100 m^2)



Yearly impact: 145 deaths attributable to $PM_{2.5}$ exposure (total population of urban area: 440,000)

(Morelli, *Environ Int*, 2019)

Intervention (2016-2030)

Decrease by 94% of emissions due to inefficient wood-burning facilities

Concentration of $PM_{2.5}$ (µg/m^3)

158 deaths avoided through the increase in **physical activity**

S. Mathy
CNRS

93 deaths avoided because of the improvement of air quality

Yearly net benefit of interventions : **484€/inhab.**

(Bouscasse, *Environ Int*, 2022)

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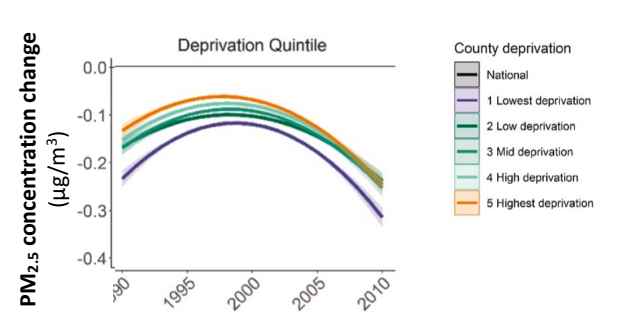
Do changes in air quality levels vary according to sociodemographic characteristics?



In the USA, improvements in air quality between 1990 and 2010 benefited more to the least socially deprived counties

(Wyatt, *Environ Int*, 2020)

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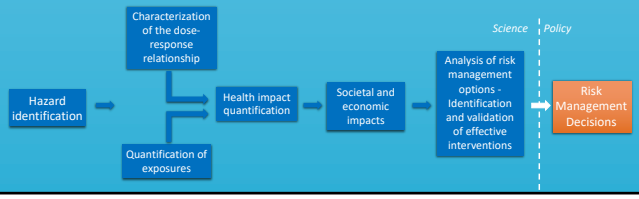
J. Risk management



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Atmospheric pollutants: some recent regulations

- 1952 : Episode de pollution de Londres
- 1955 : Air Pollution Control Act (USA)
- 1963 : Clean Air Act (USA), amendé en 1967, 1970, 1977, 1990
- 1974 : Décret relatif au contrôle des émissions polluantes dans l'atmosphère (France)
- 1980-92 : Directives européennes
  - 1980, 1985 : SO_2 et particules (TSP)
  - 1982 : plomb dans l'atmosphère
  - 1992 : ozone
- 1990 : Amendement du Clean Air Act (USA)
  - Limite annuelle : 15 µg/m³ pour $PM_{2,5}$ 100 µg/m³ pour NO_2
- 1996 : Loi sur l'air et l'utilisation rationnelle de l'énergie (France)
- 1999 : Directive européenne sur SO_2, NO_2, PM_{10} et le plomb
  - Limite annuelle (UE) : 40 µg/m³ pour PM_{10} (janvier 2005)
- 2002 : Directive européenne sur le bruit
- Avril 2008 : Directive européenne sur PM_{10} et $PM_{2,5}$
  - Valeur *cible* annuelle pour 2010 : 25 µg/m³ pour $PM_{2,5}$
  - Valeur *limite* annuelle pour 2015 : 25 µg/m³ pour $PM_{2,5}$

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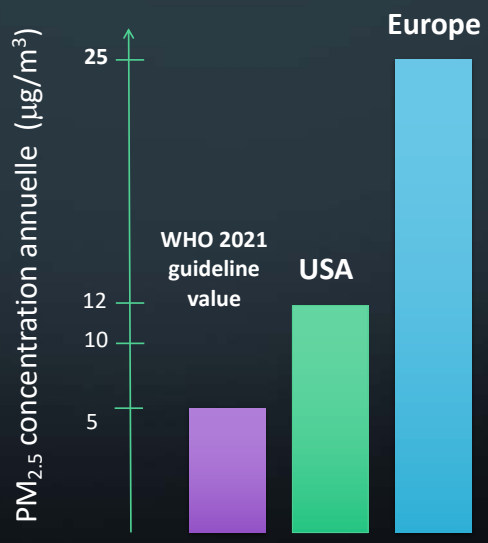
Some regulations and guidelines on $PM_{2.5}$ yearly levels



