SCIENCE DE LA DURABILITÉ

Identification of hazards and management of risks induced by environmental factors in the Anthropocene era (IDANGER)

1. Introduction – Context and concepts

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Master TRANSFORM
ENS-PSL, CERES
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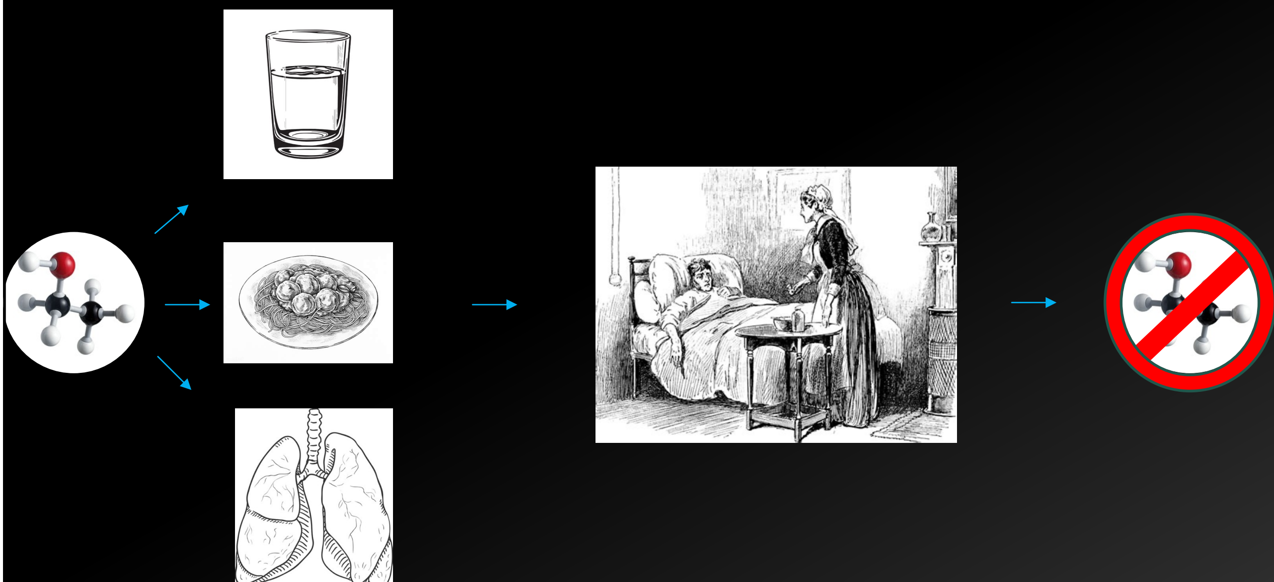
Schematic course outline



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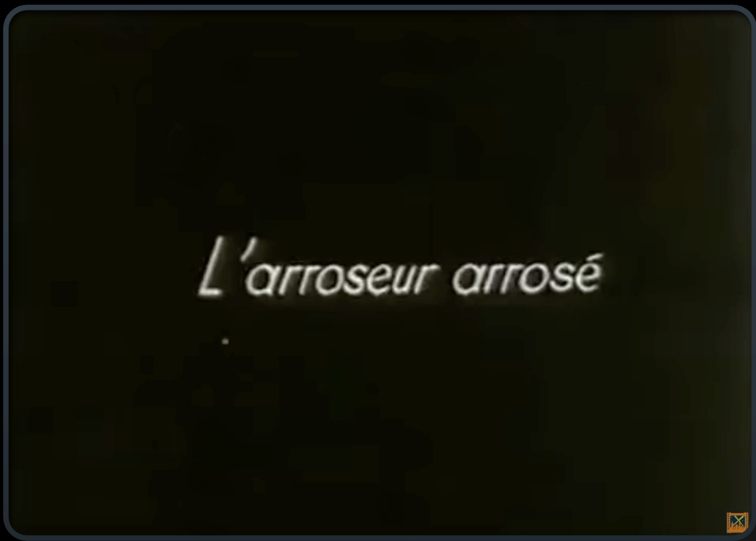

Course outline (visual)

(Lumière brothers, 1895)

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Andrew Kehoe

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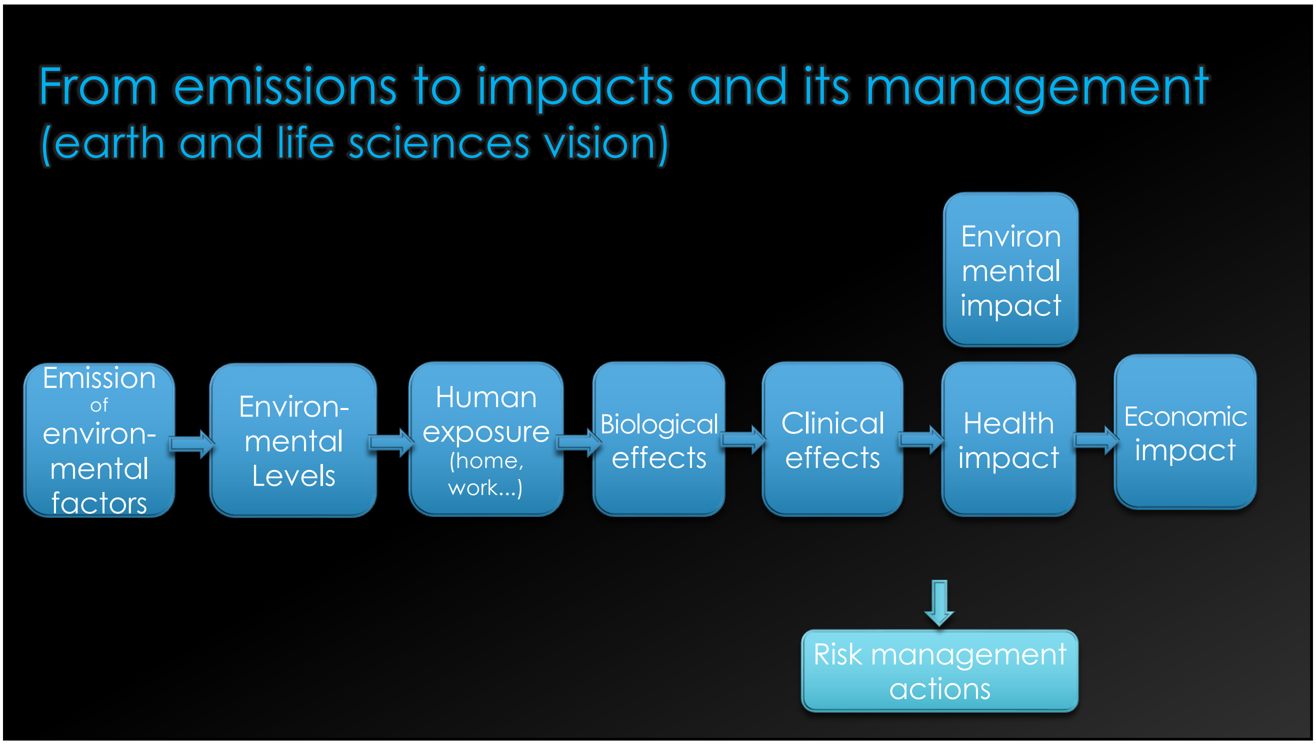
From emissions to impacts and its management
(earth and life sciences vision)
Environ mental impact
Emission of environ-mental factors
Environ-mental Levels
Human exposure (home, work...)
Biological effects
Clinical effects
Health impact
Economic impact
Risk management actions

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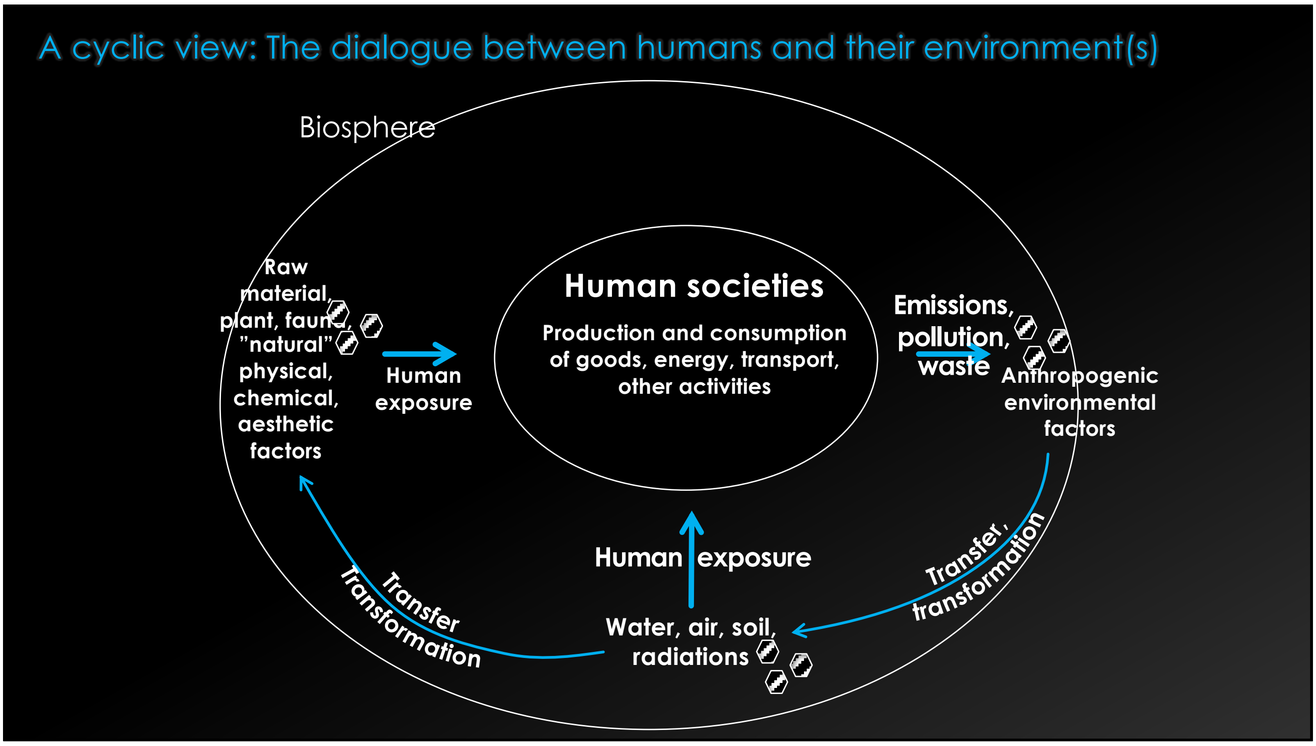
A cyclic view: The dialogue between humans and their environment(s)
Biosphere
Human societies
Production and consumption of goods, energy, transport, other activities
Raw material, plant, fauna, "natural" physical, chemical, aesthetic factors
Human exposure
Emissions, pollution, waste
Anthropogenic environmental factors
Transfer, transformation
Human exposure
Water, air, soil, radiations
Transfer
Transformation

6

A dialogue between technology and progress

Technical advances ⟷ **Societal progress**

How can societies make sure that **technical advances** do not lead to **decreases in well-being**, **inequity** (social, territorial, linked to origin or gender…), **environmental disruptions** and other hidden impacts and costs?

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A more societal perspective

Production of a « new » factor

Societal diffusion

- Across economic sectors
- Across socio-demographic groups

Environmental diffusion

- Across environmental compartments
- Across continents, between North and South…

Hazard identification

Gradual (and generally partial) restrictions of use

Across

- economic sectors
- socio-demo-graphic groups
- countries

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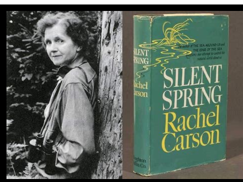
A more societal perspective



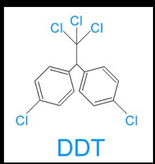
Synthesis of knowledge on environmental impacts (Carson, 1962)

Hazard identification

Societal diffusion

Across economic sectors | Across socio-demographic groups

Production of a « new » factor



Insecticidal properties (Müller, 1939)

Gradual (and generally partial) restrictions of use

Across

economic sectors | socio-demo-graphic groups | countries

Environmental diffusion

Across environmental compartments | Across continents, between North and South…

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Lecture overview

I. **Context**

Changing environment – The Anthropocene, the great acceleration

Changing populations – The epidemiologic transition

II. Connecting environment and human health

General arguments regarding the influence of the environment on health

Disciplines and approaches

III. Some concepts of risk management

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I. The human and environmental context of the Anthropocene

1. Changing environment – The Anthropocene, the great acceleration
2. Changing populations – The epidemiologic transition

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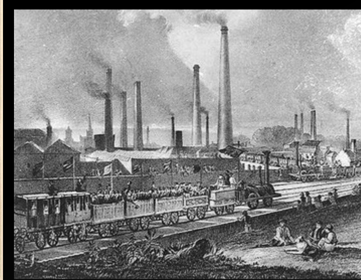
The Industrial Revolution (1784-)

Hokusai, 1830



An energy revolution:

The transition from a society based essentially on human and animal power and the wind…

…to a society drawing its energy from coal (18th Century) and then oil (from the end of the 19th Century).

A revolution of fossil fuels

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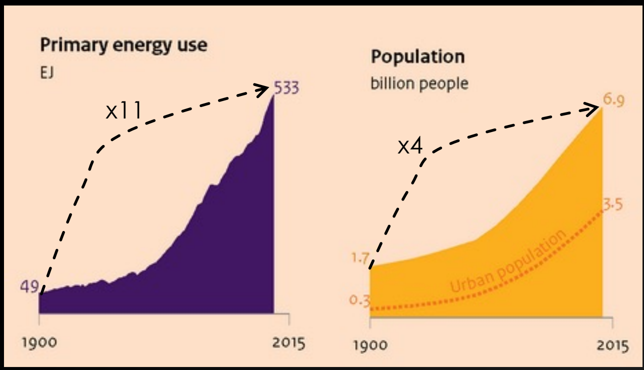
The Industrial Revolution (1784-)



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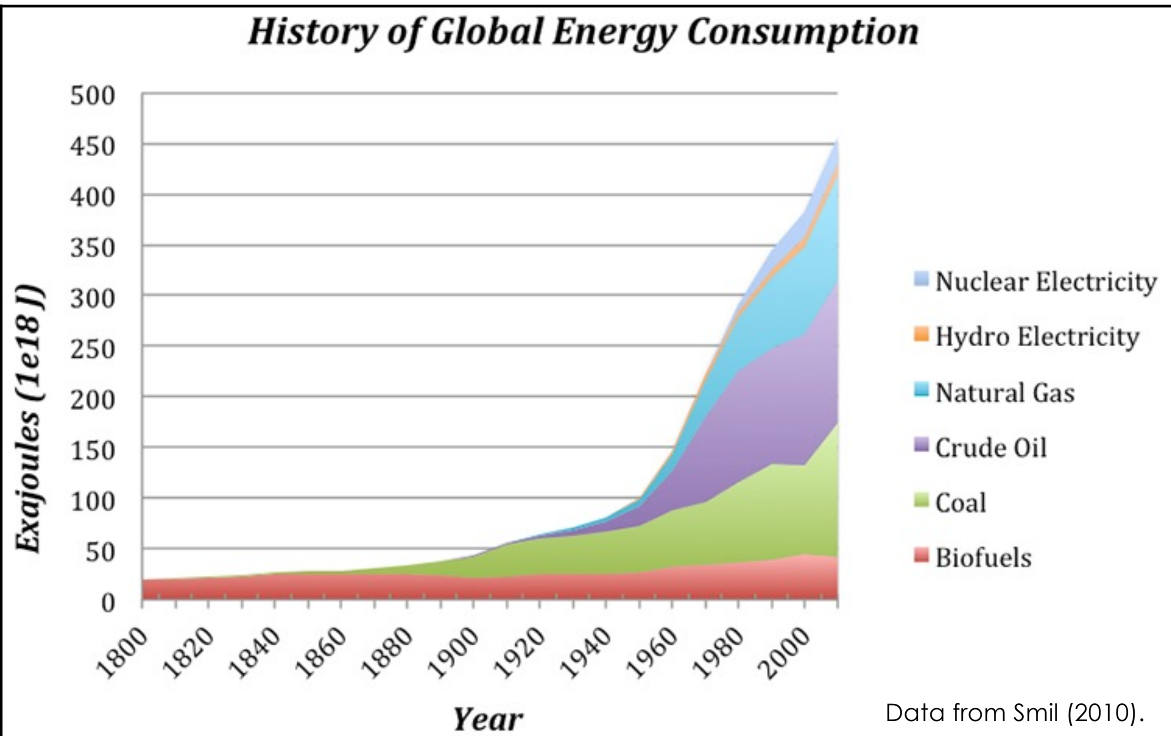

Data from Smil (2010).

