Environmental burden of disease of cadmium (Cd) and HBM indicators

Cd: **Jurgen Buekers &** Greet Schoeters (VITO), Eva Ougier& Christophe Rouselle (ANSES), Ricardo Assunção & Carla Martins (INSA), with support of JSI

Indicators: **Jurgen Buekers** & Jos Bessems (VITO), Joana Lobo Vicente & Xenia Trier (EEA), Madlen David & Janek Jubelt (UBA)

3rd HBM4EU Training School 2019

Large part of burden of Disease (BoD) and related costs attributed to environmental factors (among them chemicals)

- Prüss-Ustün et al. (2017): 22% of DALYs (environmental risks)
- Grandjean and Bellanger (2017): global costs chemical exposure +/- 10% of Global Domestic Product
- Based on limited information exposure and exposure-response functions
- Production volume of synthetic chemicals is still increasing

- Environmental burden of disease for exposure to cadmium

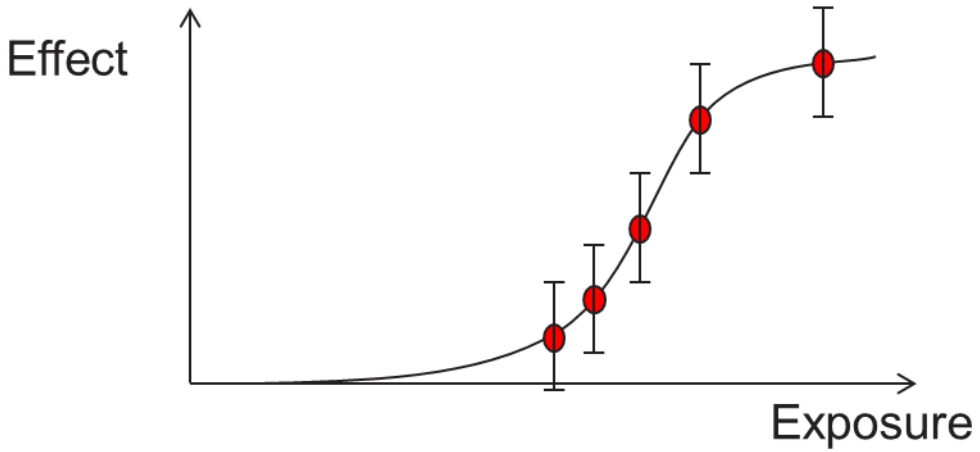
- Environment and health indicators within HBM4EU

Risk assessment

- Comparison of exposure with HBM guidance value

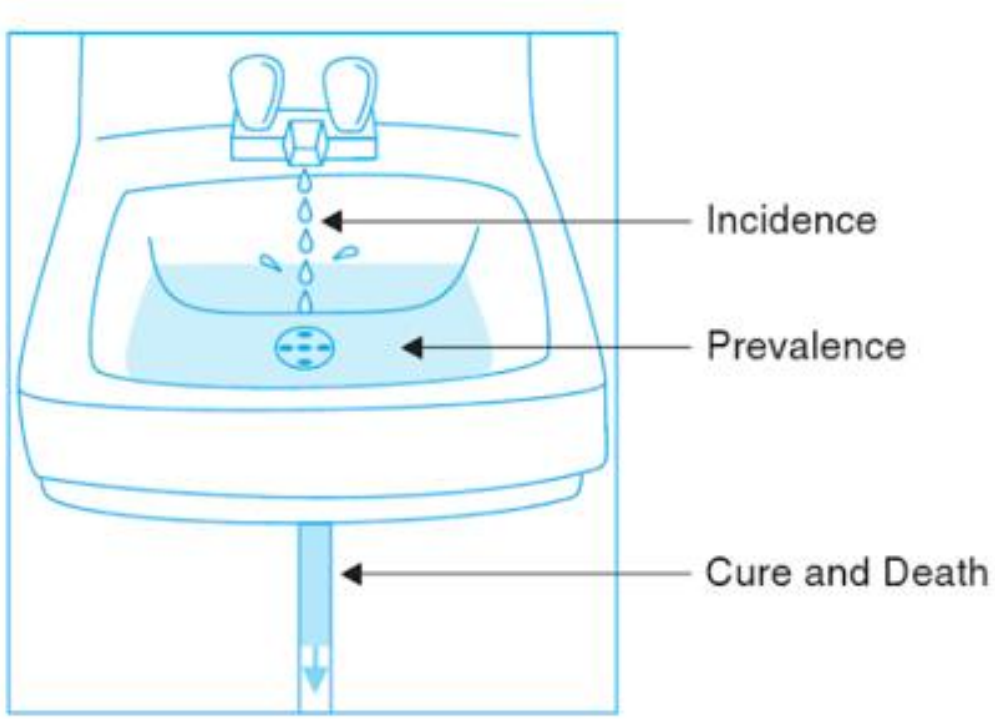
Environmental burden of disease (EBoD)

- Epidemiological exposure-response curve
- How many people have certain exposure
- How many people get a certain disease due to exposure



Some definitions

Incidence/prevalence



Relationship among incidence, prevalence, mortality and cure.

Essentials of epidemiology in public health, Ann Aschengrau, George R. Seage, 2013

Odds ratio (OR)

Case control studies

It quantifies the association between an exposure and a health outcome

	Disease (case)	No disease (controls)
Exposed	a	b
Non-exposed	c	d

Odds for disease when exposed: a/b

Odds for disease when non-exposed: c/d

Odds ratio: (a/b) / (c/d) = ad/bc

OR of 1 (no influence of exposure)

Relative risk (risk ratio)

Relative risk= Compare risk of health event between 2 groups

$$\frac{\textit{Risk of disease (incidence proportion, attack rate) in group of primary interest}}{\textit{Risk of disease (incidence proportion, attack rate) in comparison group}}$$

	Population	Disease	No disease
Exposed	N_1	a	b
Not-exposed	N_0	c	d

Risk for disease when exposed: a/N_1

Risk for disease when not exposed: c/N_0

Risk ratio: $(a/N_1) / (c/N_0) = a\ N_0/c\ N_1 = a\ (c+d) / c\ (a+b)$

It approaches the OR when the disease is rare

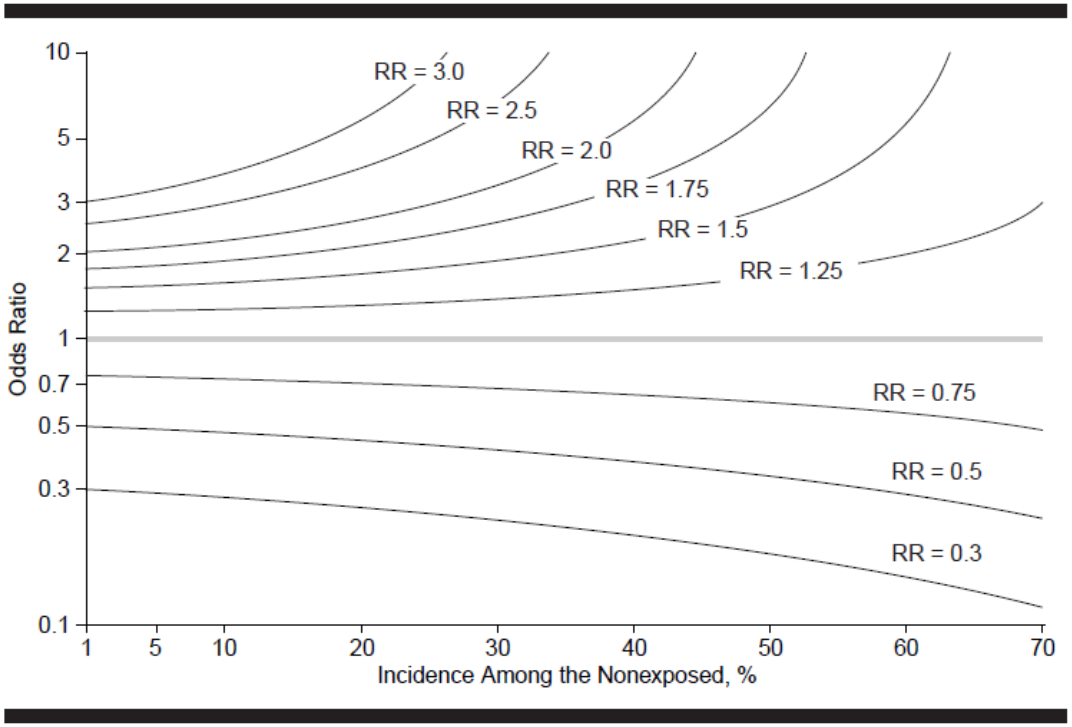
Risk ratio: $a\ (c+d) / c\ (a+b) = a\ (\cancel{c}+d) / c\ (\cancel{a}+b) \approx ad/bc$

Relationship OR and RR

What's the relative risk? (Zhang and Yu, 1998)

$$RR = \frac{OR}{(1-P_0)+(P_0 \times OR)} = \frac{OR}{(1-I_0)+(I_0 \times OR)}$$

P_0 or I_0: incidence in the non-exposed



The relationship between risk ratio (RR) and odds ratio by incidence of the outcome.

Unit risk

Extra cancer cases

IARC (International Agency on Cancer Research)