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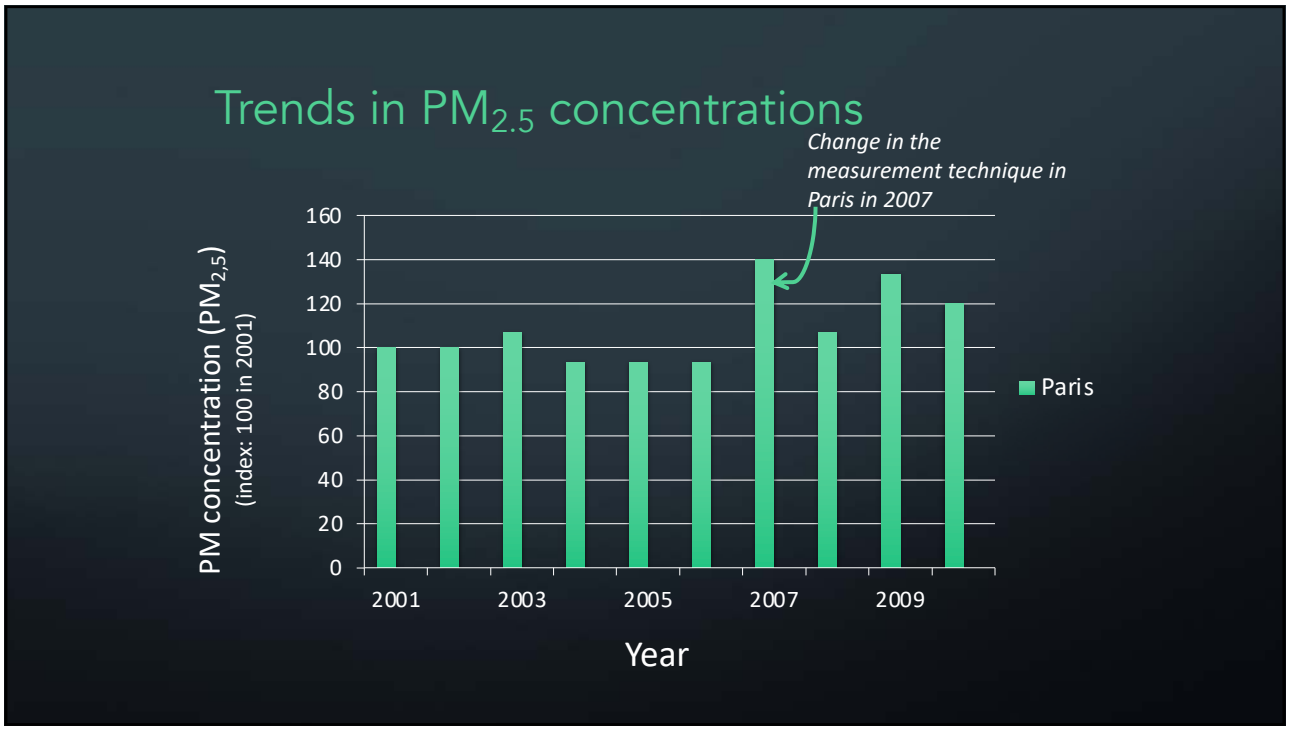
Trends in PM2.5 concentrations
Change in the measurement technique in Paris in 2007
PM concentration (PM2,5)
(index: 100 in 2001)
160
140
120
100
80
60
40
20
0
2001
2003
2005
2007
2009
Year
Paris