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The Anthropocene (Crutzen & Stoermer, 2000)

- Stoermer and Crutzen suggested that our epoch was characterized by an unprecedented influence of humans on Earth and its atmosphere at all scales
- Possible starting point: that of the **industrial Revolution** (1784, invention of the steam engine)
- Geology:
  - Current era: Cenozoic
    - Period: Quaternary
      - Epoch: *Holocene* (last 11,700 years) – that of Human history
  - The international commission on stratigraphy (ICS) and the International Union of Geological Sciences refused (2024) to baptize a new epoch "Anthropocene"
- Competing names and concepts:
  - The prefix anthropo assigns responsibility to species, not to "guilty" parties (industrialists, capitalists, colonizers, males, white people). The term hides inequalities.
  - Capitalocene (Andreas Malm), Chthulucene (Donna Haraway, 2015), urbanocene (Chwalczyk, 2020), noosphere (Teilhard de Chardin & LeRoy, 1924)…

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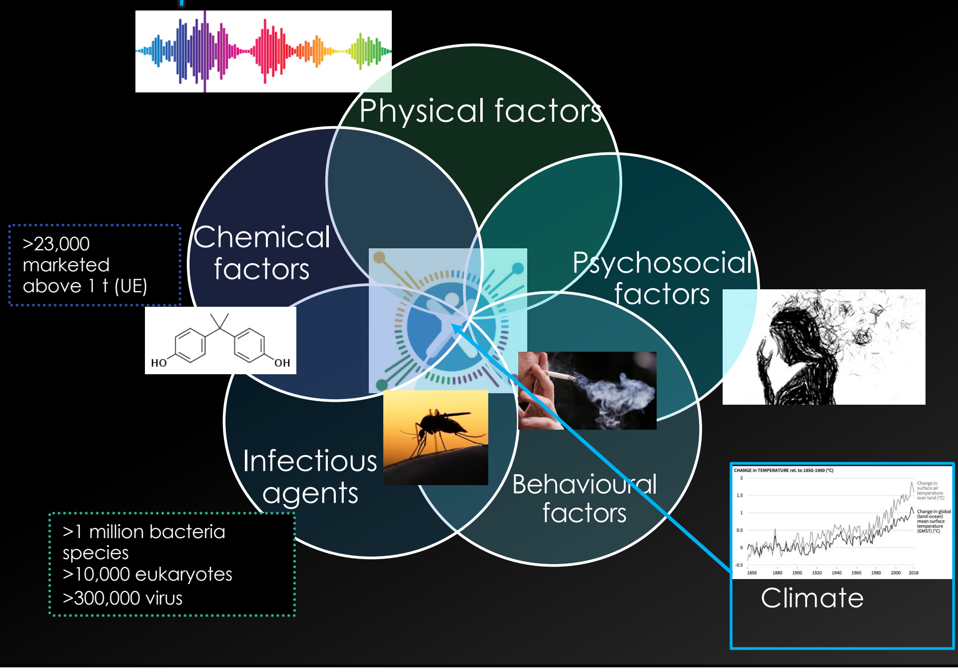
The exposome and its domains



The exposome encompasses all exposures that an individual encounters from conception onwards (from Wild C, 2005)

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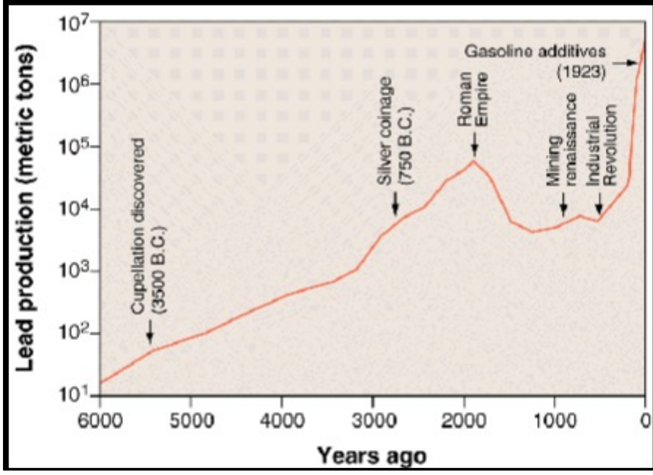
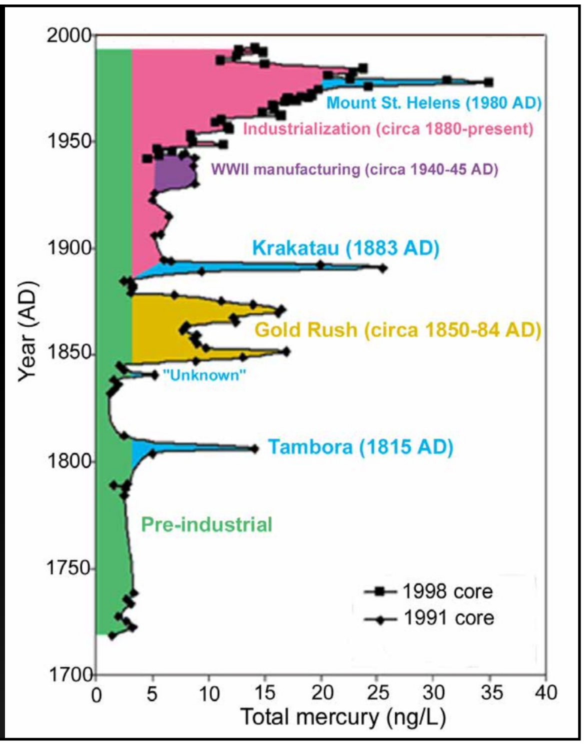
Mercury

Lead production throughout history





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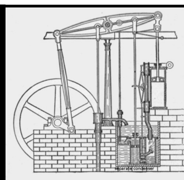
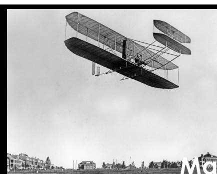
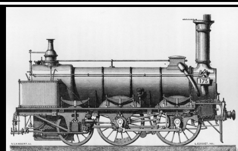
Transportation

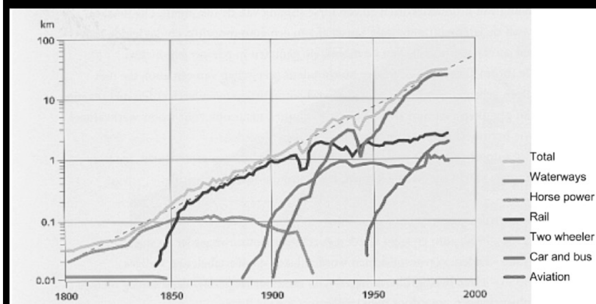




Rafts	Shoes	Wheel	Cata-marans	Compass	Steam engine	Bike Trains and metros	Plane	Mass production of automobiles
-20,000 BCE	-6,500 BCE *(ca)*	-3500 BCE	-3000 BCE	+1044	1784		1903	



Distance travelled per person per day in France



(From Gaudry, 2010)

Connections with:
- Access to food
- Air quality
- Noise
- Other dimensions of the quality of the environment
- Traffic accidents
- Social inequalities
- Physical activity

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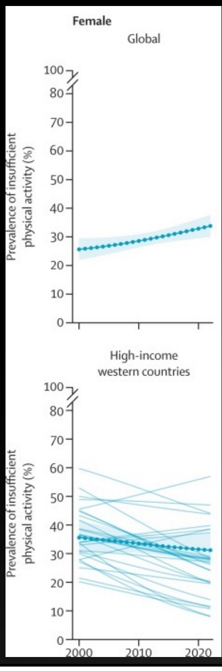
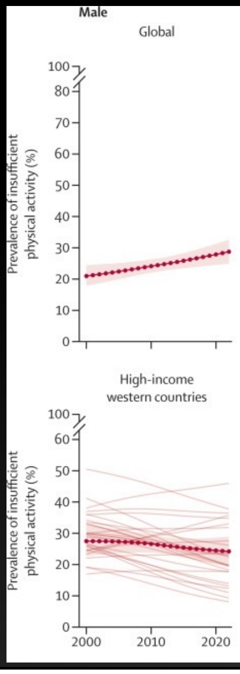
Physical activity

Trends in insufficient physical activity among adults





(Strain, 2024)

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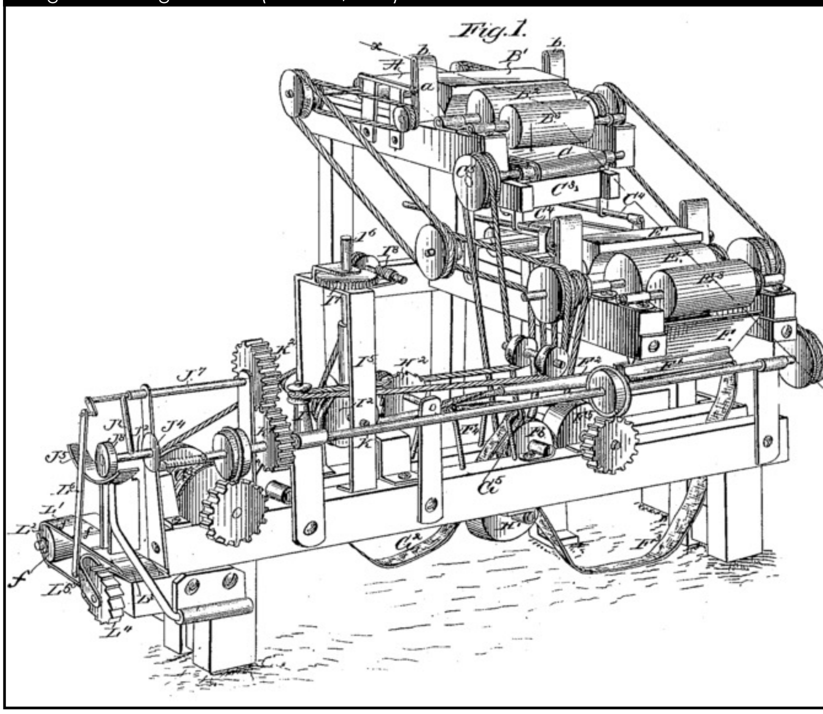
Cigarette rolling machine (Bonsack, 1880)



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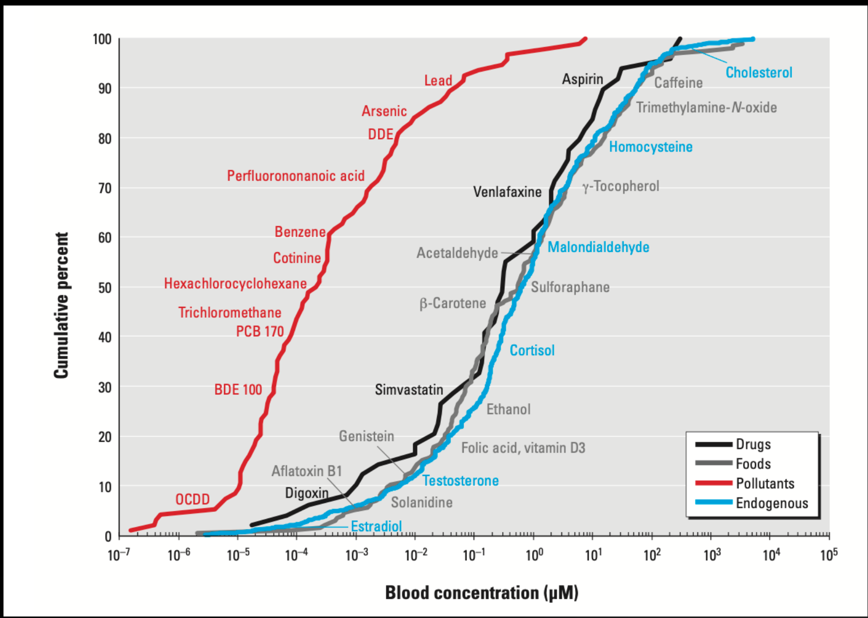
Some substances found in the blood



(Rappaport, *Env Health Perspect*, 2014)

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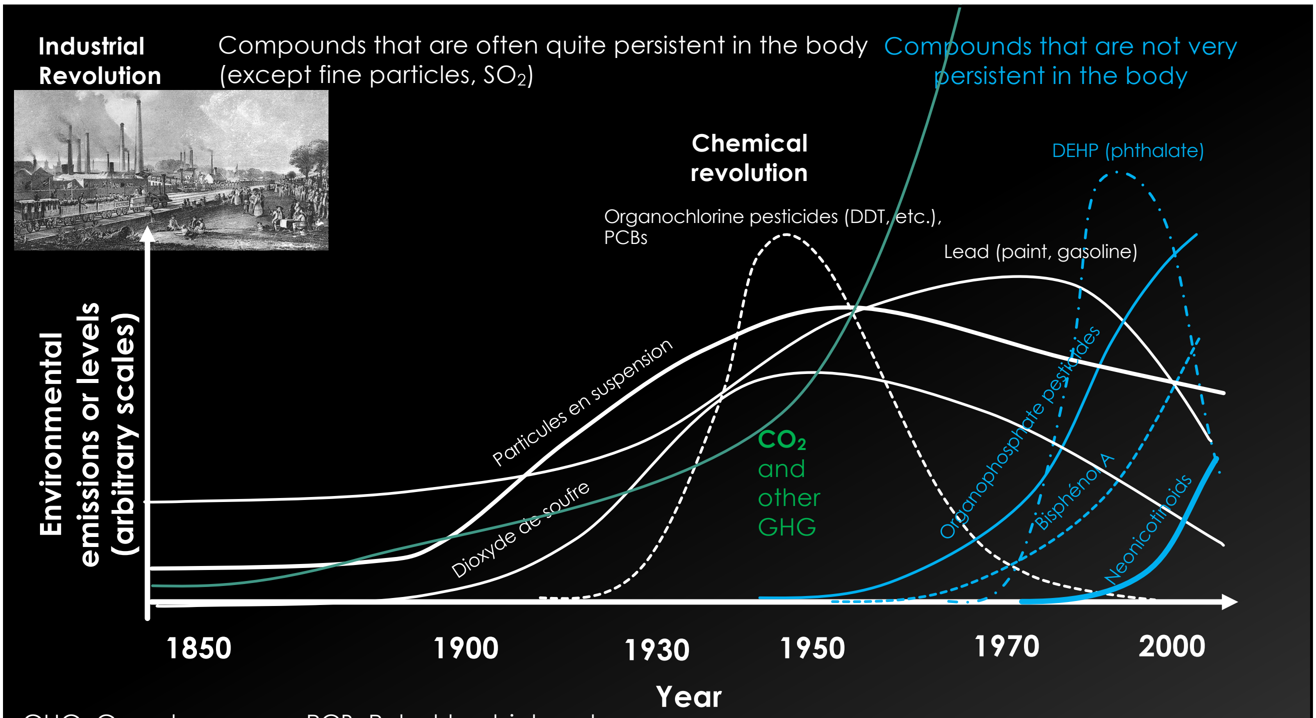

GHG: Greenhouse gas; PCB: Polychlorobiphenyls.