e.g. Ni in air 3.8×10^{-4} and lungcancer

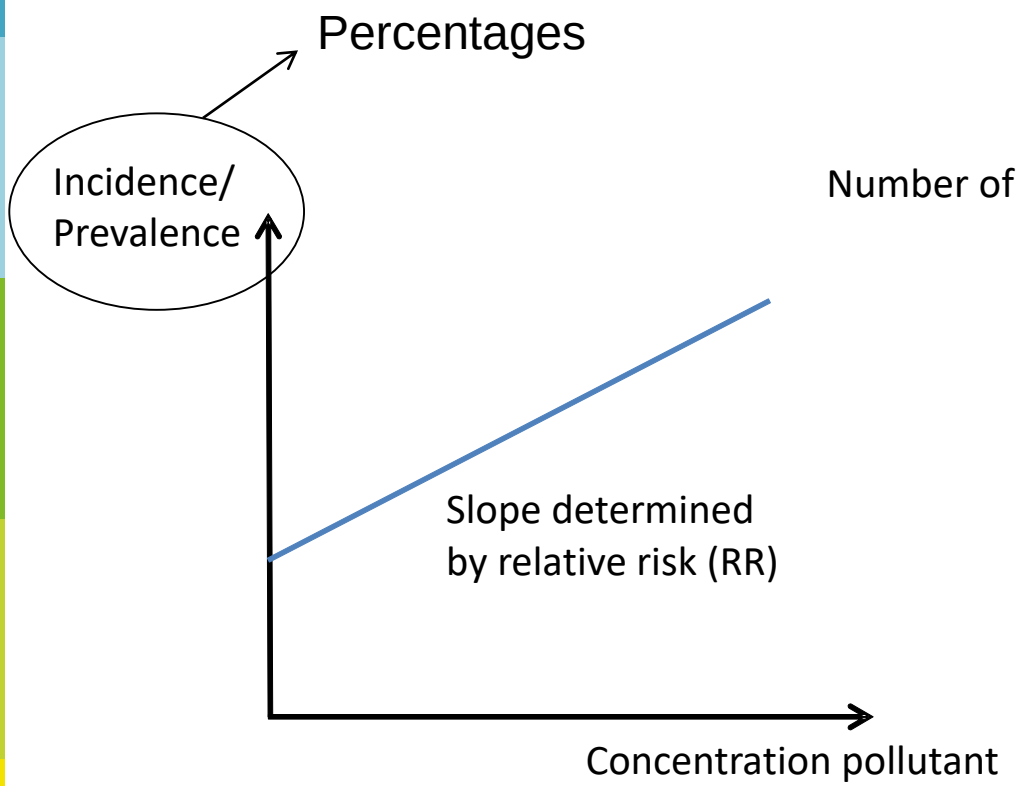
For lifetime exposure to 1 µg/m^3

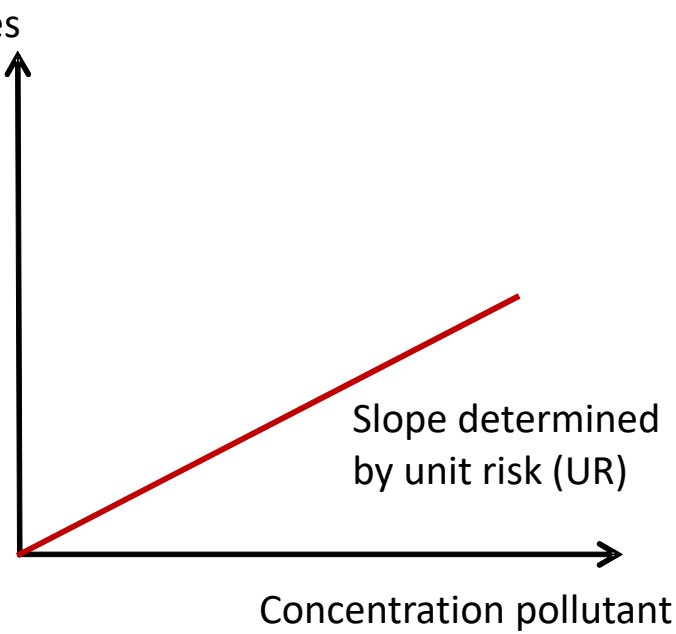
Lifetime exposed to 1 µg/m^3: $\frac{3.8}{10000}$

Independent of the background incidence

Exposure-response curves

Exposure-response functions

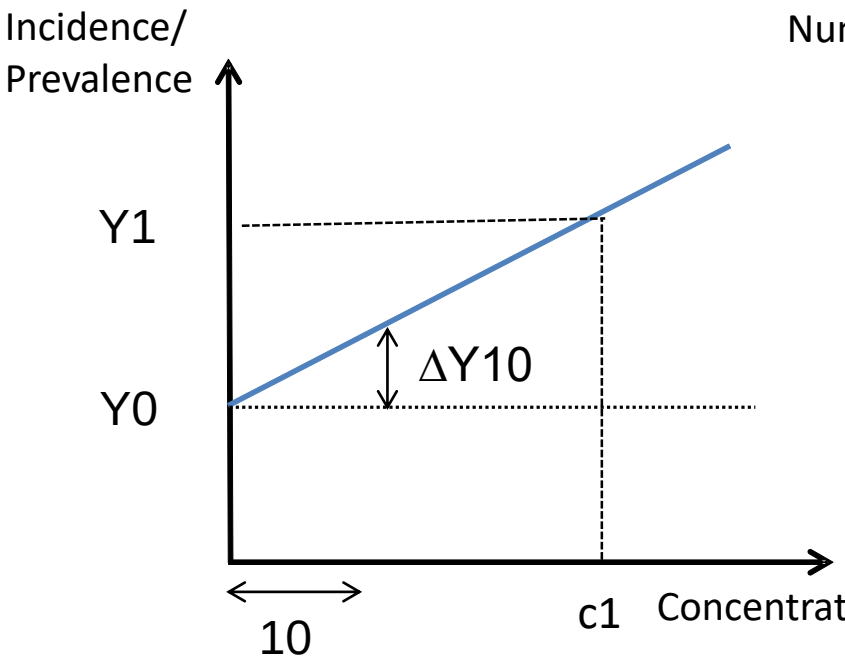


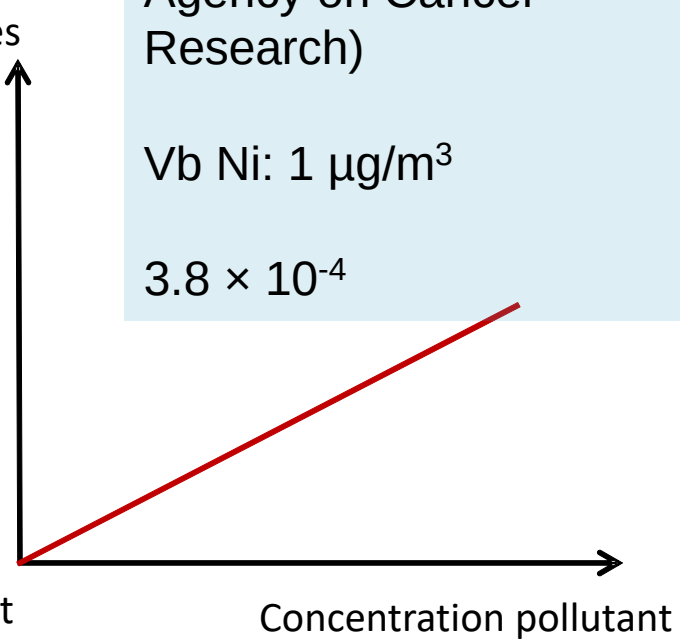


(Log) linear model

Exposure-response functions

RR10 = (Y0 + ΔY10) / Y0
RR at c1= Y1/Y0





Independent of background incidence/prevalence

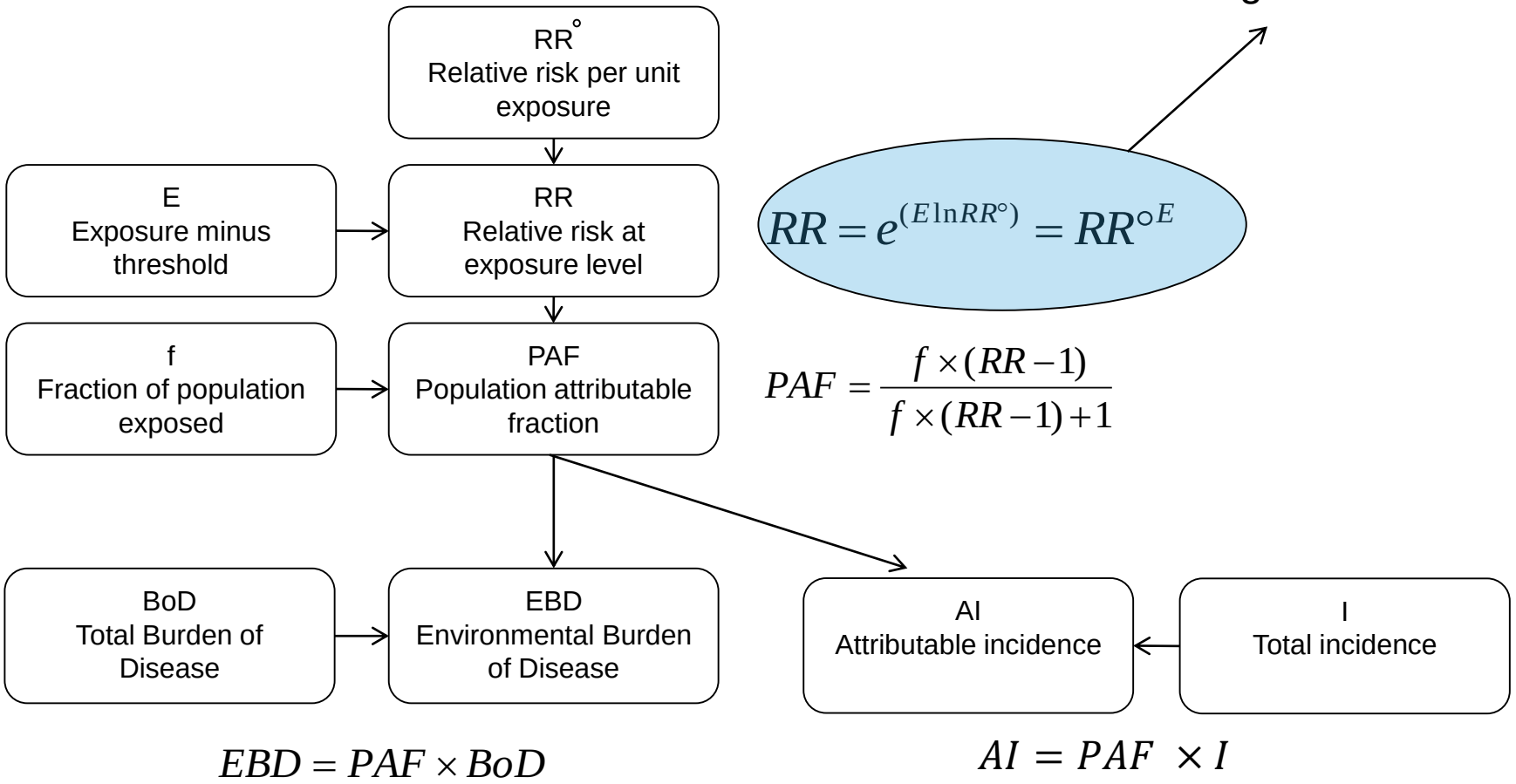
IARC (International Agency on Cancer Research)

Vb Ni: 1 µg/m^3

3.8×10^{-4}

(Log) linear model

Population attributable fraction



Log linear model

$$RR = e^{(E \ln RR^{\circ})} = RR^{\circ E}$$

$$PAF = \frac{f \times (RR - 1)}{f \times (RR - 1) + 1}$$

$$EBD = PAF \times BoD$$

$$AI = PAF \times I$$

Hänninen et al. 2011: European Perspectives on Environmental Burden of Disease Estimates for Nine Stressors in Six European Countries

Background info!

RR per unit exposure and RR at exposure

Epidemiomogical exposure-response functions often log-linear

$Y = B \exp(\beta C)$ with Y incidence, B background incidence and C concentration

$RR = Y / B = \exp(\beta C)$

$\beta = \ln(RR) / C$ or β expresses the change in incidence due to a change in unit concentration of the pollutant

$\beta = \ln(RR) / C = \ln(RR°)$

$\ln(RR) = C \times \ln(RR°)$

$RR = \exp(C \times \ln(RR°))$

$RR = \exp(\ln RR°^{C})$

$RR = RR°^{C}$

Background info!