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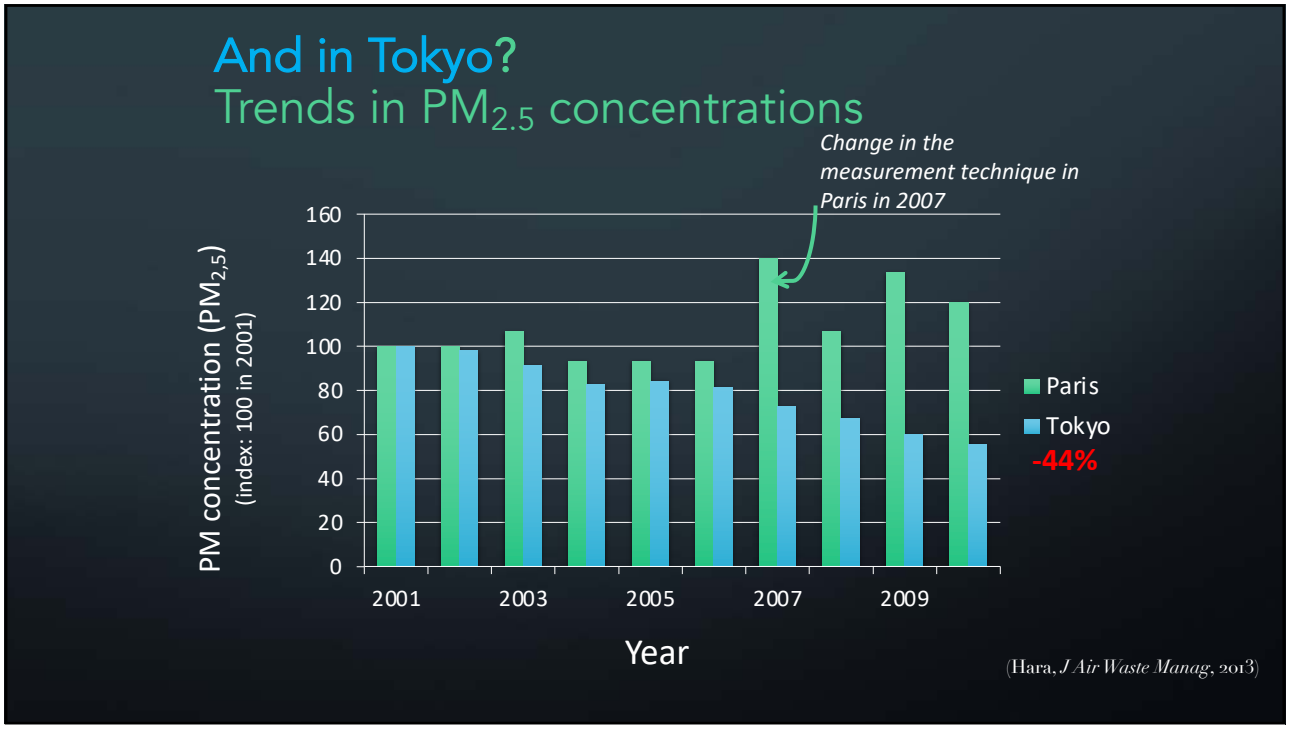
And in Tokyo?
Trends in PM2.5 concentrations
Change in the measurement technique in Paris in 2007
PM concentration (PM2,5)
(index: 100 in 2001)
160
140
120
100
80
60
40
20
0
2001
2003
2005
2007
2009
Year
Paris
Tokyo
-44%
(Hara, J Air Waste Manag, 2013)

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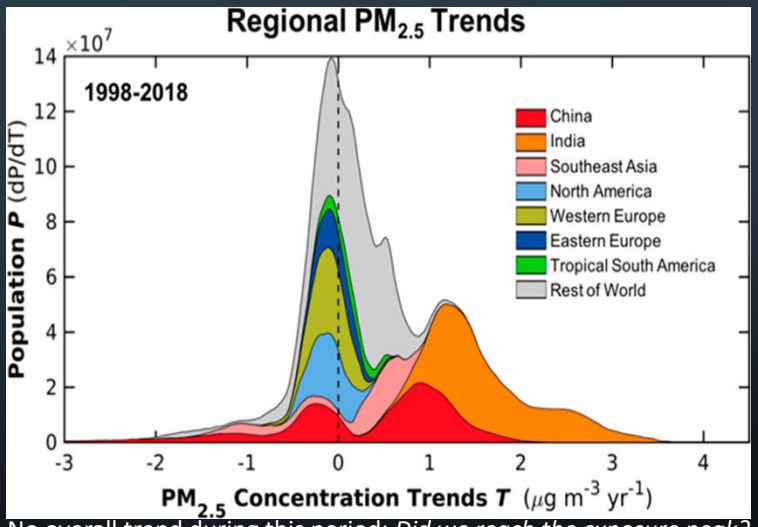
Regional trends in $PM_{2.5}$ levels (1998-2018)



1998-2018 trend:
Eastern North America: −0.28 µg/m^3/yr
Europe −0.15 µg/m^3/yr
India 1.13 µg/m^3/yr
Globally: 0.04 µg/m^3/yr

2011-2018 trend:
China: −3.37 µg/m^3/yr

No overall trend during this period: *Did we reach the exposure peak?*

(Hammer MS, *Env Sci Tech*, 2020)