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France	1750	2020
Population living from agriculture	67%	1,5%
Population living in rural areas	80%	20%

(Millet, 1857)

(Bong Joon-Ho, 2019)

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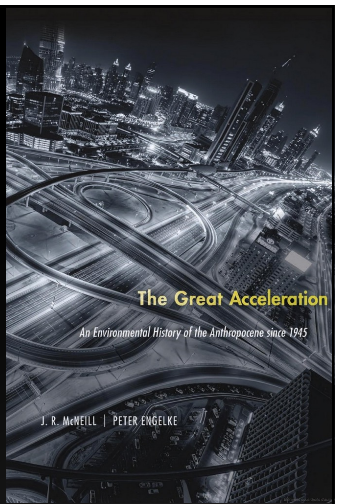
The great acceleration (McNeill, 2014)



The **Great Acceleration** is the dramatic, continuous and roughly simultaneous surge across a large range of measures of human activity, first recorded in the mid-20th century and continuing into the early 21st century.

population, economics, water usage, food production, transportation, technology, greenhouse gases, surface temperature, and natural resource usage.

Since 1950, these trends have been increasing significantly

Characteristics of human societies	Multiplicative growth factor between 1890 and 1990
World population	4
World Urban Population	13
Industrial production	40
Energy used	13
Coal production	7
Tonnage of synthetic chemicals	1,000*
Carbon dioxide (CO_2) emissions	17
Sulfur dioxide (SO_2) emissions	13
Lead emissions to the atmosphere	8

* 1,000-fold increase in chemical production (in tons) between 1930 and 2000

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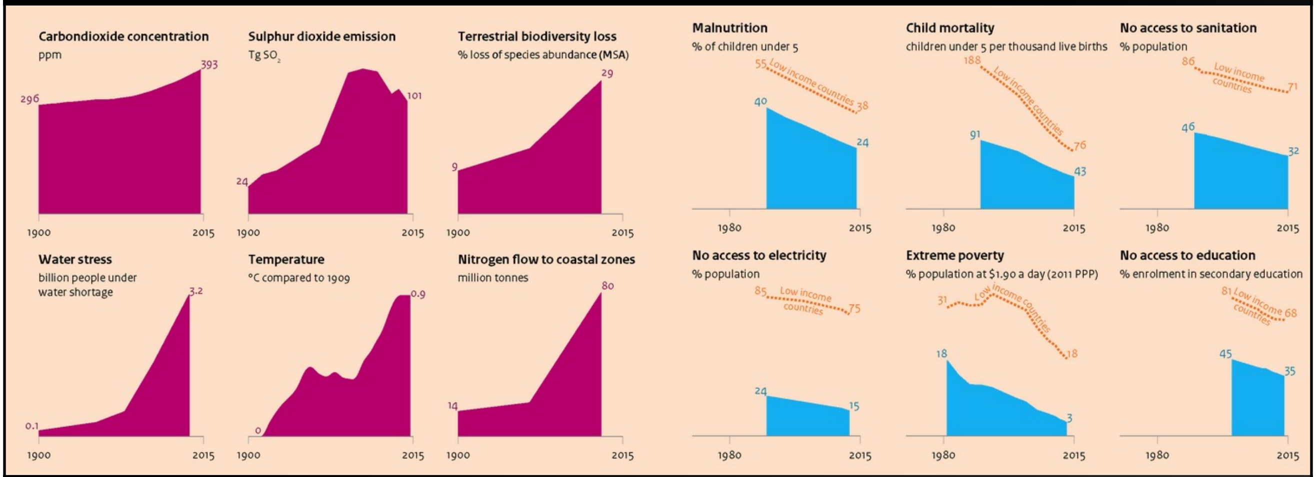

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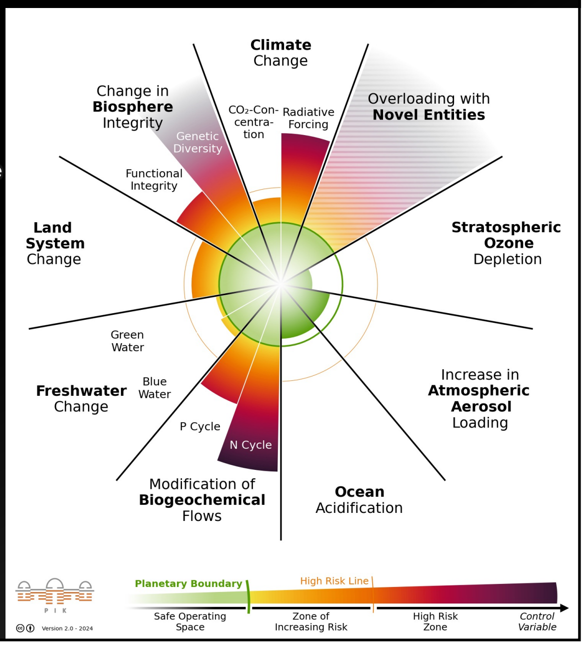
The planetary boundaries
(Rockström et al., 2009)

- The Planetary Boundaries are the « *safe limits* » for human pressure on the nine critical processes which together maintain a stable and resilient Earth.
- For novel (chemical) entities, the indicator corresponds to the percentage of synthetic chemicals released to the environment without adequate safety testing (currently not available). For aerosols, the control variable corresponds to aerosol optical depth.
- Together the boundaries mark a critical threshold for increasing risks to people and the ecosystems we are part of. Only by respecting all nine boundaries can we maintain the safe operating space for human civilization.
- It is currently estimated that 6 of the 9 limits are crossed (Richardson, 2023). Note that human health does not seem to always be considered (e.g., regarding atmospheric aerosols).
- The planetary boundaries can be seen as a concept at the science-policy interface integrating most currently identified broad environmental



See https://www.planetaryhealthcheck.org

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The development of "public relations" and of large-scale strategies to manufacture consent

- Edward Bernays, considered the father of public relations

  Member of the US Committee on Public information (CPI) during world war I "There was one basic lesson I learned in the CPI—that efforts comparable to those applied by the CPI to affect the attitudes of the enemy, of neutrals, and people of this country could be applied with equal facility to peacetime pursuits. In other words, what could be done for a nation at war could be done for organizations and people in a nation at peace." (psychological Warfare)

  Later involved in efforts to develop female smoking ("Torches of freedom", 1929)

- W. Lippmann (*Public Opinion* book, 1922) advocated for the manufacture of consent, defined as **the management of public opinion**, which he felt was necessary for democracy to flourish, since he felt that public opinion was an irrational force
- Large public relations campaigns done to promote smoking (Michaels D, Doubt is their product, 2008), dismiss environmental health issues (Conway and Oreskes, Merchants of doubt, 2010)
- 21st Century: Development of *individually targeted marketing* (Internet technologies)
- These approaches can also be used for public health campaigns (Wakefield, Lancet, 2010)

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I. The human and environmental context of the Anthropocene

1. Changing environment – The Anthropocene, the great acceleration
2. Changing populations – The epidemiologic transition

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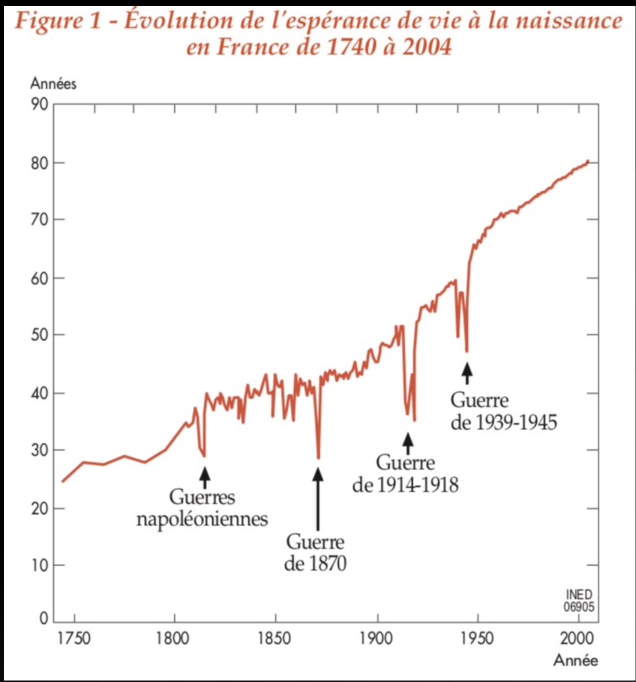

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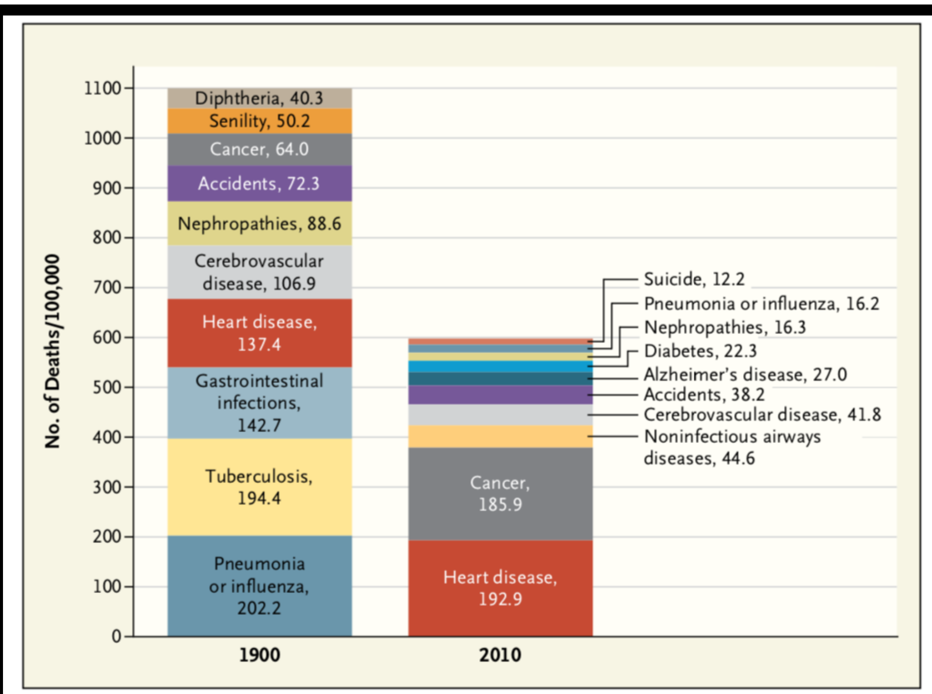

Top 10 Causes of Death: 1900 vs. 2010. (USA)

(Jones, NEJM, 2012)

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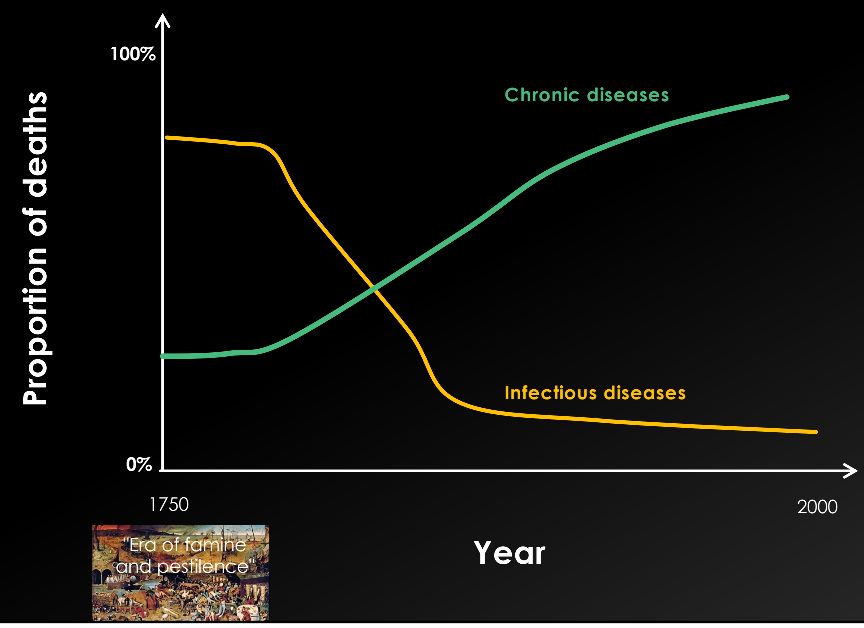
The epidemiological transition



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Le choléra lui prend son mari ; la voilà
Veuve avec la misère et quatre enfants qu'elle a.
Alors, elle se met au labeur comme un homme.
Elle est active, propre, attentive, économe ;
Pas de drap à son lit, pas d'âtre à son foyer ;
Elle ne se plaint pas, sert qui veut l'employer,
Ravaude de vieux bas, fait des nattes de paille,
Tricote, file, coud, passe les nuits, travaille
Pour nourrir ses enfants ; elle est honnête enfin.
Un jour, on va chez elle, elle est morte de faim.