Population attributable fraction (PAF)

PAF $= \frac{I_{total} - I_0}{I_{total}}$ with I_0 incidence in the non-exposed

I_{total} can also be written as a mixture of exposed and non-exposed

$I_{total} = f\, I_1 + (1\text{-}f)\, I_0$ with f the fraction of persons exposed

Therefore

$$\text{PAF} = \frac{f\, I_1 + (1-f)\, I_0 - I_0}{f\, I_1 + (1-f)\, I_0} = \frac{f\, I_1 + I_0 - f I_0 - I_0}{f I_1 + I_0 - f I_0} = \frac{f I_1 - f I_0}{f I_1 + I_0 - f I_0}$$

$$\text{PAF} = \frac{f(I_1 - I_0)}{f(I_1 - I_0) + I_0} = \frac{f\left(\frac{I_1}{I_0} - \frac{I_0}{I_0}\right)}{f\left(\frac{I_1}{I_0} - \frac{I_0}{I_0}\right) + \frac{I_0}{I_0}} \; and \; RR = \frac{I_1}{I_0}$$

$$\text{PAF} = \frac{f(RR-1)}{f(RR-1)+1}$$

Uncertainties

Knol, A., 2010. *Health and the Environment: assessing the impacts, addressing the uncertainties*, Thesis Utrecht University, the Netherlands.

1. Context uncertainty e.g. selected endpoints
2. Model structure uncertainty e.g. threshold?
3. Parameter & input data uncertainty *vb. data,* Monte Carlo analyse

Cadmium (Cd)

Toxic, carcinogenic (IARC), SVHC (ECHA)

No biological function in humans

Naturally abundant, widely distributed

Industrial, agricultural activities (fertilizer)

Soil -> crop -> human

Transfer factor larger than lead, mercury

Cigarette smoke

Food: algae formulations, offal, cocoa, crustaceans, fungi, seaweeds

Safety limits: EC No. 1881/2006: 0.05 mg/kg (some meat products) to 1 mg/kg (kidney from some animals, bivalve molluscs)

Safety limits for soils for food production and drinking water

Osteoporosis

EBoD (elderly)

Exposure

RR, OR

Incidence/prevalence

Osteoporosis hip or spine elderly women

- OR: Engström et al. (2011,2012)
- All women
- OR per unit exposure: 1.43 (1.15-1.78) per 0.42 µg Cd/g crea

µg Cd/g crea	OR (95%CI) prevalence osteoporosis
<0.5	1
0.5-0.75	1.61 (1.20-2.16)
≥0.75	1.95 (1.30-2.93)

- No osteoporosis below 0.5 µg/g crea (uncertainty)

->50y

- Low Cd-exposure

Osteoporosis

ENNS (France, 60-74y, n=421)

AMBIENT_ES (Spain, 50-65y, n=119)

Exposure and % > 0.5 µg Cd/g crea

Country	Age (years)	N	U-Cd concentrations (µg/g crea) GM	95% CI GM	P10	P25	P50	P75	P90	P95	% > 0.5 µg/g crea	% > 0.5 - 0.75 µg/g crea	% ≥ 0.75 µg/g crea
BIOAMBIENT.ES (Spain)	50-65	119	0.42	0.34 - 0.52	-	0.29	0.46	0.69	1.27	1.82	42.32%	16.35%	25.97%
ENNS (France)	60-74	421	0.43	0.40 - 0.46	0.20	0.29	0.42	0.65	0.99	1.15	40.08%	22.38%	17.69%

Prevalence of osteoporosis 30% (Spain) – similar other EU countries

RR?

µg Cd/g crea	OR (95%CI)	RR (95%CI)
<0.5	1	1
0.5-0.75	1.61 (1.20-2.16)	1.36 (1.13-1.60)
≥0.75	1.95 (1.30-2.93)	1.52 (1.19-1.86)

$$RR = \frac{OR}{(1-I_0)+(I_0 \times OR)}$$

Osteoporosis

$$PAF = \frac{f \times (RR - 1)}{f \times (RR - 1) + 1}$$

Multilevel exposure

Spain

Women 50-65y: 4.3×10^6

µg Cd/g crea	RR (95%CI)	% Exposed	AF (partial)	Prevalence	Attributable prevalence	Attributable cases
<0.5	1					
0.5-0.75	1.36 (1.13-1.60)	16.35	0.06	30%	0.06 × 30%= 1.67%	1.67% × 4.3 × 10^6 = 71318
≥0.75	1.52 (1.19-1.86)	25.97	0.12	30%	3.57%	151341
Sum						222659

What is now the population attributable fraction?

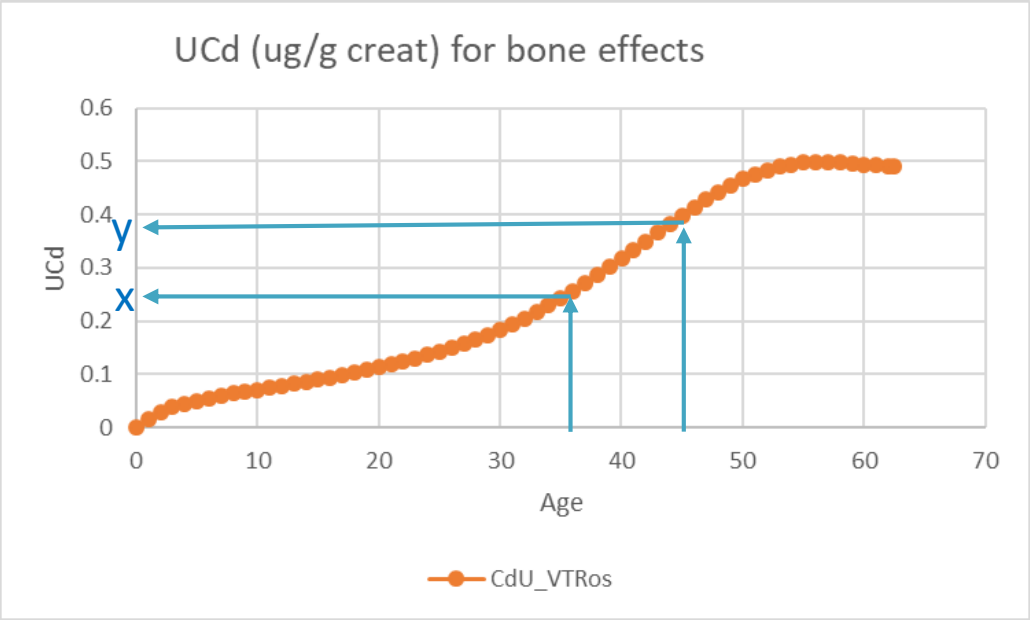
PAF= 0.16

$$PAR_F = \frac{\sum_{s=1}^{S} p_s(RR_s - 1)}{1 + \sum_{s=1}^{S} p_s(RR_s - 1)}$$

Osteoporosis

DEMOCOPHES

Cd in 16 EU countries (35-40y, >40-45y)



A life-time PBPK model was used to identify the "alert" levels of U-Cd at each age which lead to reach the 0.5 µg/g crea at age 55-60 years

Body weight and creatinine excretion evolutions in model

Assumptions!

- Constant dietary intake
- Identical for all EU countries

Fractions of women exceeding a certain level of urinary Cd crea for their age range

Country	N (women at age 35-40)*	% > x µg/g crea (prevalence expo)	AF 1	ADB 1 (cases)	N (women at age 41-45)*	% > y µg/g crea (prevalence expo)	AF 2	ADB 2 (cases)	Total number of cases
Be	443119	16.1%	0.054	7406	391833	7.7%	0.026	3211	10617

1. CKD

CKD

Exposure

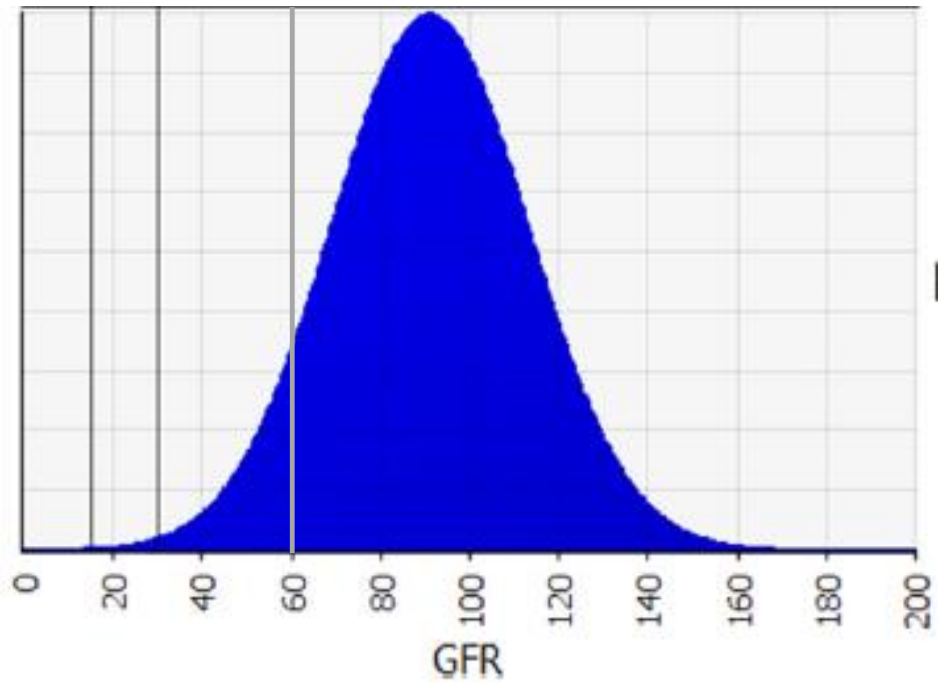
ENNS (France, 60-74y, n=421)

AMBIENT_ES (Spain, 50-65y, n=119)

Study (Country)	Age of participants (women), years	N	U-Cd concentrations (µg/g crea)							
			GM	95% CI GM	P10	P25	P50	P75	P90	P95
BIOAMBIENT_ES (Spain)	**50-65**	119	0.42	0.34-0.52	-	0.29	0.46	0.69	**1.27**	**1.82**
ENNS (France)	**60-74**	421	0.43	0.4-0.46	0.20	0.29	0.42	0.65	**0.99**	**1.15**

CKD (chronic kidney disease) elderly women

Definition CKD: GFR (glomerular filtration rate) < 60 ml/min/1.73m^2

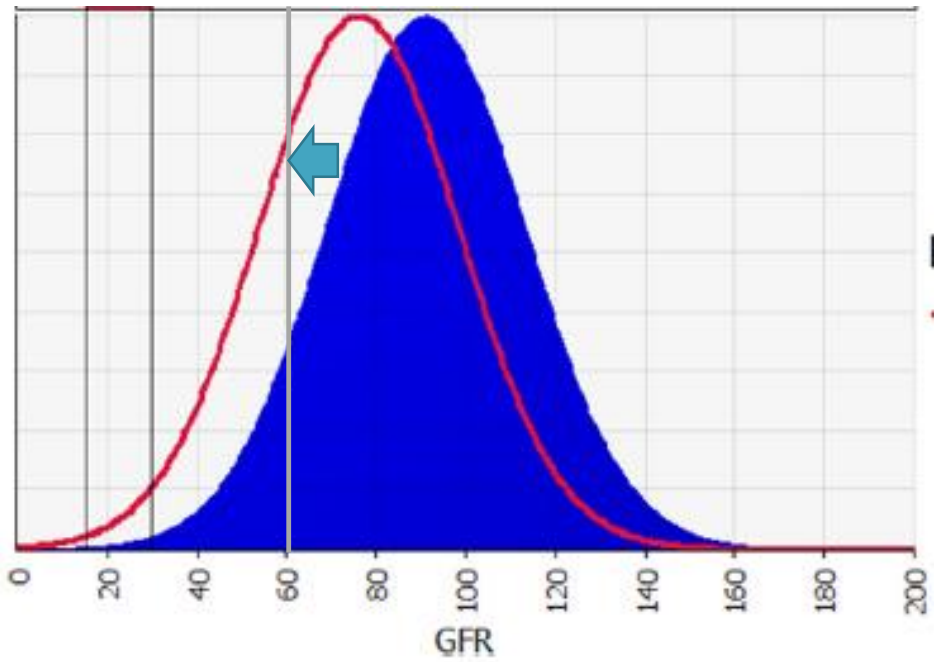


Zhang et al., 2019

Stage	ml/min/1.73m^2	Consequences
3	30-59	Some patients: swelling of hands and feet, back pain,
4	15-30	Dialysis
5	0-15	Dialysis, transplant