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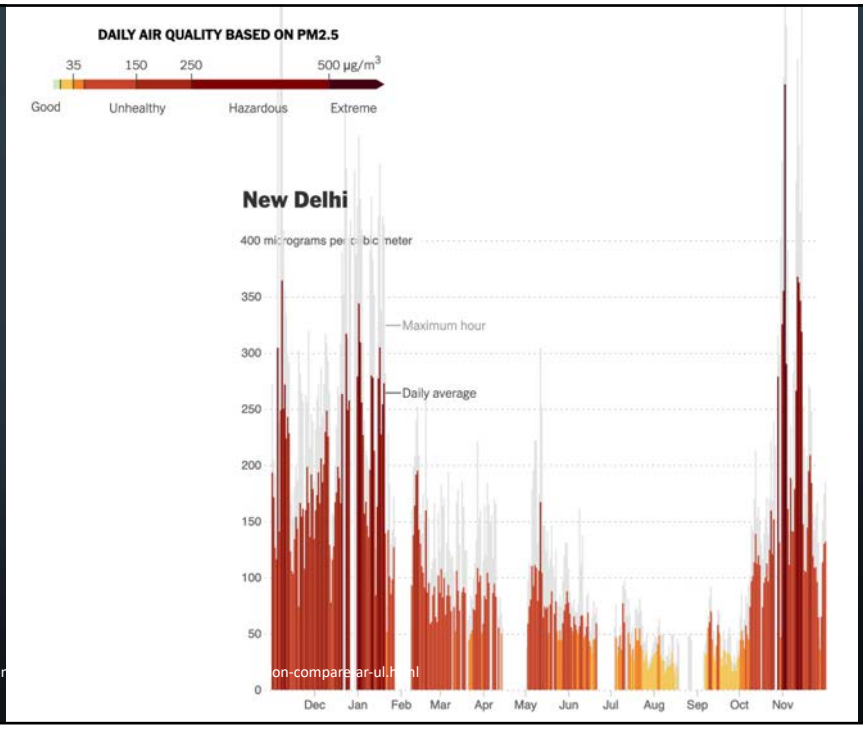

https://www.nytimes.com/ir

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Conclusion

- Various approaches allowed to identify various effects of atmospheric pollution (in particular, but not only, $PM_{2.5}$) during the last decades
  - Before-after studies, temporal ecological studies (time-series), cohort studies…
- Atmospheric pollutants have a certain effect on non-accidental mortality, cardiovascular and respiratory morbidity.
  - Huge societal cost
  - Frail people but not only them are affected
  - Large mortality displacement: not only frail people are impacted
  - No evidence of a threshold effect
- Other likely or very likely effects of $PM_{2.5}$, e.g., on foetal growth, preeclampsia, on the central nervous system, possibly type II diabetes
- Actions on various sources of PM have been developed in several parts of the world in the past (targeting e.g., road traffic, residential sources or both). Such actions are likely to be cost-efficient.

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The relations between human health and the environment in the Anthropocene

Course overview

COLLÈGE DE FRANCE 1530

#1 – 31 March 2022
Inaugural lecture: Causes and external conditions of diseases and health

#2 - 6 April 2022
Lead: the oldest enemy of human health

Seminar: **Lead, legal poison: uses and regulations of toxic in the nineteenth century**
Pr. Judith Rainhorn, Université Paris-1 Panthéon-Sorbonne (Paris)

#3 - 13 April 2022
Fine particulate matter: effects on mortality and cardiovascular and respiratory morbidity

Seminar: Air pollution effects on the central nervous system
Pr. Marc Weisskopf, Cecil K. and Philip Drinker Professor of Environmental Epidemiology and Physiology, Harvard TH Chan School of Public Health (Boston)

#4 - 20 April 2022
Fine particulate matter: new metrics, recently identified targets

Seminar: The Human Sensor – Toxicology in Real People in the Real World
Pr. Ian Mudway, Imperial College London, MRC for Environment and Health (London)

#5 - 11 May 2022
'Legacy' endocrine disruptors: the convergence between basic biology, (eco)toxicology, clinical research and epidemiology

Seminar: Endocrine disruption and nuclear receptors: mechanisms and impact on health
Dr. William Bourget, Centre de Biologie Structurale, Univ Montpellier, CNRS, Inserm (Montpellier)

#6 - 18 May 2022
Contemporary endocrine disruptors: assessing the health effects of non-persistent compounds

Seminar: Bad cocktails – the evaluation of combined exposures
Pr. Andreas Kortenkamp, Brunell University (London)

#7 - 25 May 2022
The Exposome: Promises and Challenges of a New Concept

Seminar: Biosurveillance de la population vivant en France.
Dr. Clémence Fillol, Santé publique France

#8 – 1 June 2022
A Global Vision: The Burden of Disease Attributable to the Environment

Seminar: Causality in public health research
Pr. Federica Russo, Philosophe des Sciences, Techniques, et Information, Université d'Amsterdam

#9 - 8 June 2022
Climate change and human health

Seminar: on the Anthropocene concept
Dr. Jean-Baptiste Fressoz, CNRS et EHESS

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