Victor Hugo
(écrit en 1840)
In *Les Contemplations*

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Résumé

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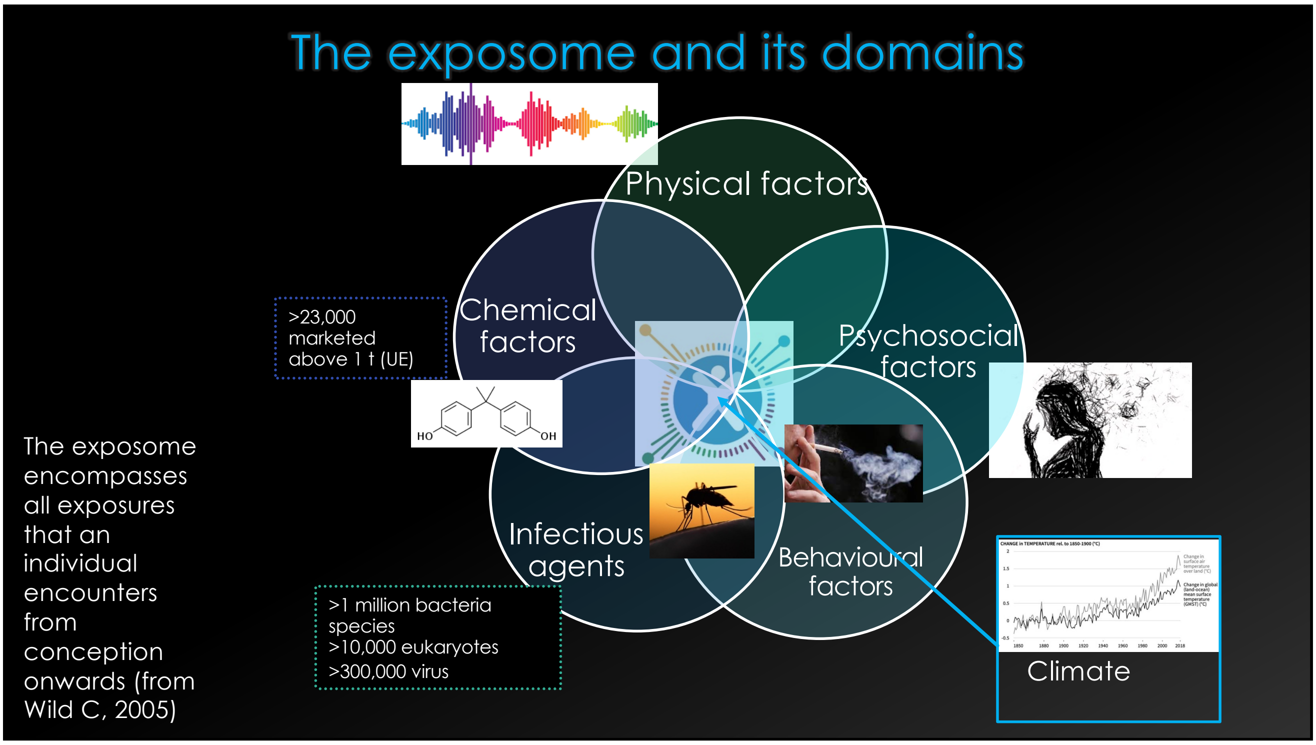

The exposome and its domains
Physical factors
Chemical factors
Psychosocial factors
Infectious agents
Behavioural factors
>23,000 marketed above 1 t (UE)
HO
OH
>1 million bacteria species
>10,000 eukaryotes
>300,000 virus
Climate
The exposome encompasses all exposures that an individual encounters from conception onwards (from Wild C, 2005)

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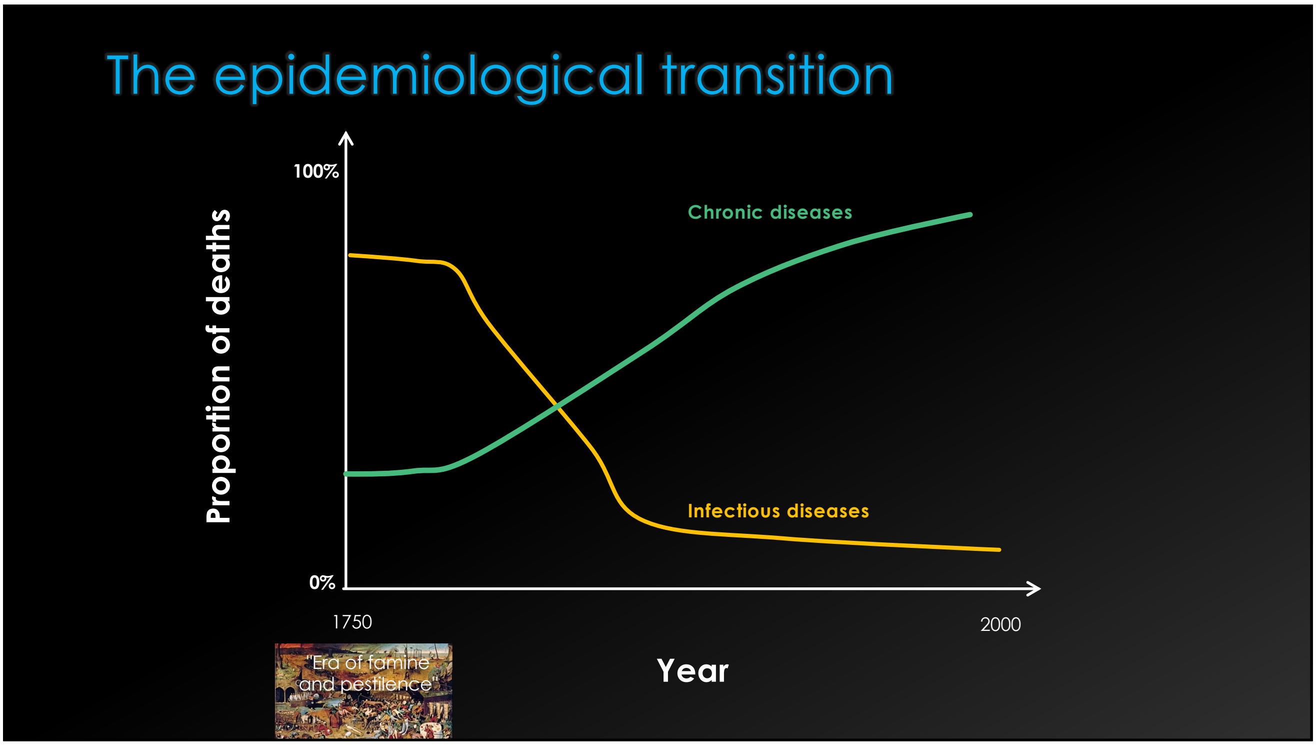

The epidemiological transition
100%
Proportion of deaths
Chronic diseases
Infectious diseases
0%
1750
2000
Year
"Era of famine and pestilence"

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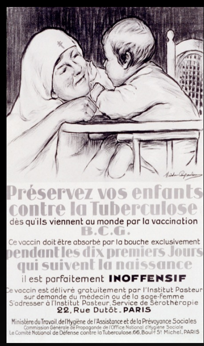
The drivers of the epidemiological transition

Sewer

Housing

Cold chain

Vaccination



Antibiotics (1940-)

Transforming agriculture

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II. Connecting the environment and human health

1. General arguments regarding the influence of the environment on health
2. Disciplines and approaches

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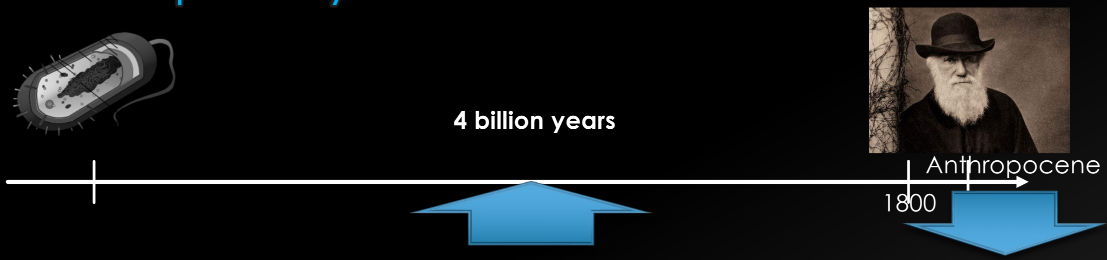
In the long term, the human species has been shaped by its environment



Climate, environment, viruses, bacteria, flora, fauna...

In the shorter term, it has profoundly modified this environment (biodiversity, climate, emissions of chemical substances, etc.).

Can these changes affect our health?

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Heritability§ of traits and selected chronic diseases

Phenotype	**Heritability** (from familial studies)
Type 1 diabetes	60-90 %
Eye colour	80 % *
Waist	80 %
Autism spectrum disorders	80 % ***
Schizophrenia	70-80 %
Crohn's disease	60-80 %
Multiple Sclerosis	30-80 %
Thyroid cancer	53 % **
Cholesterol (HDL)	50 %
Obesity (BMI)	40-60 %
Type 2 diabetes	30-60 %
Breast Cancer	25** - 30 %
Testicular cancer	25 % **
Cancer of the nervous system	12 % **
Lung cancer	8 % **
Leukaemia	≈ 1 % **

§ Share of risk variability due to genetic inheritance

From: Visscher *et al.*, 2012, unless otherwise indicated; * Bräuer et Chopra, 1978 ; ** Czene *et al.*, 2002 ; *** Sandin *et al.*, 2017.
See Slama, Le Mal du Dehors, Quae, 2017.

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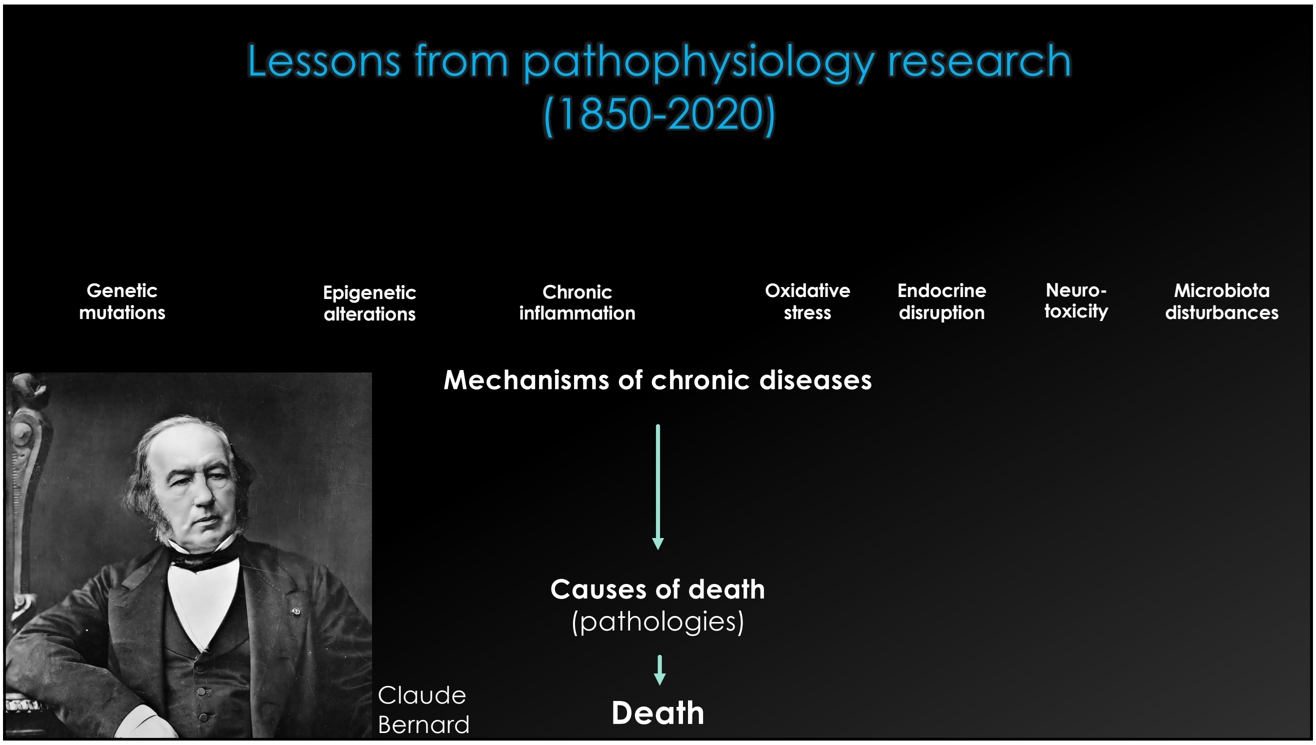
Lessons from pathophysiology research
(1850-2020)
Genetic mutations
Epigenetic alterations
Chronic inflammation
Oxidative stress
Endocrine disruption
Neuro-toxicity
Microbiota disturbances
Mechanisms of chronic diseases
Causes of death
(pathologies)
Death
Claude Bernard

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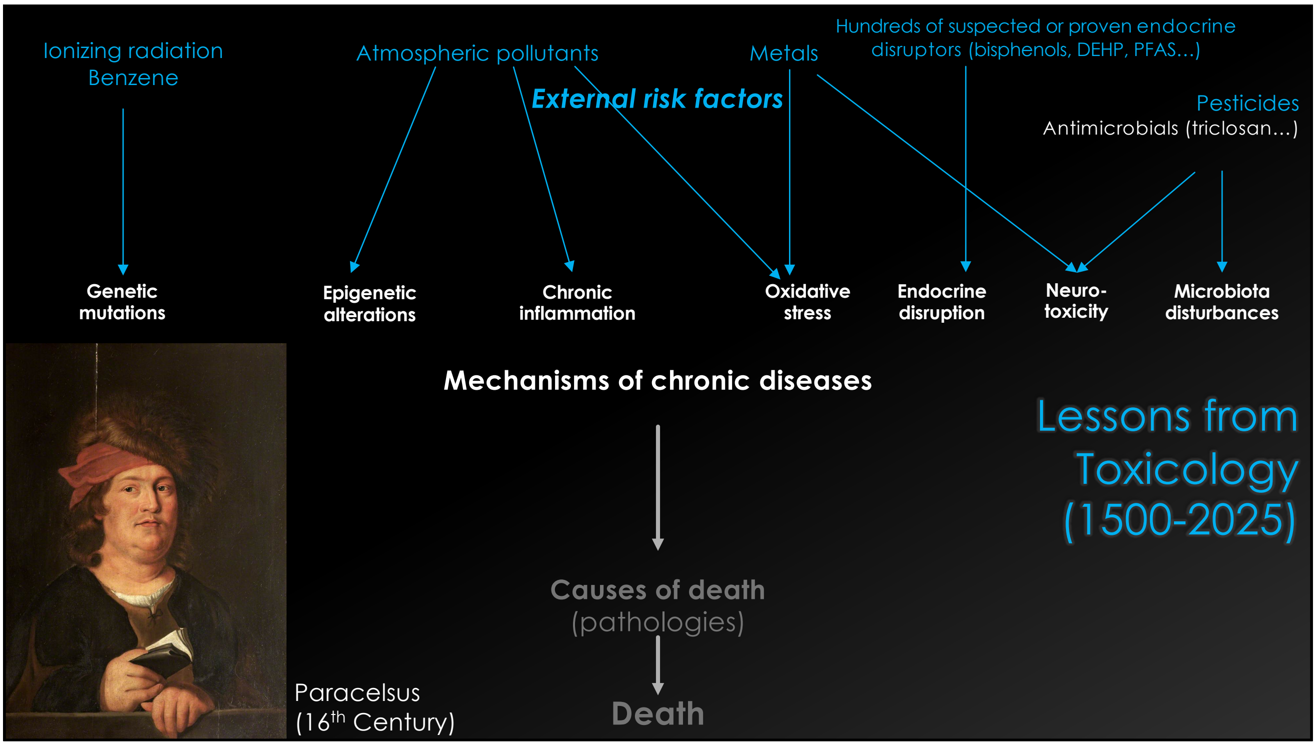
Ionizing radiation
Benzene
Atmospheric pollutants
Metals
Hundreds of suspected or proven endocrine disruptors (bisphenols, DEHP, PFAS…)
External risk factors
Pesticides
Antimicrobials (triclosan…)
Genetic mutations
Epigenetic alterations
Chronic inflammation
Oxidative stress
Endocrine disruption
Neuro-toxicity
Microbiota disturbances
Mechanisms of chronic diseases
Lessons from Toxicology (1500-2025)
Causes of death
(pathologies)
Death
Paracelsus
(16th Century)