CKD

Age related

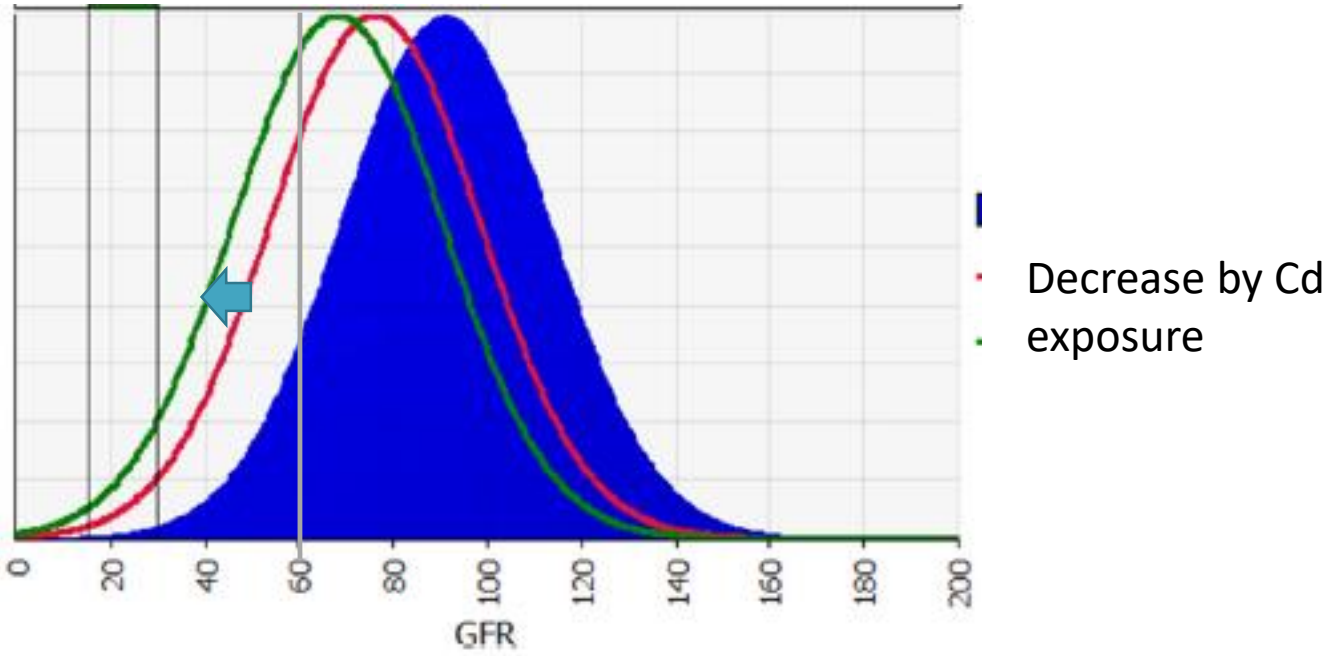


Decrease by ageing

$X_{\alpha+n} = X_{\alpha} - 0.8\ n$ (after 30 or 40 years)
with
α the age category at which GFR is known
n the number of years to be added to come to age at which we want to know GFR

CKD

Cd exposure related



Without ageing: $X_{cd} = X\ (1\text{-}0.058(UCd\text{-}1))$

Exposure response: Akesson et al. (2005) and translated by Ginsberg et al. (2012) towards GFR: 5.8% decrease in GFR per µg Cd/g crea
Threshold: 1 µg Cd/g crea
Low Cd exposure

With ageing and Cd exposure included: $X_{\alpha+n,cd} = (X_{\alpha}\text{- } 0.8\ n)(1 - 0.058\ (UCd\text{-}1))$

Cd exposure

ENNS (France, 60-74y, n=421)

AMBIENT_ES (Spain, 50-65y, n=119)

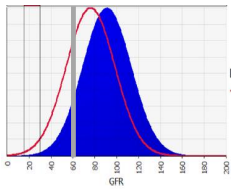
Study (Country)	Age of participants (women), years	N	U-Cd concentrations (µg/g crea)							
			GM	95% CI GM	P10	P25	P50	P75	P90	P95
BIOAMBIENT_ES (Spain)	50-65	119	0.42	0.34-0.52	-	0.29	0.46	0.69	1.27	1.82
ENNS (France)	60-74	421	0.43	0.4-0.46	0.20	0.29	0.42	0.65	0.99	1.15

GFR (literature)

Country	GFR, mean (SD) (ml/min/1.73 m^2)	Mean Age (years)	Reference
Spain	84.6 (36.7)	49.5	Otero et al., 2010
France	71.0 (15.0)	68.3	Bacchetta et al., 2010

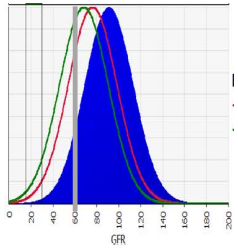
Shift in GFR due to age

Spain: Mean GFR for 57.5y? → 84.6 – (57.5-49.5) x 0.8 = 78.2



Shift in GFR due to Cd (e.g. Spain) at P90 at P95 UCd

Spain	Age and Cd exposure-related GFR decrease (ml/min/1.73 m²) Age 57.5 (mean age of BIOAMBIENT_ES women)
P90 U-Cd concentration (1.27 µg/g crea) of the BIOAMBIENT_ES study	76.97 (SD 36.7)
P95 U-Cd concentration (1.82 µg/g crea) of the BIOAMBIENT_ES study	74.5 (SD 36.7)



Example for CKD stage 5 (0-15 ml/min/1.73m²)

	Prevalence
Age 49.5	2.89%
Age 57.5	4.25%
Age 57.5 and Cd at Cd P90	4.57%
Age 57.5 and Cd at Cd P95	5.25%
Shift in prevalence at Cd P90	4.57-4.25= 0.32%
Shift in prevalence at Cd P95	5.25-4.25= 1%
Attributable prevalence taken into account % of people exposed	=0.32% × 5% + 1% ×5% = 0.07%
Number of attributable cases in women 50-65y	= 0.07% × 4.3 ×10⁶ = **2781**

AF = 0.07/4.25= 0.02

All CKD stages

CKD stage	AF
3-5	**0.01**

Total number of cases Spain women 50-64y: 15230

BIOAMBIENT_ES

Osteoporosis (uncertainty!)

0.5 µg Cd/g crea

PAF: 0.16

CKD

1 µg Cd/g crea

PAF: 0.01

Risk assessment EFSA, JECFA, ATSDR

Dietary intake values

HBM?

Critical effect = kidney disfunction

Accumulation of Cd

Elderly people

Increased evidence for bone effects at low-level exposure

Risk assessment EFSA, JECFA, ATSDR

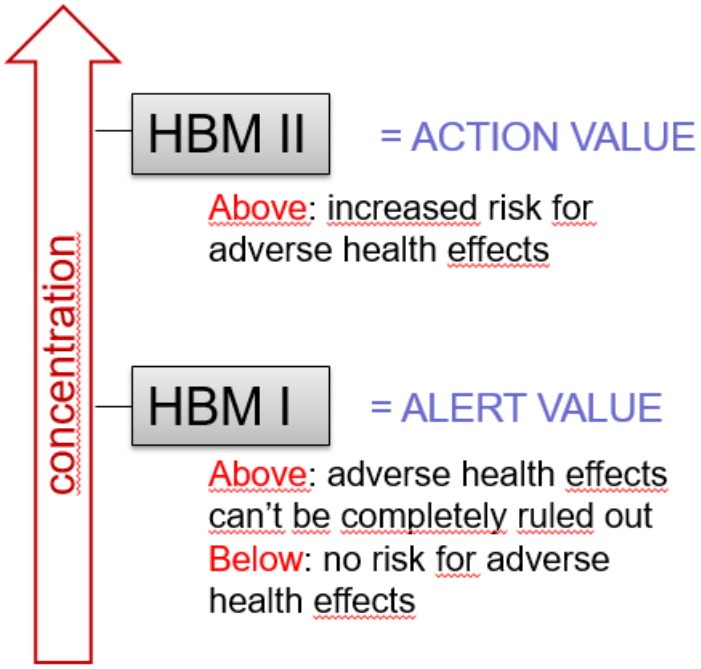
Derivation of Cd dietary intake limit values and health-based guidance values for U-Cd

	EFSA (2009)	JECFA (2010)	ATSDR (2012)
Key study	Pooled analysis from EFSA (35 epidemiologic studies)		Meta-analysis of environmental exposure studies
Evaluation of tubular proteinuria & U-Cd excretion	β2-microglobulin & U-Cd (µg/g crea) (Exclusively for a population over 50 years of age)		Low molecular weight proteinuria & U-Cd (µg/g crea) (selected studies reported a dose-response relationship in sufficient detail so that the dose-response function could be reproduced independently)
Critical U-Cd (µg/g crea)	1 µg/g crea ($BMDL_5$ of 4 µg/g crea and specific adjustment factor of 3,9 to account for human variability in U-Cd within each dose-subgroup in the analysis)	5.24 µg/g crea (4.94-5.57) (point of gradient change in the slope)	0.5 µg/g crea (95% lower confidence limit associated with 10% increased risk of low molecular weight proteinuria)
Dietary Cd assessment model	Adapted from Amzal et al., 2009	Adapted from Amzal et al., 2009 (Cd half-life)	Kjellstrom & Nordberg, 1978
Toxicological reference value (oral)	TWI 2.5 µg/kg bw/week TDI 0.36 µg/kg bw/day	PTMI 2.25 µg/kg bw/month PTWI 5.6 µg/kg bw/week	MRL 0.1 µg/kg bw/day

HBM guidance values

HBMI-value: 1 µg/g crea (1µg/L)

adults



A value above the HBMI is an indicator, a raised flag, that the risk is increased, not meaning that health effects are already present, seeing e.g. the uncertainties and safety factors applied. It is an indicator that there is a concern of the exposure with regard to health-based criteria and is signal for policy-makers.