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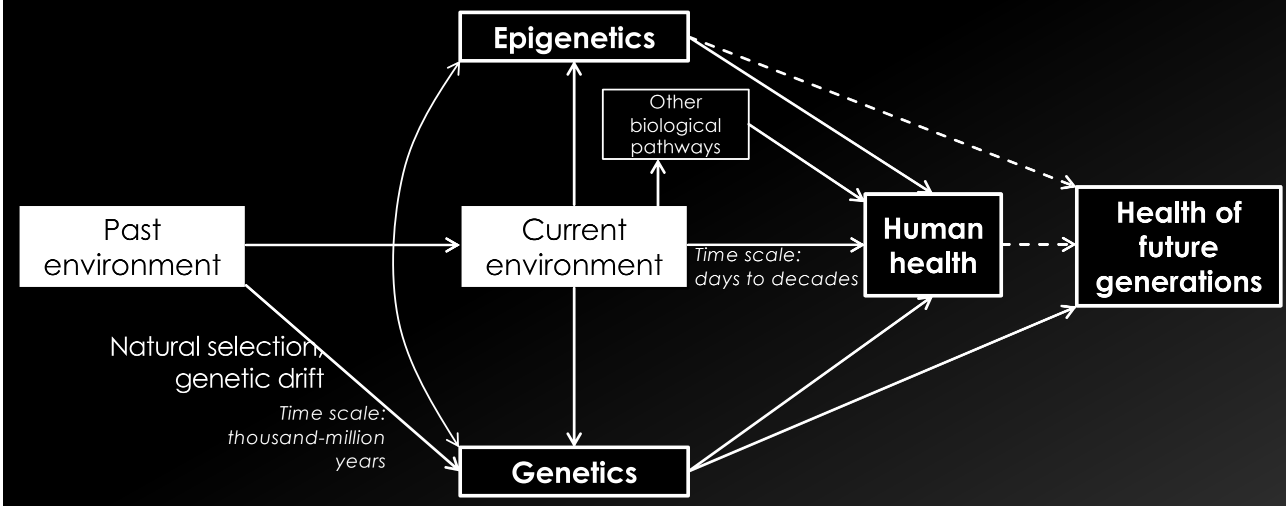
Environment, genes on health: long-term vision



(From Slama, 2017)

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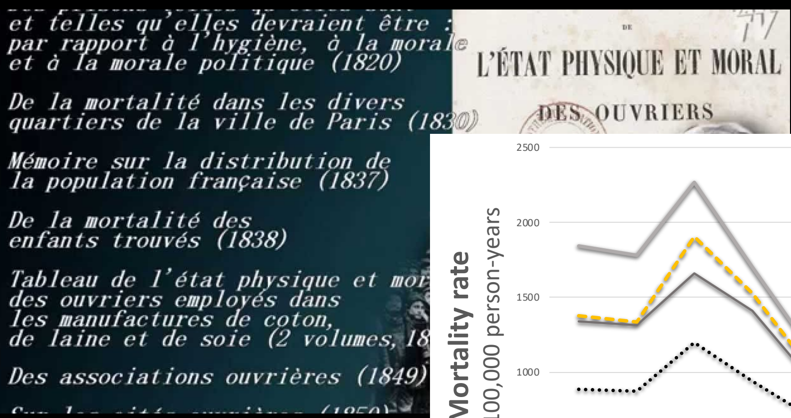
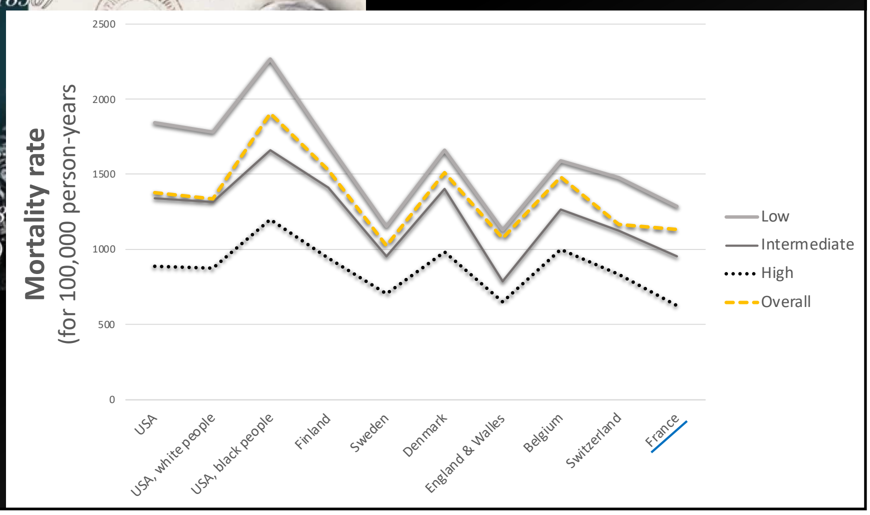
Social health inequalities



Louis-René de Villermé
(1782-1863)



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General arguments regarding the influence of the environment on health - *overview*

- The long-term view / evolution
- Family studies / heritability
- GWAS (Genome-wide association studies) of chronic diseases
- Understanding of the fine-scale mechanisms of chronic diseases and toxicological work on the induction of these mechanisms by various environmental contaminants
- Social health inequalities
- The examples of tobacco, alcohol, atmospheric pollutants…

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II. Connecting the environment and human health

1. General arguments regarding the influence of the environment on health
2. Disciplines and approaches

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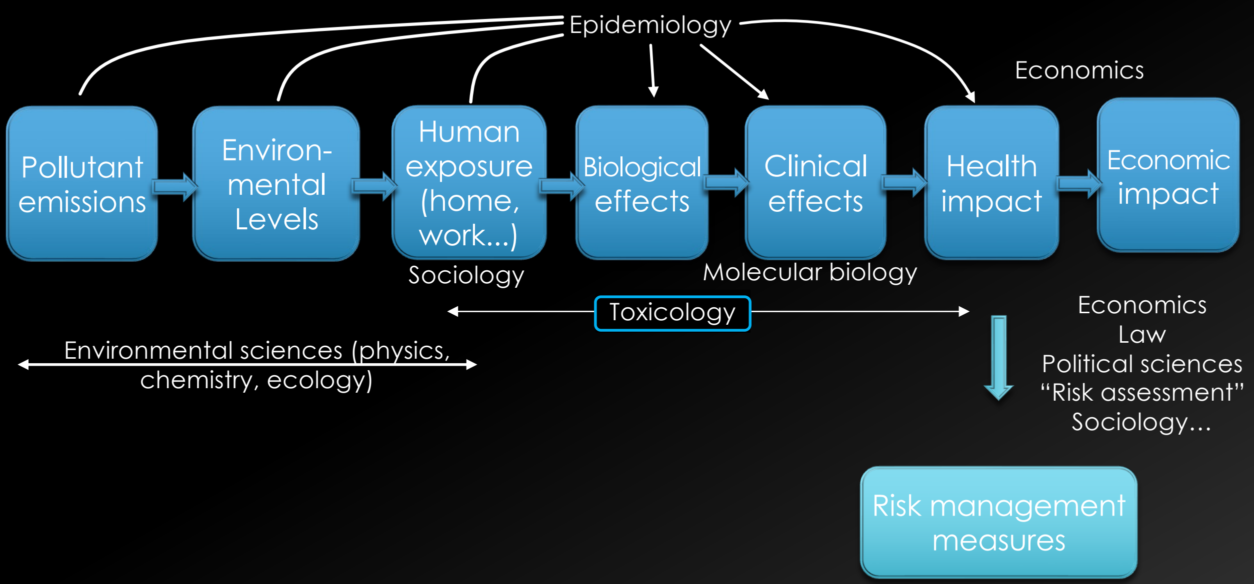
Disciplines involved



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Toxicology

- Originally defined as the "science of poisons"
- Sometimes also defined as the "science of safety"
- Complementary
- Often presented as consisting of
  - Toxicokinetics (or pharmacokinetics)
  - Toxicodynamics

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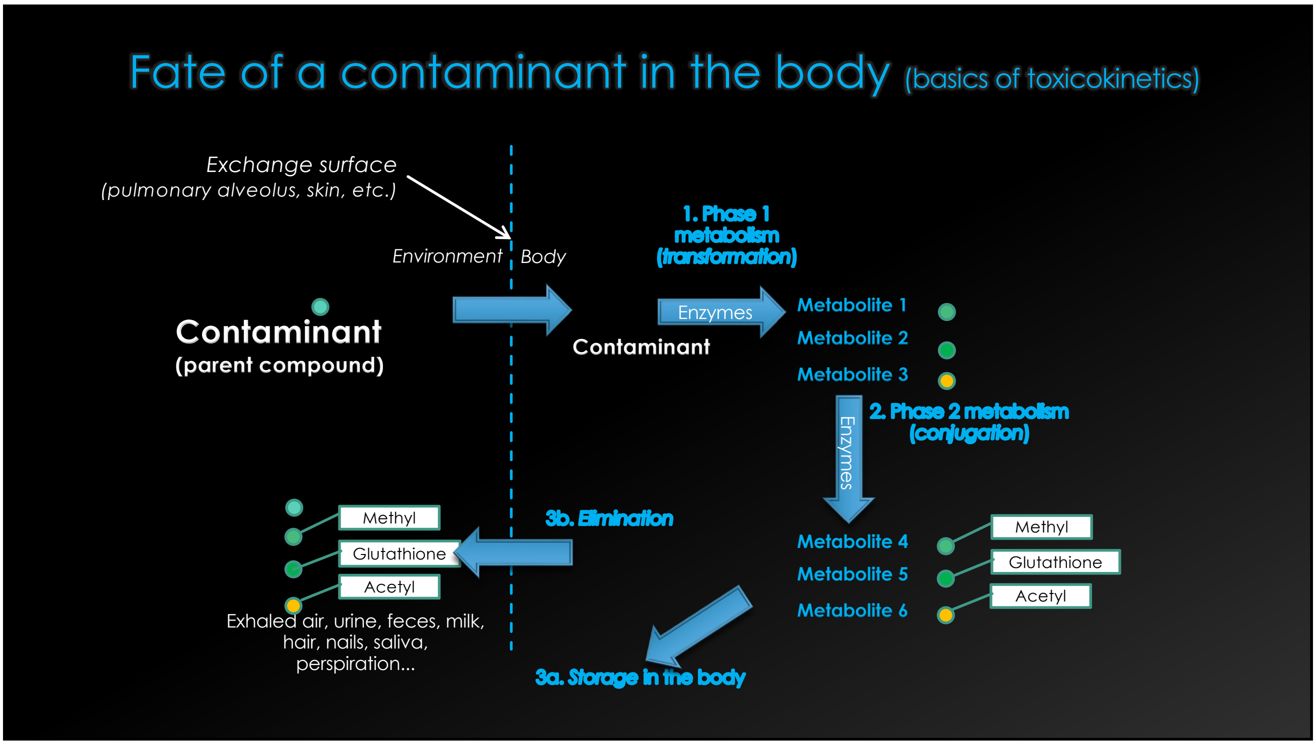

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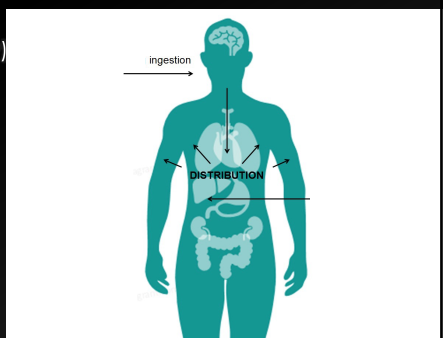
3 main **exposure routes**: inhalation, ingestion, dermal contact

- Lungs
  - Surface: 140 m²
  - 24 kg of air inhaled every day (20 m³)
  - Thickness: 0.2-0.4 µm
  - Non-selective as regards gases absorbed (but in terms of granulometry)
- Digestive tract
  - Surface: 200 m²
  - 2 kg of liquids and 1.5 kg of solids ingested every day
  - Thickness: 10-12 µm
  - To a certain extent selective as regards to what enters the body
- Skin
  - Surface: 2 m²
  - Thickness: 100 mm



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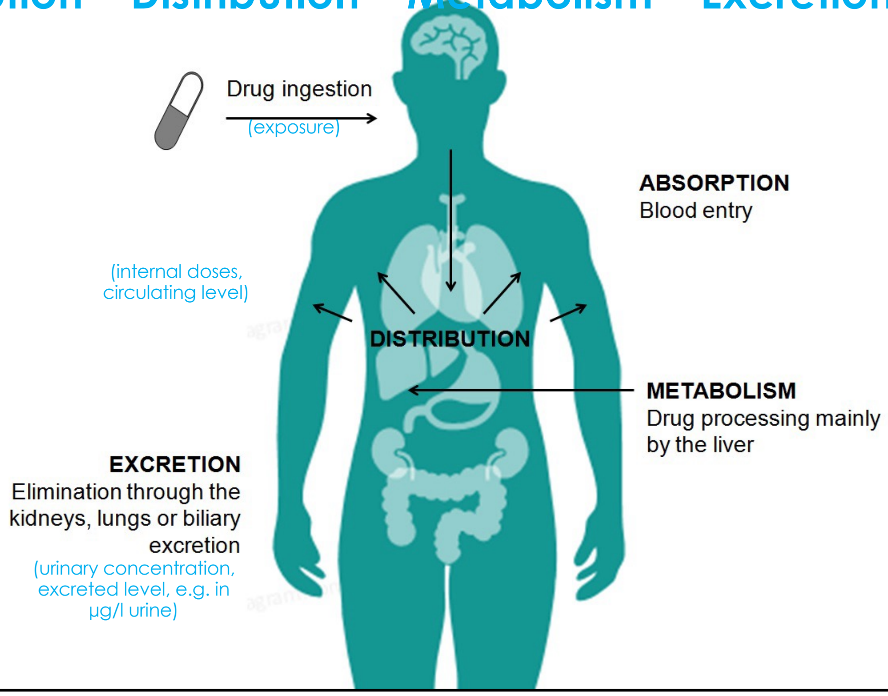
Absorption – Distribution – Metabolism – Excretion (ADME)



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Sources (emissions) → Environmental levels → Personal exposure → Internal dose → Dose to the target organs → Effects

- Environmental levels
  - Concentration (µg/m^3, or mg/l…)
- Exposure
  - Contact between the pollutant and an area of exchange of the organism(nose, mouth, eyes, skin, digestive tract…)
  - Can be estimated as the product of the compound level in each micro-environment times the time spent in this environment (or the amount absorbed) summed over all micro-environments

$$E_{i\,totale} = \sum_j C_{ij} T_{ij}$$

T_{ij}: Time spent by subject i in microenvironnement j

C_{ij}: Concentration of the pollutant in microenvironnement j

- Dose
  - Amount of pollutant in the body.
  - unit: quantity (g)
- Biologically active dose
  - Amount of pollutant (and its active metabolites) reaching the biological target (e.g., a specific tissue)

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Causality in environmental health

A ⟶ B

What does "A causes B" *mean?*

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Causality in science

- Causality is a complex and debated concept in philosophy and epistemology
- Some claim that many sciences do not require a concept of causality
  - In physics, the notion of cause is not applicable, or at lease useless
  - Causality as the relic of a prescientific view of the world (Russel, 1912, quoted by Blanchart)
- *Functional view:* causal notions play a crucial role in distinguishing effective from ineffective strategies (Cartwright, quoted in Blanchart)
  - Relevant in biology/medicine: What treatments/approaches can be used to cure or avoid a given disease?
- Epidemiologists (and economists and others) have known for a long time that two events can systematically co-occur without one influencing the other (e.g., concept of confounding)
- **Counterfactual** framework (Lewis, 1973); **Potential outcome framework** from Neyman-Rubin
- Recent mathematical developments: causal inference, **structural causal models** (SCM)(e.g., Pearl J)

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Causality in environmental health sciences

3 questions

1. What is causation conceptually?	**2. How to estimate causality (or the LoE) using environmental health data?**	**3. . How to assess the causal nature of an association (or the LoE) on the basis of the existing scientific literature on a topic?**
Conceptual problem *What does "A causes B" mean?*	Analytical problem *How can I make the* ***data*** *speak regarding a specific causal question?*	Analytical/research synthesis problem *How can I make the* ***published literature*** *speak regarding a specific causal question?* (not discussed here)

LoE: Level of evidence regarding the possible effect of A on B

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Causality in environmental health – A practical perspective - *Concepts*

1. What is causation conceptually?

- **Necessary causes**
  - B cannot happen in the absence of A
  - See Hume (*An enquiry concerning human understanding*, 1748): "We may define a cause to be an object, followed by another,...where, if the first object had not been, the second had never existed."
- **Sufficient causes**
  - B will happen if A alone is present
- **In environmental health, it is clear that, generally, causes are neither necessary nor sufficient**
  - Tobacco smoke → Lung cancer example
  - Tobacco smoke exposure is not necessary for lung cancer to occur (some non-smokers unexposed to passive smoking develop lung cancer)
  - Tobacco smoke exposure is not sufficient for lung cancer to occur (some lifestyle smokers live until 90 without developing lung cancer)
  - Yet, tobacco smoke is a cause of lung cancer

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2. How to estimate causality (or the LoE) using environmental health data?