Risk assessment

External doses (EFSA)

"Conclusions were that the mean Cd exposure for adults across Europe was close to, or slightly exceeding the TWI of 2.5 µg/kg bw/week. The exposure of some subgroups of population, such as vegetarians, children, smokers and people living in highly contaminated areas was determined to exceed the TWI by about 2-fold."

and

"EFSA concluded that there was a need to reduce exposure to Cd at the population level"

Internal doses

ENNS (France, 60-74y, n=421)

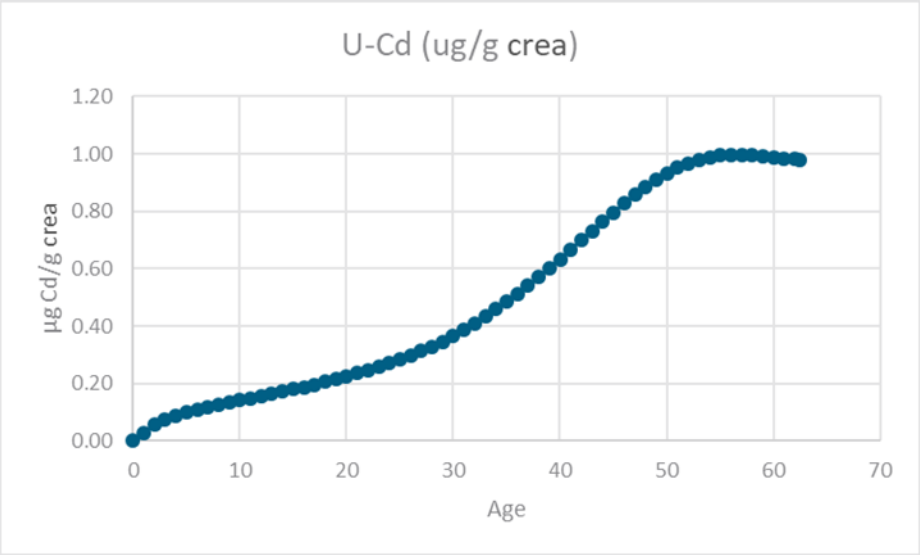
AMBIENT_ES (Spain, 50-65y, n=119)

Study (Country)	Age of participants (women), years	N	U-Cd concentrations (µg/g crea)							% > 1 µg/g crea
			GM	95% CI GM	P10	P25	P50	P75	P90	P95	
BIOAMBIENT_ES (Spain)	50-65	119	0.42	0.34-0.52	-	0.29	0.46	0.69	1.27	1.82	17.4%
ENNS (France)	60-74	421	0.43	0.4-0.46	0.20	0.29	0.42	0.65	0.99	1.15	8.0%

Internal doses

DEMOCOPHES

Cd in 16 EU countries (35-40y, >40-45y)



Spain, Ireland, Poland and Romania
P95 > age specific U-Cd alert value

A life-time PBPK model was used to identify the "alert" levels of U-Cd at each age which lead to reach the U-Cd HBM-GV of 1 µg/g crea at age 55-60 years

Body weight and creatinine excretion evolutions in model

Assumptions!

- Constant dietary intake
- Identical for all EU countries

These results lends further support to the EFSA conclusion that Cd exposure in the general population should be reduced

Indicators

1. A definition of an Environment Health Indicator (EHI)

An expression of the link between environment and health targeted at an issue of specific policy or management concern and presented in a form, which facilitates interpretation for effective decision making

(Corvalan, Briggs and Kjellstrom 2000)

Types of environmental health indicator

Environmental health indicators can thus be:

- *Health-based: describing a health outcome that is attributable to a known or suspected environmental cause.*

  E.g. Mortality rate in adults due to exposure to fine particulate matter

- *Exposure-based: describing an exposure (or potential for exposure) that might lead to a definable health effect.*

  E.g. Exposure to PFOS in children

- *Focus on exposure-based (results indicator and impact indicator)*

1. Indicators

- Tool to condense complex scientific information in a few key descriptors
- “Scientific data does not speaks for itself!”
- Communicate to non-expert audience
- Choice of descriptor linked to the (policy) question
- Policy questions HBM?
    - Does the body burden varies over country, age, sex?
    - Does the body burden varies by socioeconomic status (SES)?
    - Has a policy to reduce exposure shown effect (time)?
    - Is the health of a population at risk?
- Activities on E&H: EEA, WHO, Eurostat, OECD, UN SDGs (e.g. nr. 3: good health & well-being; nr. 10: reduced inequalities)

Power of indicators is comparisons

- over time (trends)
- geographic areas
- groups of people

and the focus on the most essential domains of health.

What indicators can (theoretically) do

- Give “early warning” of new problems
- Highlight causes and points for intervention
- Target action where it is needed
- Compare and assess policy options
- Prioritise actions
- Translate policy into management
- Monitor progress and distance to targets
- Monitor policy effects and effectiveness
- Raise awareness about roles and responsibilities
- Inform the public about policy actions
- Justify policies

Briggs, 1999

The information chain

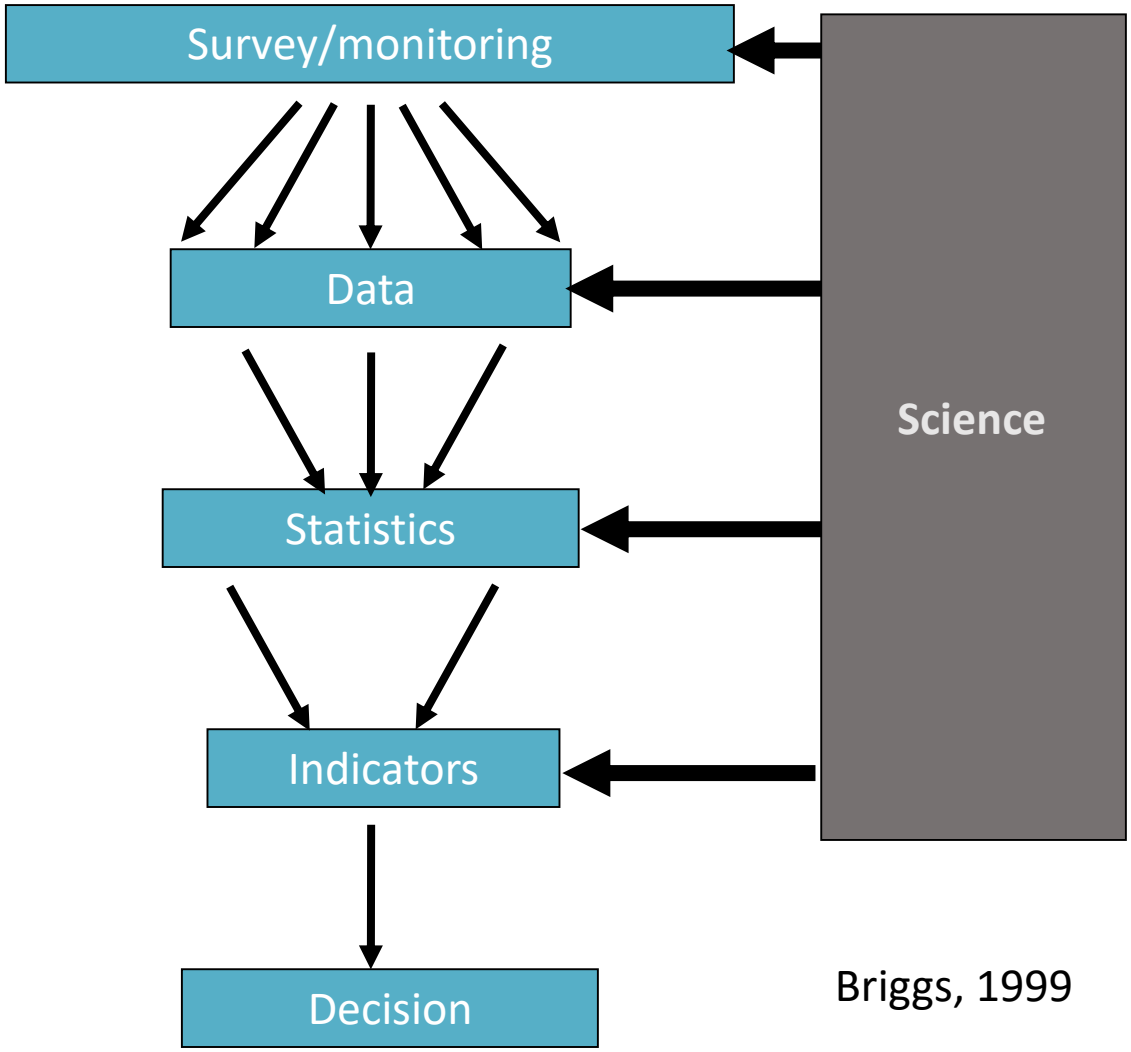
Measurements

Compilation

Aggregation

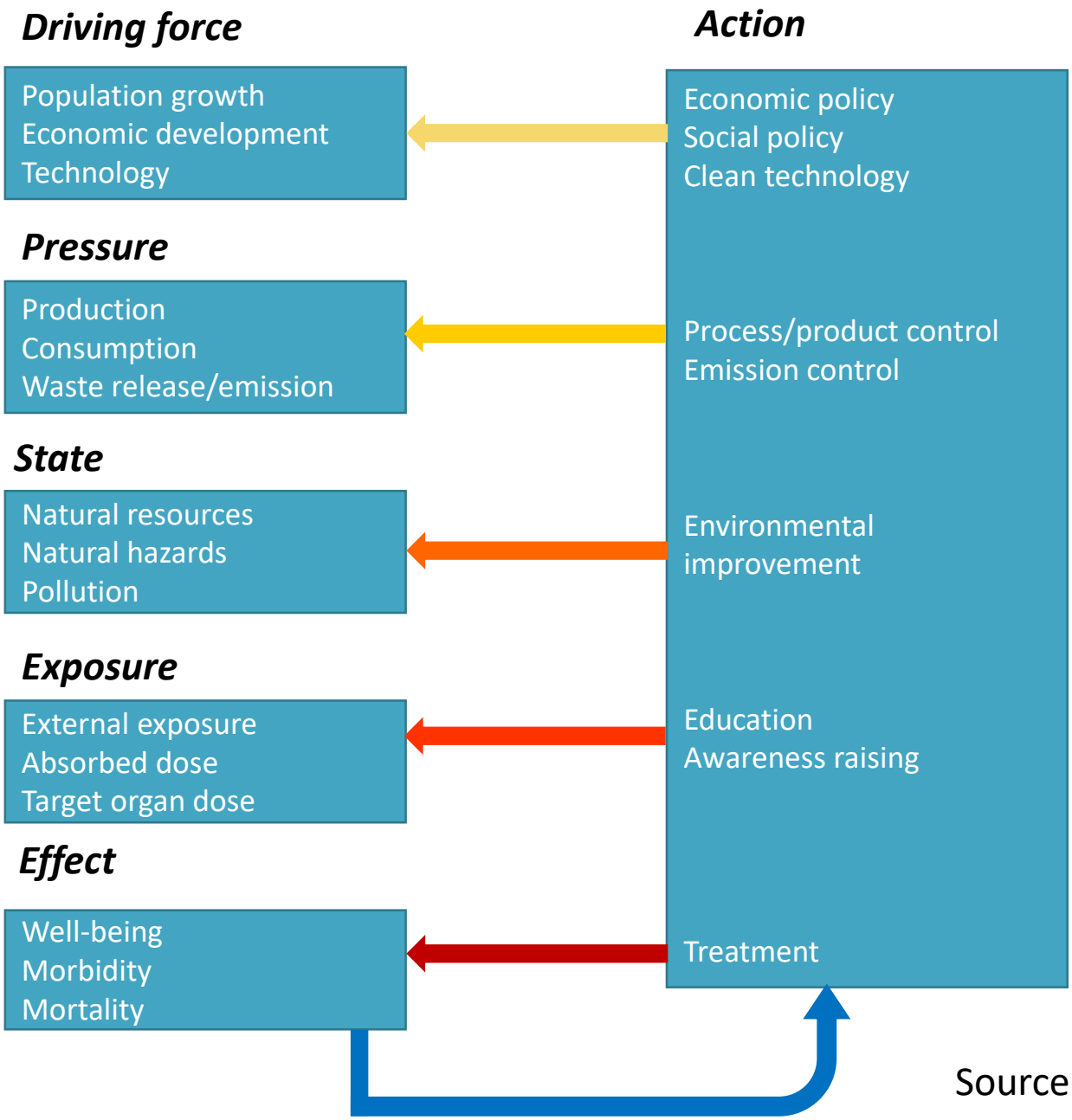
Synthesis/ interpretation

Application



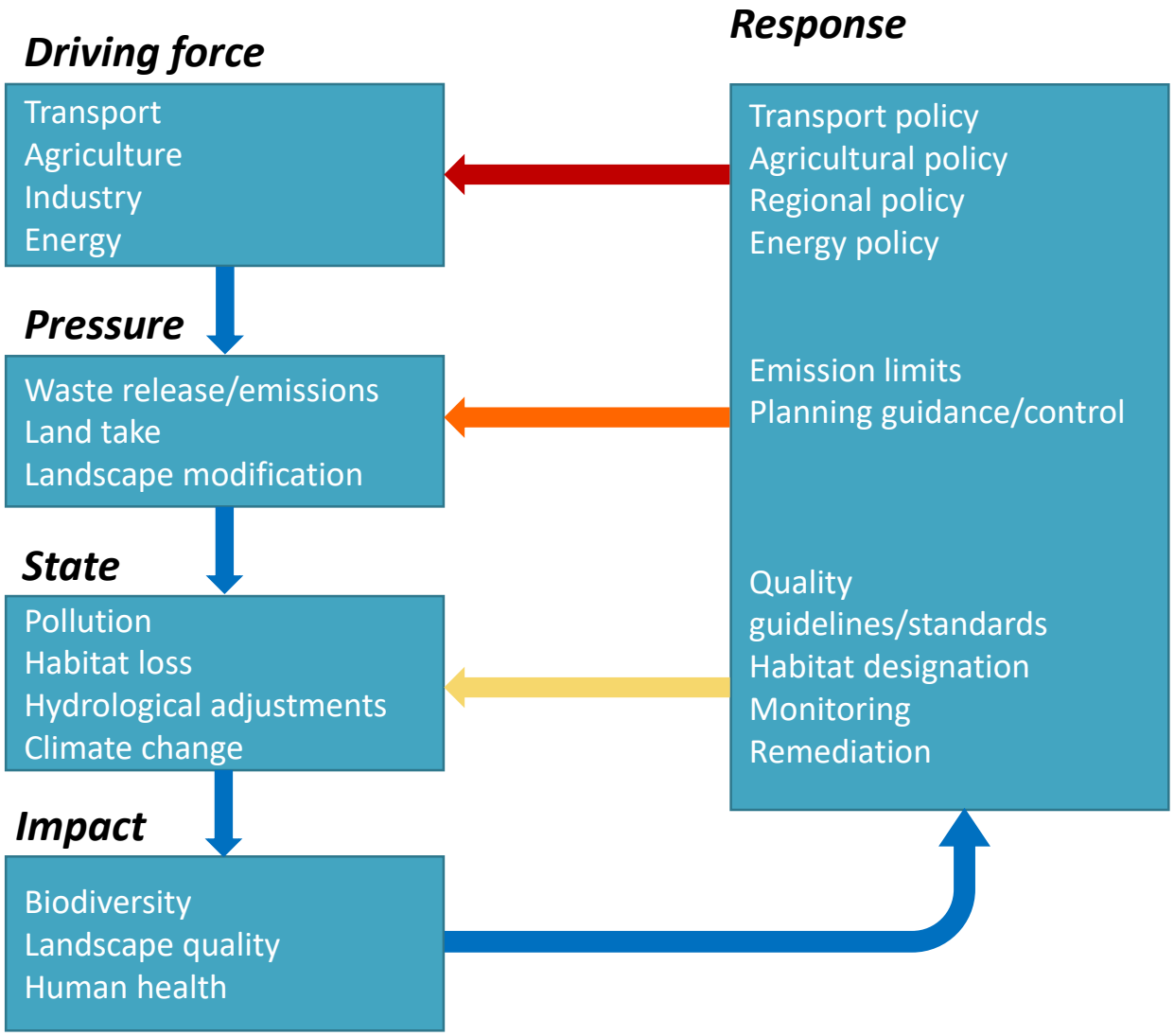
Briggs, 1999

DPSEEA framework



Source WHO

DPSIR chain



Source OECD (Pressure-State-Response model)
Applied by EEA

1. Metadata: descriptive
2. Aggregated data
3. Individual data

Important to include next to aggregated data also metadata in indicator

contextualisation

1. ECHI

Lack of environmental health indicators in the ECHI list

Two ECHI indicators dealing with environmental health:

1. '*Smoking*' providing information about the regularity people smoke cigarettes

2. '*PM10 and PM2.5 particulate matter exposure*'

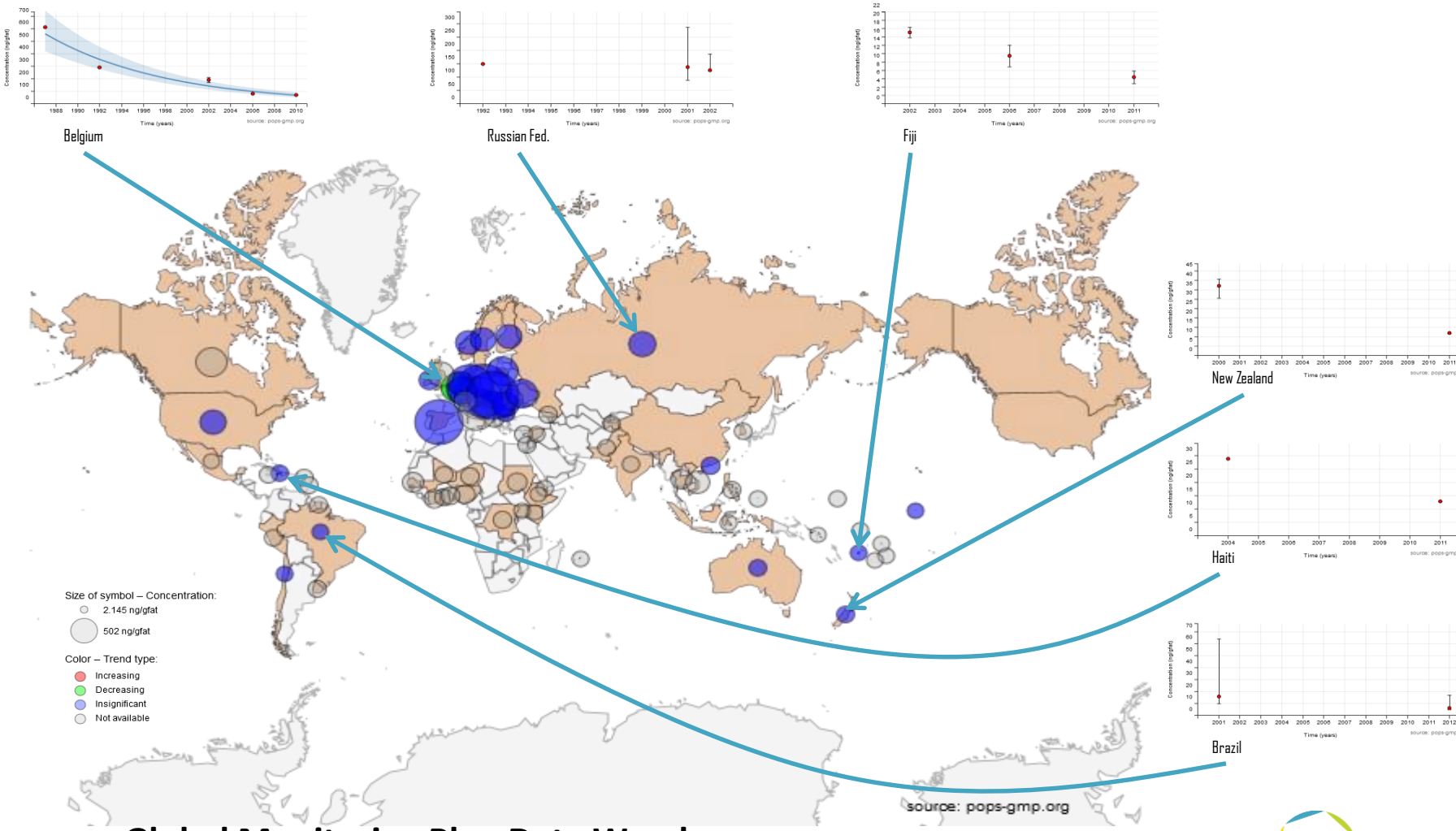
https://ec.europa.eu/health/indicators_data/indicators_nl

Examples of indicators

- Geographical area
- SES
- Gender
- Age
- Time
- Risk

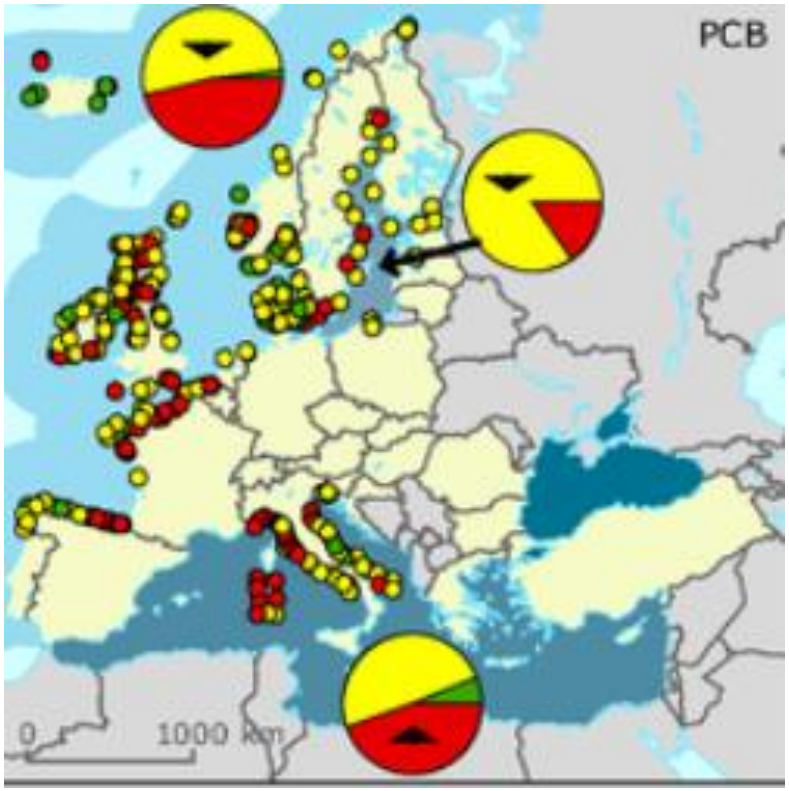
1. Stockholm convention on POPs

Indicator PCBs in human milk (sum 6 PCB)