We consider

- a population of N individual units (people, mice, cities…) indexed by i=1…N

Assume that we randomly allocate each unit to either treatment x_1 or to treatment x_0 (e.g., placebo), so that both groups are identical in expectation.

Estimate the difference in Y between the subjects assigned to x_1 and those assigned to x_0 and take it as a relevant estimate of the average value of Y_{i1}-Y_{i0}

Alternative:

If Y is a transient outcome (e.g., blood pressure, but not "being alive at 70") and if exposure is reversible and does not have carry-over effect (e.g., x_1=nasal irritant and Y=sneezing), then it is possible to perform a crossover trial:

- Expose each subject to x_1, assess Y_i and assume that it is a good estimate of Y_{i1}
- Expose each subject to x_0, assess Yi and assume that it is a good estimate of Y_{i0}
- Estimate Y_{i1}-Y_{i0}

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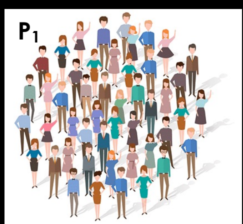
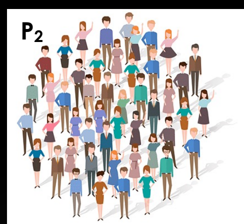
Estimating the causal effect in the (ideal) randomized situation

2 "comparable" population samples of size N (living in the same environment)



Receives 'treatment' x_1



Receives 'treatment' x_2

Follow-up for duration **Δt**

Count cases of the target disease (**n_1**)

Count cases of the target disease (**n_2**)

$n_1 - n_2$ is the estimated causal effect of treatment x_1, compared to treatment x_2, on the occurrence of the disease (during the time period **Δt**).

In practice, a confidence interval can be constructed around $n_1 - n_2$ to take into account random fluctuations, allowing to conclude if $n_1 - n_2$ is *not* compatible with the value 0 corresponding to a lack of effect ('*null* hypothesis'). If is compatible with the null hypothesis, then no strong conclusion can be drawn regarding the difference between both treatments.

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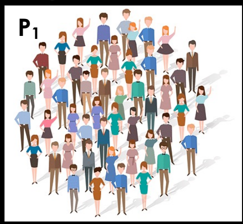
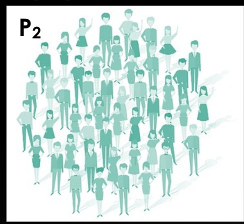
2. How to estimate causality (or the LoE) using environmental health data?

What can be done if exposure cannot be randomized (if both populations are likely to differ)?

7% are exposed to Z (a known risk factor for disease Y)





70% are exposed to Z

Z

X - - - - - - - → Y

Z is a cause of both Y and X, implying that it will distort any observable effect of X on Y.
In particular, even if X does not causally influence Y, the existence of Z may create a spurious (non causal) statistical association between X and Y.
Z is called a confounder for the association between X and Y.

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Z Temperature

X Eating ice cream - - - - - - - → Y Drowning

There may be more people drowning when sales of ice cream are high (than low), but this apparent effect is likely confounded by temperature.
This is because, when temperatures are high, people both tend to eat more ice cream and also more often go swimming.
Drowning and eating ice cream share a common cause (high temperatures).

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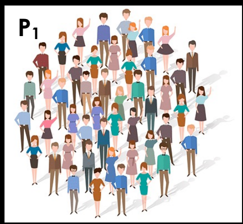
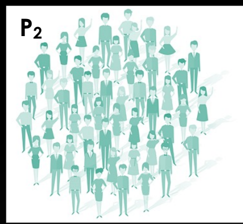
Estimating the causal effect in the non-randomized situation

2 "distinct" population samples of size N

7% are exposed to Z (a known risk factor for disease Y)





70% are exposed to Z

Receives 'treatment' x_1 | Receives 'treatment' x_2

Follow-up for duration **Δt**

Count cases of the target disease (**n_1**)
Correct (statistically) for the effect of Z (and any other confounder) on Y
→ **n'_1** (corrected number of cases)

Count cases of the target disease (**n_2**)
Correct (statistically) for the effect of Z (and any other confounder) on Y
→ **n'_2** (corrected number of cases)

$n'_1 - n'_2$ is the estimated causal effect of treatment x_1, compared to treatment x_2, on the occurrence of the disease (during the time period **Δt**).

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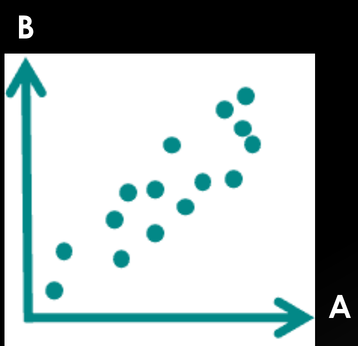
Which situations can induce a statistical association between A and B?



Scientific name	Occurrence	Example
Causality	1. **A causes B** (A → B).	Exposure to tobacco smoke causes lung cancer.
Reverse causality (protopathic bias, in a clinical context)	2. **B causes A (B → A).**	There is a statistical relationship between aspirin intake and the risk of death, not because of a causal effect of aspirin on mortality, but because people with conditions that may soon lead to death are more likely to take aspirin to treat the symptoms of these conditions.
Sampling Fluctuations	3. The association observed in the study sample is not what would have been observed if the entire target population had been recruited, in spite of the sample being drawn at random. The number of observations (subjects) in the study is too small to accurately characterize the association between A and B (even assuming that the subjects are a random sample of the population).	If only 10 exposed and 10 unexposed subjects are studied for the effects of smoking, there may be fewer cases of lung cancer in those who smoke. This association would be reversed with a much larger number of subjects. This issue can be addressed by increasing the number of observations, contrarily to the sources of bias described below.
Measurement error	4. A or B is incorrectly measured, resulting in an unintended association (or a change in the existing association) between A and B.	In a retrospective study, it is possible that healthy people may make less effort to answer the question about their past exposure to the factor under study, and therefore under-report it more often than subjects who developed the disease and tend to look for an explanation (recall error, a specific type of measurement error).
Confounding factor (confounding bias)	5. A and B share a common cause X, which perturbs the observed association between A and B when X is ignored.	The association between air pollution (A) and mortality (B) can be distorted by temperature (X), which can influence both A and B.
Selection bias	6. A and B share a common consequence X on which the association is conditioned. In other words, the way in which the study's observations are selected induces (or distorts) the relationship between A and B.	"Healthy Worker Effect": If a retrospective study is conducted in an occupational setting, recruiting only the population that is still employed in the considered factory at the time of the study, workers who had been exposed to an occupational factor and who developed the disease because of this exposure and had to quit the company are not taken into account. This exclusion of a part of the exposed population who became sick is expected to underestimate the effect of exposure on disease risk.

(From Slama, QUAE, 2017)

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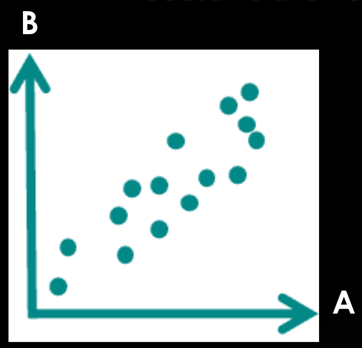
Correlation is not causation

- Correlation can exist in the absence of a causal relation
- A causal relation can exist without the 2 corresponding variables being correlated



≠ A → B

Of course, this does not imply that observational studies cannot be used to infer causation!
This is because observational studies do not necessarily rely on correlations, but generally on causal inference modelling (e.g., multiple regression adjusted for confounders)

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Causality in environmental health – A practical perspective – *Concepts*: embedded (nested) causes/explanatory level

« Tobacco smoke is a cause of lung cancer. »

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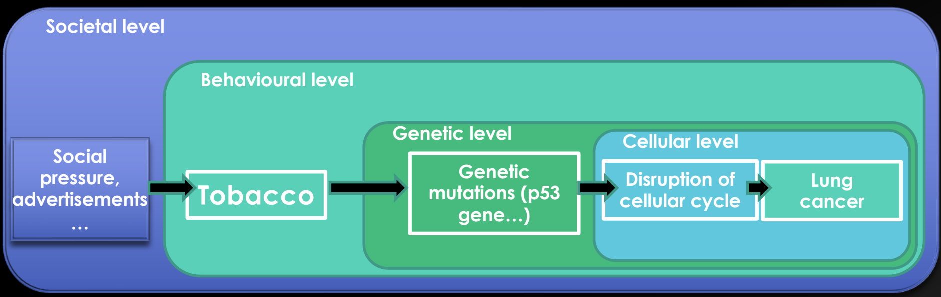
Explanatory level

Example of lung cancer



« Tobacco smoke is a cause of lung cancer. »

« Genetic mutations cause cancer. »

« Cancer occurrence corresponds to a disruption of cellular cycle. »

« Advertisements (/or peer pressure) caused the lung cancer epidemics. »

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Explanatory level

Environmental versus genetic causes (Rothman, Epidemiology: an introduction, OUP, 2002)

- Generally, there is no opposition or complementarity between genetic and environmental causes of a disease.
- The respective share of genetic and environmental factors depends on the chosen explanatory level
- At the cellular level, most mechanisms have a genetic component: « **Everything is genetic** »
- At another scale, genetic mutations or gene expression can be influenced by environmental exposures : « **Everything is environmental** »
- Extreme point of view: human evolution is driven by the environment; hence, on an evolutionary scale, our genetic characteristics are partly shaped by environmental factors.

- Example of phenylketonuria (PKU):
  - Due to a mutation of the gene of phenylalanine hydroxylase
  - Its manifestation (mental health retardation) can be prevented by a diet intervention (diet poor in phenylalanine)

Therefore, it can be said that the disease has an environmental (or at least non-genetic) component.

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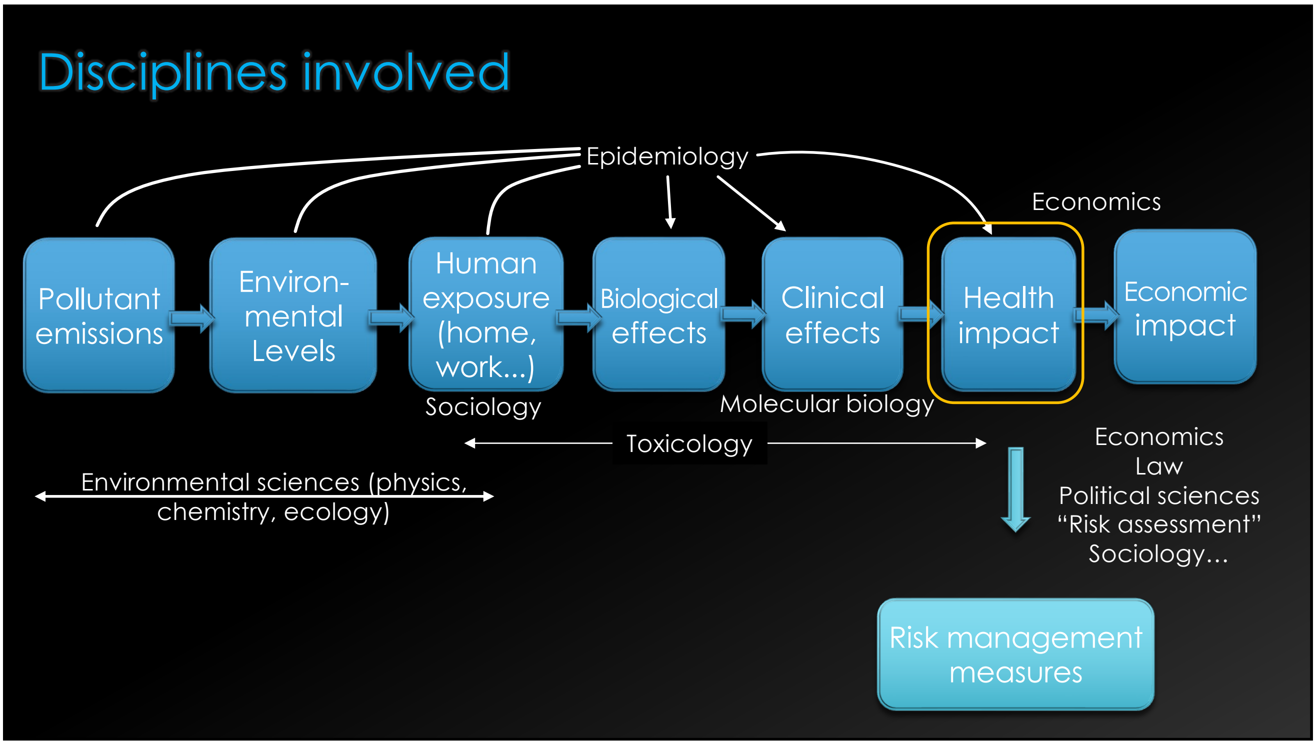
Disciplines involved
Epidemiology
Economics
Pollutant emissions
Environ-mental Levels
Human exposure (home, work...)
Biological effects
Clinical effects
Health impact
Economic impact
Sociology
Molecular biology
Toxicology
Environmental sciences (physics, chemistry, ecology)
Economics
Law
Political sciences
“Risk assessment”
Sociology...
Risk management measures