Global Monitoring Plan Data Warehouse

1. EEA: Hazardous substances in marine organisms in European seas



Substances Species and tissue	Latin name	Low/ High	µg/kg	Basis	Reference	Comment
CADMIUM						
						= 220 ppb r.w.
PCB (CB28)						
Mussels	*Mytilus*[1] *sp.*	Low	0,75	D	OSPAR 2008	BAC limit
Mussels	*Mytilus sp.*	High	3,2	D	OSPAR 2008	EAC limit
Atlantic cod, liver	*Gadus morhua*	Low	0,2	W	OSPAR 2008	BAC limit times 2 (OSPAR[2])
Atlantic cod, liver	*Gadus morhua*	High	64	L	OSPAR 2008	EAC limit
Herring, muscle	*Clupea harengus*	Low	2	W	OSPAR 2008	BAC limit times 20 (OSPAR[2])
Herring, muscle	*Clupea harengus*	High	64	L	OSPAR 2008	EAC limit
PCB (CB 52)						
Mussels	*Mytilus*[1] *sp.*	Low	0,75	D	OSPAR 2008	BAC limit
Mussels	*Mytilus sp.*	High	5,4	D	OSPAR 2008	EAC limit
Atlantic cod, liver	*Gadus morhua*	Low	0,16	W	OSPAR 2008	BAC limit times 2 (OSPAR[2])
Atlantic cod, liver	*Gadus morhua*	High	108	L	OSPAR 2008	EAC limit
Herring, muscle	*Clupea harengus*	Low	1,6	W	OSPAR 2008	BAC limit times 20 (OSPAR[2])
Herring, muscle	*Clupea harengus*	High	108	L	OSPAR 2008	EAC limit

Concentrations

- Low
- Moderate
- High

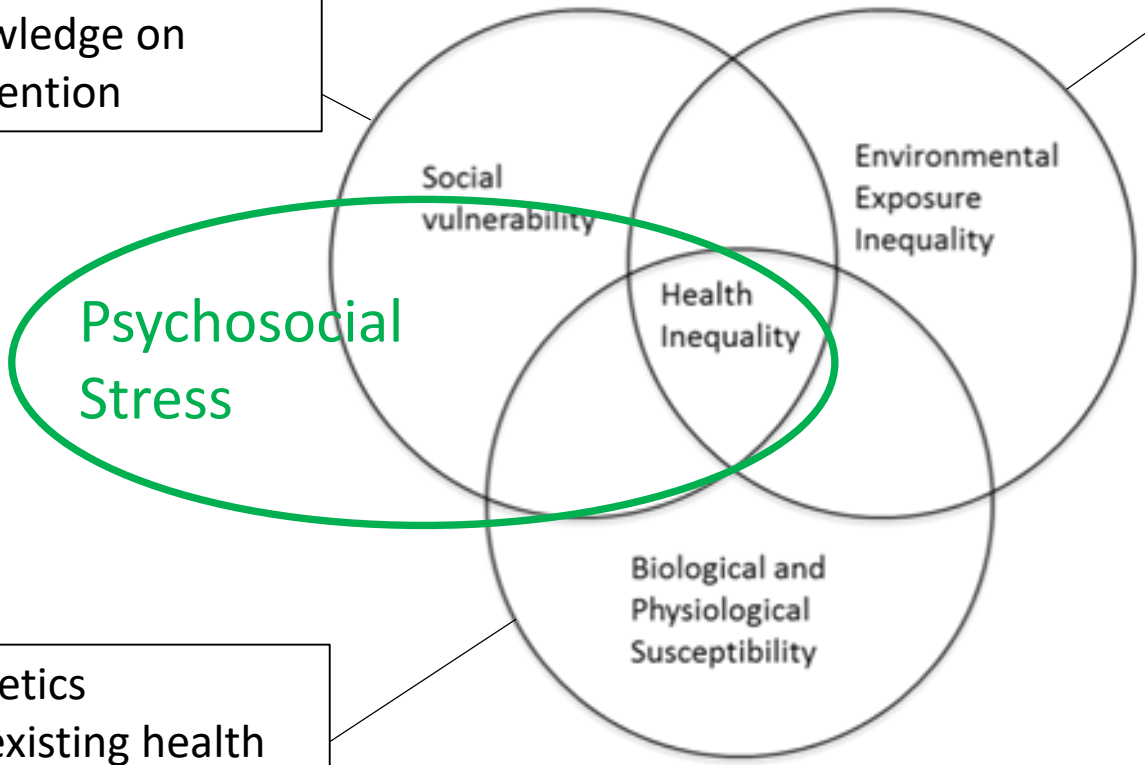
Trend up Trend down

Examples of indicators

- Geographical area
- SES
- Gender
- Age
- Time
- Risk

Health inequalities – Combination of factors

- Access to healthcare
- Knowledge on prevention



- Outdoor
- Indoor
- Occupational
- Dietary (e.g. fast food)
- Green space

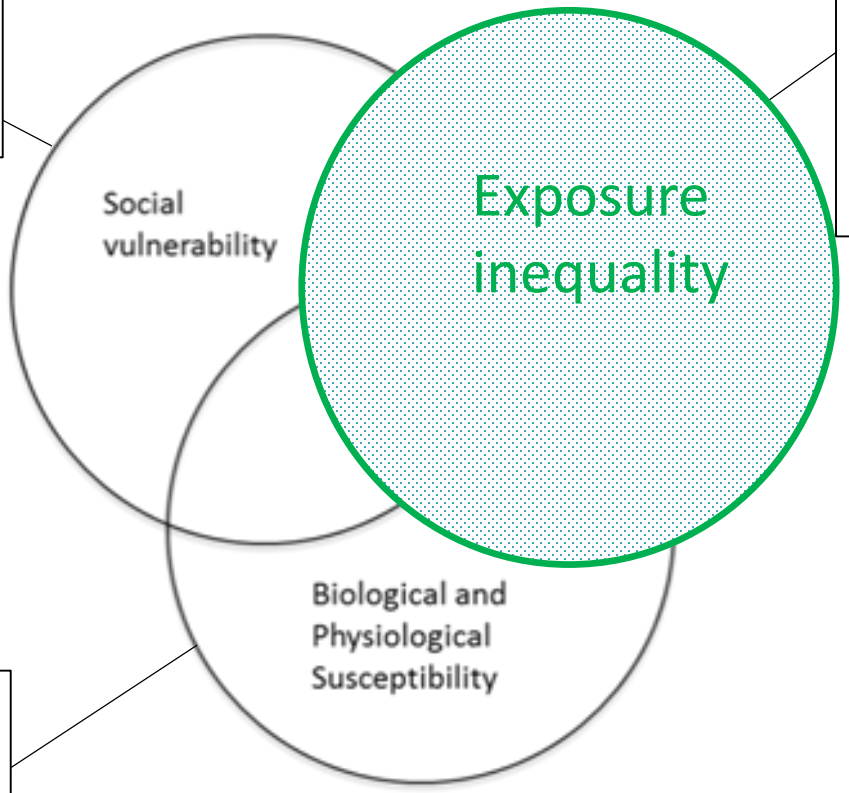
- Genetics
- Preexisting health conditions

"*Social inclusion by design*"

Morello-Frosch et al., 2011
Frumkin, 2016

Health inequalities – Combination of factors

- Access to healthcare
- Knowledge on prevention



- Outdoor
- Indoor
- Occupational
- Dietary (e.g. fast food)
- Green space

- Genetics
- Preexisting health conditions

Morello-Frosch et al., 2011
Frumkin, 2016

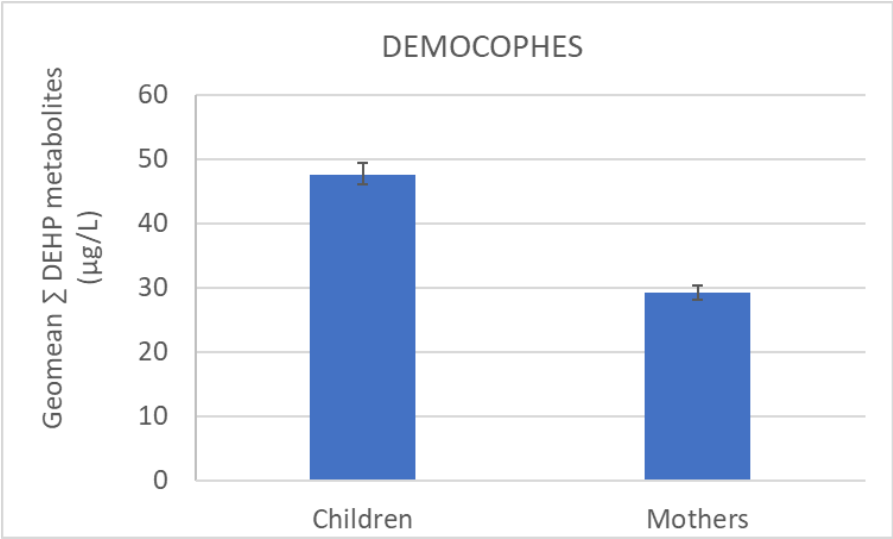
Figure will be added when report will appear (next Wednesday)

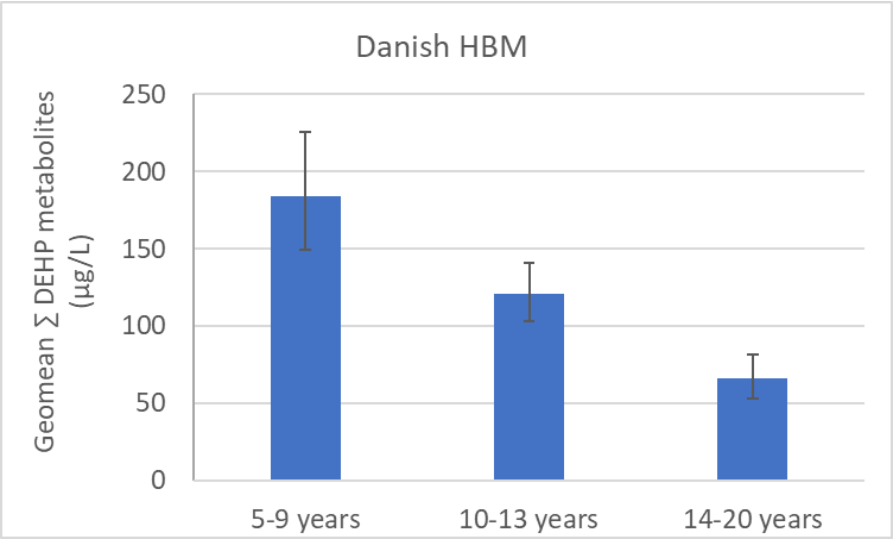
Environmental health inequalities in Europe – second assessment report 2019

Inequalties in chemical exposure (Buekers et al.)