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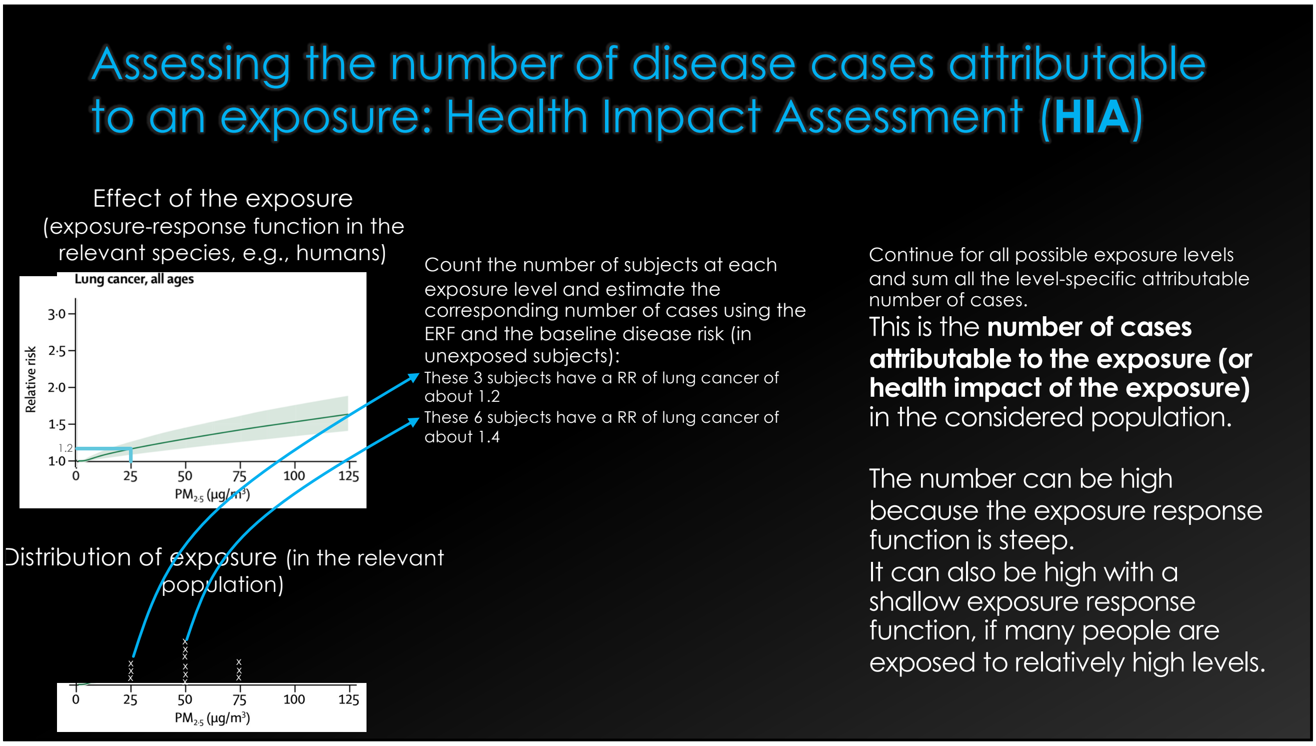
Assessing the number of disease cases attributable to an exposure: Health Impact Assessment (HIA)
Effect of the exposure (exposure-response function in the relevant species, e.g., humans)
Lung cancer, all ages
Relative risk
PM2.5 (μg/m³)
Distribution of exposure (in the relevant population)
Count the number of subjects at each exposure level and estimate the corresponding number of cases using the ERF and the baseline disease risk (in unexposed subjects):
These 3 subjects have a RR of lung cancer of about 1.2
These 6 subjects have a RR of lung cancer of about 1.4
Continue for all possible exposure levels and sum all the level-specific attributable number of cases.
This is the number of cases attributable to the exposure (or health impact of the exposure) in the considered population.
The number can be high because the exposure response function is steep.
It can also be high with a shallow exposure response function, if many people are exposed to relatively high levels.

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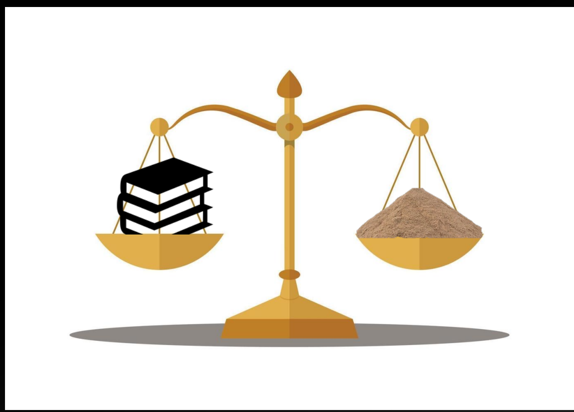
A large (health) impact may result from the accumulation of a large number of very small impacts



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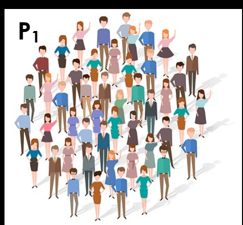
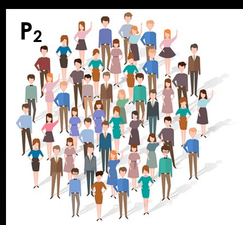
Estimating the causal effect using a HIA approach

2 population samples of size N



Exposure: distribution observed in the population



Exposure=0 for everyone **(counterfactual scenario)**

Estimate cases of the target disease (**n_1**)

Estimate cases of the target disease (**n_2**)

$n_1 - n_2$ is the estimated causal effect of exposure with its current distribution, compared to a hypothetical situation of a zero exposure, on the occurrence of the disease.

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III. Some concepts of risk management

1. Overview
2. Some principles of regulatory toxicology

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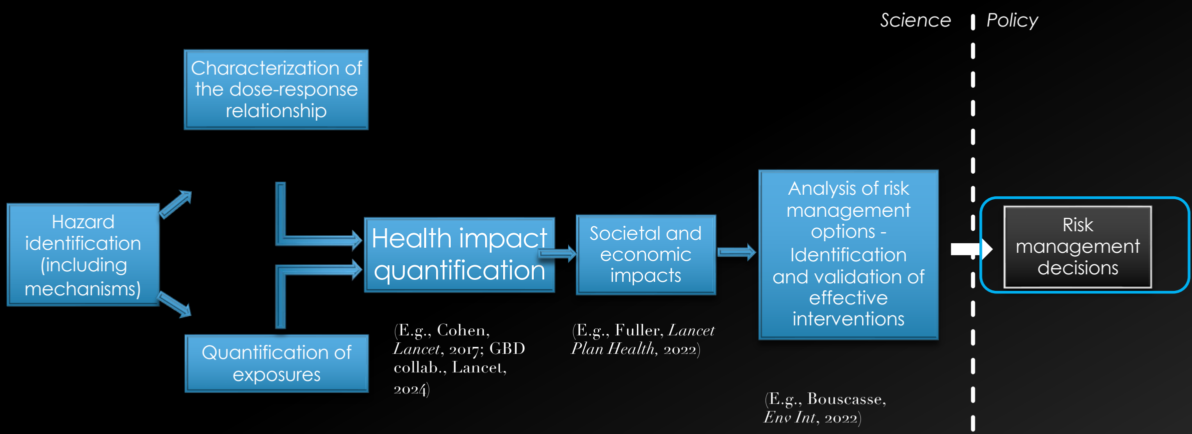
Environmental health research in support of public decision-making



In practice, all the steps on the scientific side need not to be conducted before a risk management decision is taken.

Adapted from (Slama, 2022) and strongly adapted from the NTP Redbook (1983)

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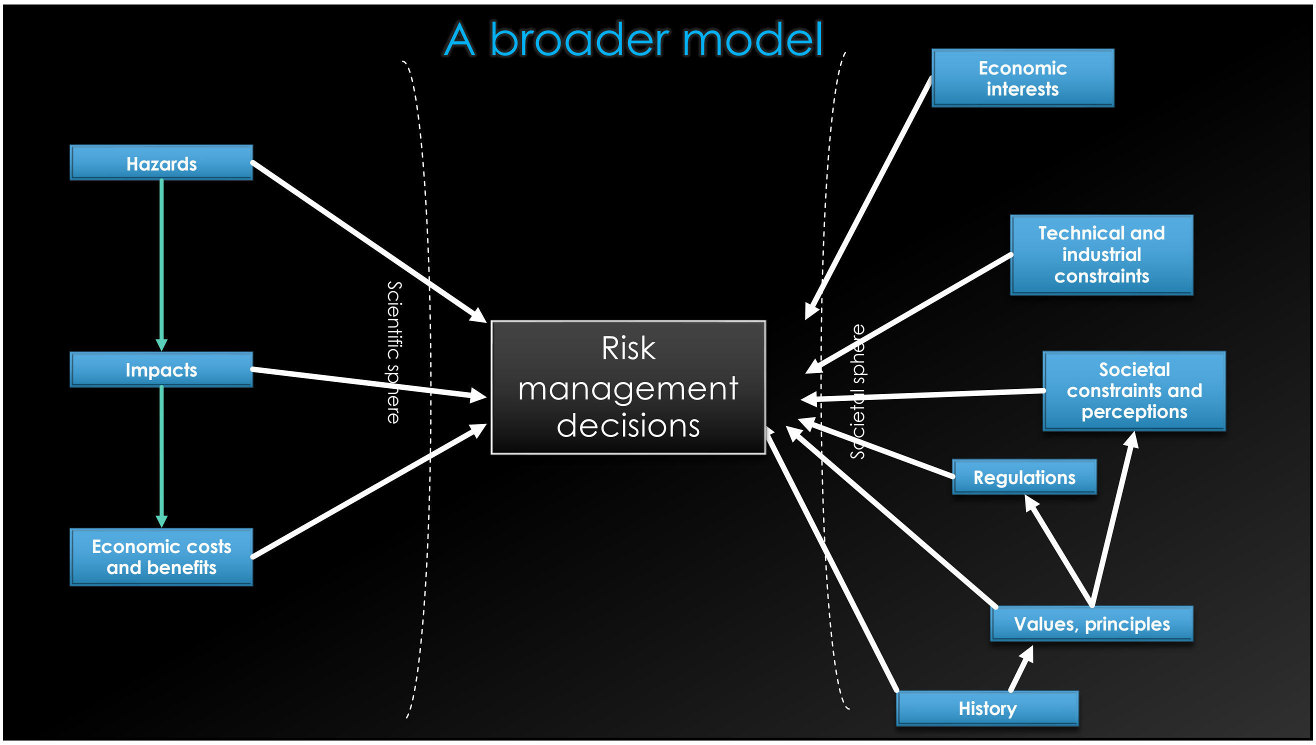

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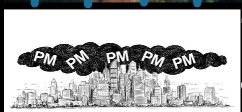
Hazard and risk (impact)

"Tigers can kill humans" — **Risk ≈ 0** (France; about 15/year worldwide)



"Particulate matter is carcinogenic" — **Risk ≈ 310,000 deaths/year worldwide** (and about 7 million deaths/year worldwide, all death causes altogether)

Hazard identification

Health **impact** quantification

Hazard:
Something with the potential to cause harm.
Qualitative notion attached to a substance (or factor) independently of the context.

Risk (impact):
Probability of occurrence of the harm in a given context (or corresponding number of cases).
Quantitative notion (probability of occurrence or number of cases), context specific.

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Level of action
Mode of action (tool)
Target of the action (e.g. specific health of exposure level)
Consideration of uncertainties
Perimeter and level of the decision
Mode of decision of the risk management decisions

Risk management decisions

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What level(s) of action?

Prevention | **Therapy**

Action Level

Research (Generating knowledge useful for action)

Sources → Environments → Exposure → Patients

Behaviours → Exposure



Health expenditure
France, 2022
Total: €314 billion

4%
That is to say 13 billion €
for primary, secondary prevention
(including Covid-19 tests and vaccines)

96%
(DREES, 2023)

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Acting at the source vs. at the target

- Acting at the source
  - Example of climate change: trying to limit emissions rather than simply adapt to a changing climate
- Acting at the target
  - Close to where exposure takes place
  - Extreme situation: removing humans from hazardous places
  - Examples of cars: children not "allowed" to play in streets anymore
- Regulation
  - Some pieces of regulation tend to call for "rectifying pollution at source" (EU).
- See similar issues in other areas (fight against criminality, drug traffic…)

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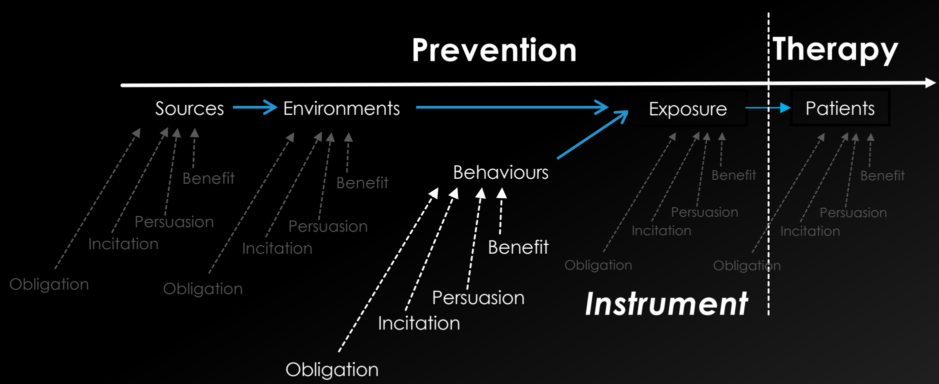
What instrument(s)?



There are few examples of major public health problems that have been solved by using a single instrument at a single level: actions at several levels and with different instruments simultaneously are needed

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Instruments that can be used to manage environmental health issues (broader typology)

Instrument	Possible forms	Examples
Non market-based		
Prescriptive regulation	Ban, emission limits, (technological) standards	EU air quality regulation, Stockholm POP convention
Provision	Compensation funds, state provisions…	National park, International Oil Pollution Compensation Funds, FIVP
Commons	Non property-based community governance of common goods (E. Ostrom)	Communal meadows, forests…
Market-based		
Property rights	Tradable emission permits*. "Coasian" tool * See https://www.perc.org/2020/07/06/are-property-rights-a-solution-to-pollution/	CO_2 or SO_2 emission rights
Penalties	Taxes against bad actors/behaviours. "Pigouvian" tools (Pigou, 1920)	Polluter-payer principle, fines regarding water pollution…
Subsidies	Favouring good actors/ behaviours	Prime Renov', subsidies for green [and brown] energy producers
Persuasion	Education, information, social marketing, training, nudge, labels	WHO air quality guidelines, organic food labels…
Legal actions (justice)	Individual or class action, possibly linked with the vigilance principles, lack of information to customers…	

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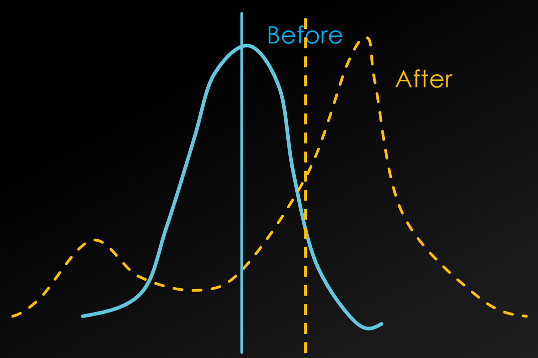
Consideration of socio-demographic (or origin-related) inequalities

- Sometimes (often?) improving health *overall* can lead to increases in health inequalities inside the population



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Possible impact of lockdown policies on social gradients in COVID-19 infection (France, spring 2020)

The overall COVID-19 infection rate strongly decreased after the 1st lockdown, while the social gradient in infection rate reversed.