Examples of indicators

- Geographical area
- SES
- Gender
- Age
- Time
- Risk





"Toy directive"

Examples of indicators

- Geographical area
- SES
- Gender
- Age
- Time
- Risk

Blood lead

Exhibit 1. Blood lead concentrations for the U.S. population age 1 year and older by sex, 1999–2016

Information on the statistical significance of the trends in this exhibit is not presented here. For more information about uncertainty, variability, and statistical analysis, view the technical documentation for this indicator.

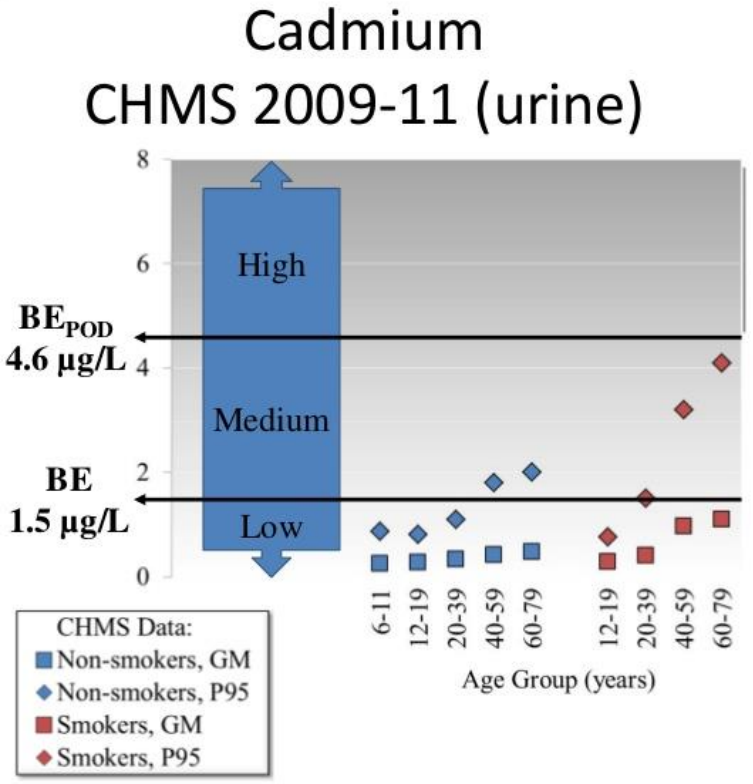
Data source: CDC, 2018

Examples of indicators

- Geographical area
- SES
- Gender
- Age
- Time
- Risk

HBM in a health risk context

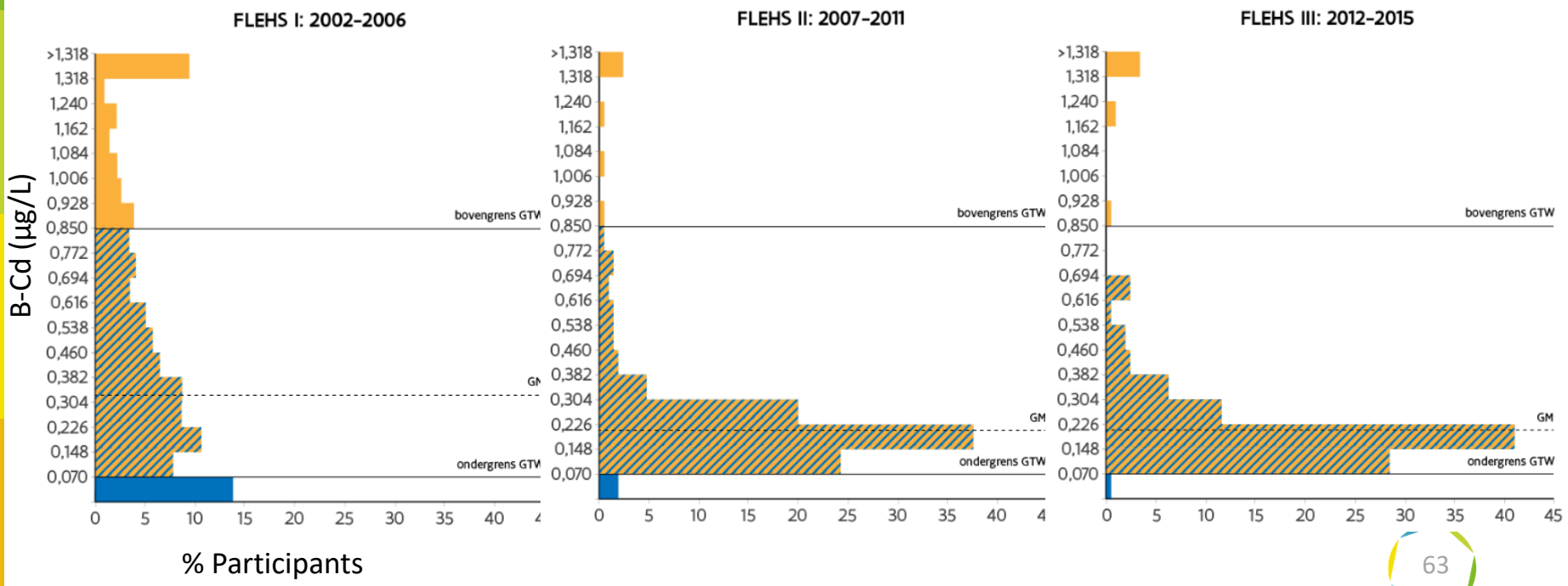
Santé Canada Health Canada



Interpreting population level biomontirong: Data in a risk based context: A Canadian perspective

https://www.slideshare.net/KateJones7/71-

1. Flemish
2. https://www.milieurapport.be/milieuthemas/milieu-gezondheid/humane-biomonitoring/blootstelling-aan-cadmium-concentraties-in-bloed-van-jongeren



1. Indicator criteria (Expert consultation)

- Policy, societal relevance (BoD useful, build-up, health inequalities)
- Possibilities for prevention and/or reduction
- Data availability & robustness (across EU)
- Transparent and easy to communicate (layered)
- Align with other indicators e.g. ECHI
- Context
- *Etc.*

1. Indicator types (Eurostat)

Result indicator: descriptive, state, referring to HBM exposure concentrations (P50, P95), HBM reference values

Impact indicator: performance, distance to target, normative HBM guidance values

a) Percentage of exceedance (P): % > HBM GV (mention number of samples!) (BRIDGEHEALTH)

b) Extent of exceedance (E): P95 / HBM GV (prioritization)

Depending of level of disaggregation: indicator split up by age, sex, SES

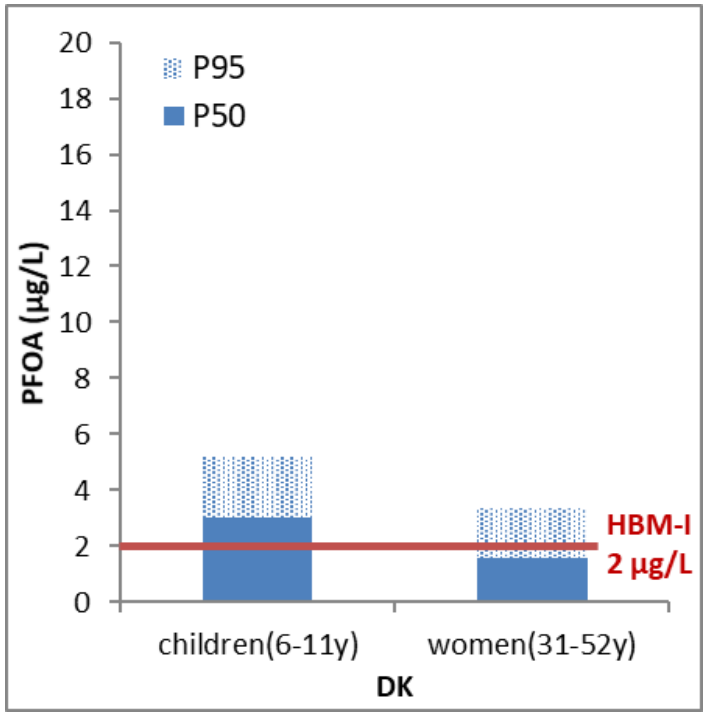
1. DEMOCOPHES

This project has received funding from the European Union's Life programme under Agreement LIFE09/ENV/BE/000410.

- 17 countries
- Consistent at European scale
- Child-mother pairs
- 3688 persons
- 2011-2012

- Published data: Cd, Hg, cotinine, BPA, PFOA, PFOS
- Aggregated data

1. HBM data in risk context - age



Morck et al., 2015

	n	P50 (µg/L)	P95 (µg/L)	HBM-I (µg/L)	Percentage of exceedance (P)	Extent of exceedance (E) based on P95
Children	116	3.02	5.21	2	>50%	2.61
Mothers	143	1.59	3.38	2	<50%	1.69

- High persistency
- PFOA: SVHC (ECHA)

As time goes by…

Contact

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project engineer VITO

studies: environmental engineering

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 733032.

1. HBM-I and BE values

The HBM-I value is not equal but conceptually similar with the biomonitoring equivalent (BE) of Summit Toxicology (Hays et al. (2008)) representing an internal concentration consistent with a defined external exposure guidance value (e.g. tolerable daily intake, reference dose) below which no adverse health effects are expected

Log-linear models: The term "log linear" is used in a number of different ways in multivariate statistics. Here, we mean a model where the dependent or "left hand" variable has been expressed on a logarithmic scale and the independent or "right hand" variable has been expressed in a linear metric. Usually, the natural log is used, so that the model looks like: ln(Y) = a + b (X) or, taking the anti-logs of both sides: Y = exp (a + b (X)).

Y= exp(a) . exp (b(X)) = constant value . exp (b(X))
Y= B exp(b(X))

HBB

German HBM values

concentration

HBM II = ACTION VALUE

Above: increased risk for adverse health effects

HBM I = ALERT VALUE

Above: adverse health effects can't be completely ruled out
Below: no risk for adverse health effects

Biomonitoring equivalents

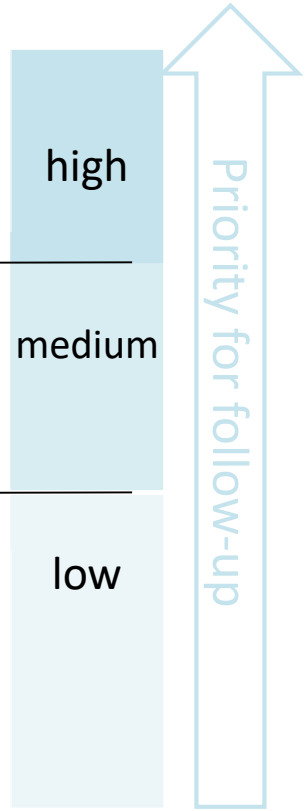
Derived from external exposure

Concentration consistent with point of departure (NOAEL, LOAEL)
→ no uncertainty factors

BEPOD

BE

Concentration consistent with defined exposure guidance values (RfD, MRL, TDI)
→ Similar HBM I
→ Incl uncertainty factors



1. Human biomonitoring

Integrated exposure
Individual
HES Health Examination Survey
Biomarkers
- Exposure
- Effect
- Susceptibility

Questionnaires (SES)

Determinants?