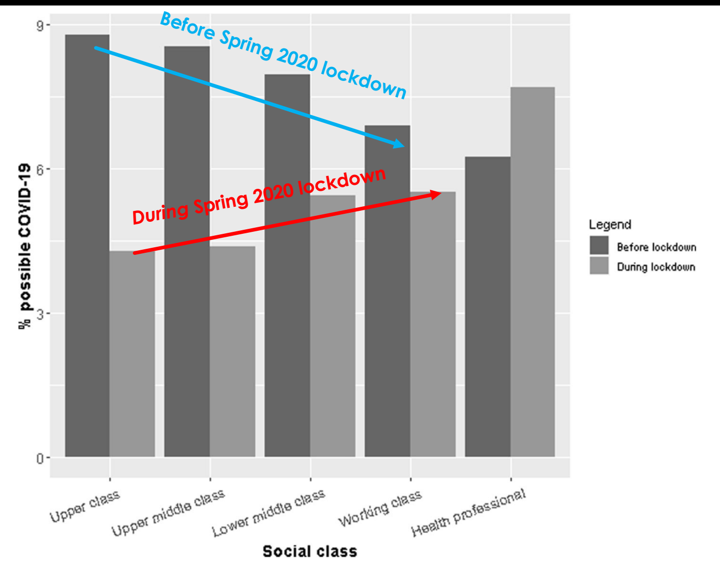

Fig. 1 Percentage of individuals likely to be infected before or during lockdown by social class

10,101 volunteers from SAPRIS cohorts, France

(Bajos, *BMC Pub H*, 2021)

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Which (health) target?

- Explicit target
  - Zero exposure (or zero hazard)
  - Zero risk
  - Other explicit (tolerable) risk level
    - E.g., "<1 death per 100,000 person-years"
- No explicit (health or environmental) target
  - E.g., ALARA approach (as low as reasonably achievable) or "minimize risk"

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Perimeter of the risk management decisions

- Economic sector considered
  - E.g., cosmetic, transport, toys, drugs, pesticides… or all sectors altogether (cross-sectorial or horizontal regulation)
- Number of risk factors simultaneously considered
  - It can be one compound at a time; one group of factors at a time (e.g., group of specific air pollutants: PM, NOx, O_3, SO_2); one family of compounds (e.g., PFAS?)
  - *Mixture adjustment factor* (MAF) debate
- Level of decision, political and geographical area(s) considered
  - Local, national, continent (EU-wide), international…

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Mode of decision

- Dedicated arena (e.g., environmental agency) or political decision
- Relying or not on expertise (scientific, social…), on participatory democracy…
- Consideration of economic costs of decisions (yes/no)
  - If yes: may be explicit (e.g., via a cost-benefit analysis) or not, scientifically done or not (e.g., considering only specific actors of society)

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Consideration of uncertainties: **the precautionary principle** (PP)

		Level of evidence: **Low** (high uncertainties)	Level of evidence: **High** (little uncertainty)
Risk, damage	Potentially low	Area where the absence of a management measure can be justified	**Prevention**
	Potentially high	Measures according to the **Precautionary Principle**	**Prevention**

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Risk management in the broader context: **From P to PP and PPP**

		Level of evidence: **Low** (high uncertainties)	Level of evidence: **High** (little uncertainty)
Risk, damage	Potentially low	Area where the absence of a management measure can be justified	**P**
	Potentially high	**PP**	**P**
	Past	**PPP**	**PPP**

P: Prevention
PP: Precautionary principle
PPP: Polluter pays principle

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PPP, BPP, PCP

- PPP (polluter pays principle)
  - Those agents who pollute should pay to address the created pollution (externatilities)
- BPP (beneficiary-payer principle)
  - Those who benefit from acts/policy, which requires the use of emissions should pay. Note the difference between this and the polluters pays principle. The beneficiary pays principle has no interest in whether you emit or how much you have emitted.
- PCP (principle of capacity to pay)

https://climateethics.co.uk/index.php/2021/01/07/who-should-pay-for-climate-change-the-beneficial-pays-principle/
https://www.idunn.no/doi/10.18261/issn.1504-2901-2021-02-03-07

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Principle	Mitigation context	Adaptation context
Polluter pays	Actors should pay in proportion to the amount of climate change they have caused.	Actors should pay in proportion to the amount of climate change they have caused.
Beneficiary pays	Actors should pay in proportion to the level of benefit they have derived from actions which caused climate change.	Actors who will benefit from a specific climate adaptation measure should pay a high proportion towards that measure.
Ability to pay	Actors should pay in proportion to their financial capacities.	Actors should pay in proportion to their financial capacities.

https://theconversation.com/cop29-who-pays-for-climate-action-in-developing-nations-and-how-much-becomes-more-urgent-242678

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III. Some concepts of risk management

1. Overview
2. Some principles of regulatory toxicology

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Regulatory toxicology

- Defined as a branch of toxicology at the interface with risk management
- In principle complementary to "toxicology" (or academic toxicology)
- In practice sometimes opposed to it, in particular because of blurred frontiers between scientific facts and risk management positions, and of the strong influence of the industry/OECD on the practice of regulatory toxicology
  - See e.g. debates on "thresholds" and DTI (Carrington CD, *Tox Appl Pharmaco*, 2010), bisphenol A, good laboratory practices (Myers, EHP, 2009)
- Central for the regulation of chemicals (but generally not other environmental health factors)

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Some structuring concepts of regulatory toxicology

- Hazard
- Risk
- NOAEL (no observed adverse effect level)
- Daily tolerable intake (DTI)
- Benchmark dose

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Some structuring concepts

- Hazard
  - Something with the potential to cause harm.
  - Qualitative notion attached to a substance (or factor) independently of the context.
- Risk
  - Probability of occurrence of the harm in a given context (or corresponding number of cases).
  - Quantitative notion (probability of occurrence or number of cases), context specific.
- NOAEL (no observed adverse effect level)
- Tolerable Daily Intake (TDI), and acceptable daily intake (ADI)
  - Daily amount of a chemical contaminant that has been assessed *safe* for human being exposure on long-term basis (usually whole lifetime)
- Benchmark dose
  - The benchmark dose corresponds to the dose associated with a specific change in the considered biological response (e.g., a 5% decrease in organ weight). doses below the BMDL are those likely to correspond to a change in the biological response lower than 5% (or whatever other value chosen as benchmark response).

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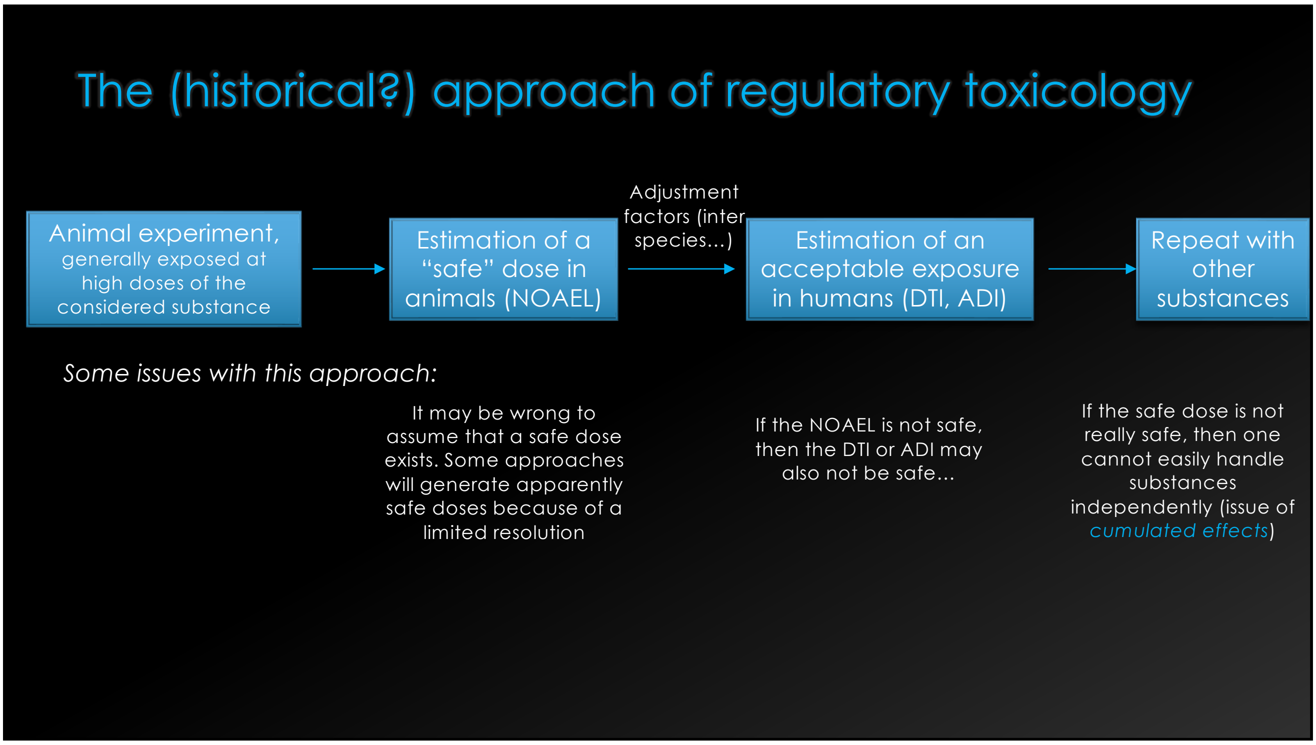
The (historical?) approach of regulatory toxicology
Animal experiment, generally exposed at high doses of the considered substance
Estimation of a "safe" dose in animals (NOAEL)
Adjustment factors (inter species...)
Estimation of an acceptable exposure in humans (DTI, ADI)
Repeat with other substances
Some issues with this approach:
It may be wrong to assume that a safe dose exists. Some approaches will generate apparently safe doses because of a limited resolution
If the NOAEL is not safe, then the DTI or ADI may also not be safe...
If the safe dose is not really safe, then one cannot easily handle substances independently (issue of cumulated effects)

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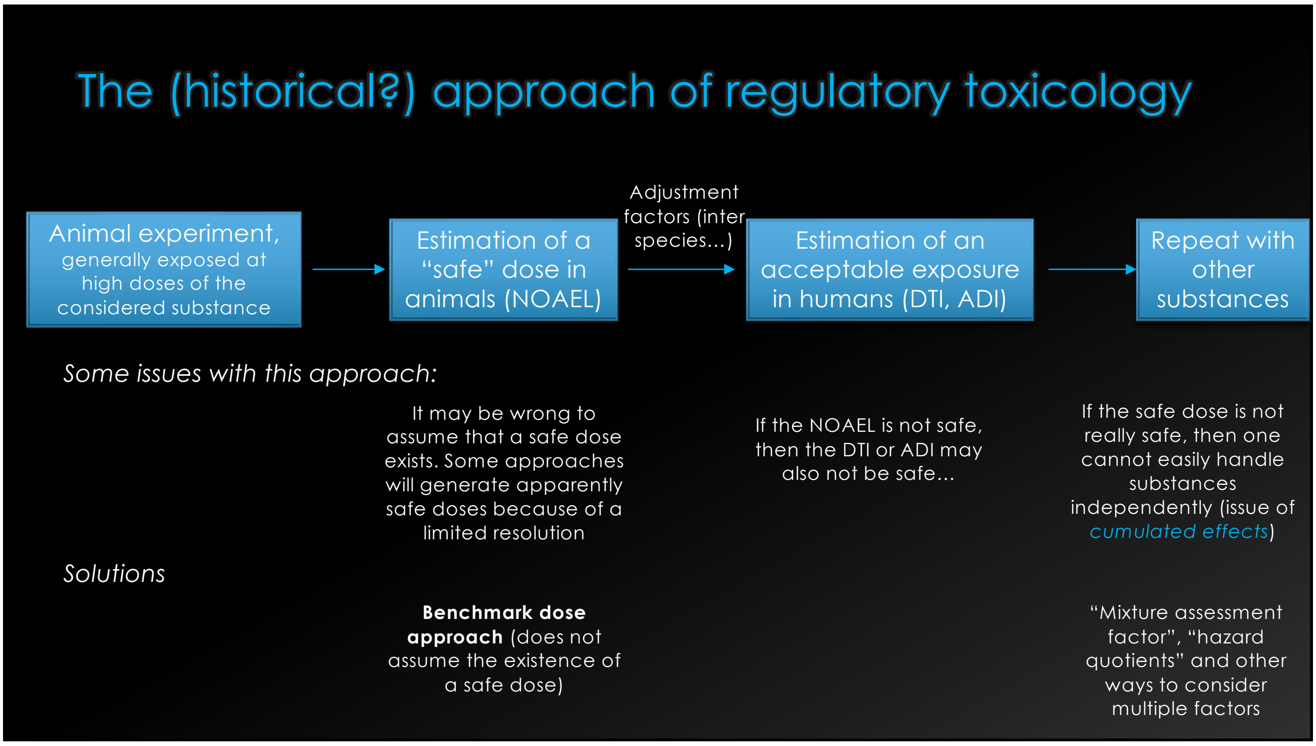
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Adjustment factors (inter species...)
Estimation of an acceptable exposure in humans (DTI, ADI)
Repeat with other substances
Some issues with this approach:
It may be wrong to assume that a safe dose exists. Some approaches will generate apparently safe doses because of a limited resolution
If the NOAEL is not safe, then the DTI or ADI may also not be safe...
If the safe dose is not really safe, then one cannot easily handle substances independently (issue of cumulated effects)
Solutions
Benchmark dose approach (does not assume the existence of a safe dose)
"Mixture assessment factor", "hazard quotients" and other ways to consider multiple factors

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IV. Concluding remarks

1. Managing risks induced by environmental factors: Challenges and tensions
2. Overview of the course

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Some challenges and sources of tension

- Large number of factors (exposures) that need to be considered
- Tensions between access to the market (for the industry) and testing/safety requirements and the associated time and costs
- Weakness of public-funded research (and, generally, lack of mechanism binding the research funds with needs)
- Reliance on some fragile or not very rigorous seemingly scientific approaches or concepts of risk management in the
- Weaknesses and heterogeneity (across sectors) of the "theoretical" risk management framework
- Multiple possibilities to disrupt the work of environmental health research and knowledge diffusion

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Overview of the whole course

1. Introduction
2. Introduction (2)
3. Lead
4. Tobacco
5. Ionising radiations
6. Atmospheric pollutants
7. Persistent Organic Pollutants (POPs)
8. Perfluroalkyl substances (PFAS)
9. Endocrine disruptors
10. Pesticides
11. Alcohol
12. The gasoline-powered car
13. Conclusion

Note: one of these lectures will probably be skipped

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Liste des projets étudiants proposés – *V2*

- La gestion des composés perfluorés (PFAS) (en France ou dans l'UE)
- Le secteur des transports en Europe en 2050
- Faut-il interdire le glyphosate ?
- Le principe de précaution
- PPP (principe pollueur payeur) ou PCP (principe de capacité à payer) ?
- Pertinence, limites éthiques et pratiques des analyses coût-bénéfice
- La taxe Carbone, le bon outil pour lutter contre le changement climatique ?
- Gérer la crise de la biodiversité
- Généralisation du *Nutriscore* dans l'UE
- Le marketing : malédiction ou opportunité pour la santé environnementale ?

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