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The basics of environmental risk assessment and how it relates to other environmental management tools

Luís Nunes

Yamagushi, July 2025

Main environmental management tools

They are needed to counterbalance the following effects:

Capitalist systems require perpetual growth on a finite planet;

Short-term decision cycles conflict with long-term environmental timescales;

Those benefiting from environmental destruction have more influence than those bearing the costs;

Human cognition struggles with abstract, global, long-term environmental problems;

Dominant values prioritize material progress over environmental stewardship;

Existing systems create path dependence that resists fundamental change;

Individual rational behavior leads to collectively irrational environmental outcomes.

They all resume to issues of environmental ethics... which are personal!

Let´s do a simple exercise to show how complex it is to find the right balance between human development and preservation of natural resources.

I would like you to fill in a survey, designated the *New Ecological Paradigm*.

It serves to assess the individual environmental ethics of citizens.

There are no right or wrong answers.

The results reflect the similarity or diversity of personal environmental ethics.

Populations with similar ethics will agree with common sustainable development strategies;

While those with different will struggle to agree, avoiding or postponing the decisions (e.g., measures to mitigate climate change).

Please follow this link and answer a survey about environmental ethics:

The New Ecological Paradigm survey (NEP)

Take at most 10 min.

https://forms.office.com/Pages/Resp
onsePage.aspx?id=MQkPE_aguUSuh
bnxbImtgnkngR0sCxpJhcC88DOeBh
1UQjJVUFJCRTI0Q0JCUkoyTUM1
VFI0N0FVNi4u

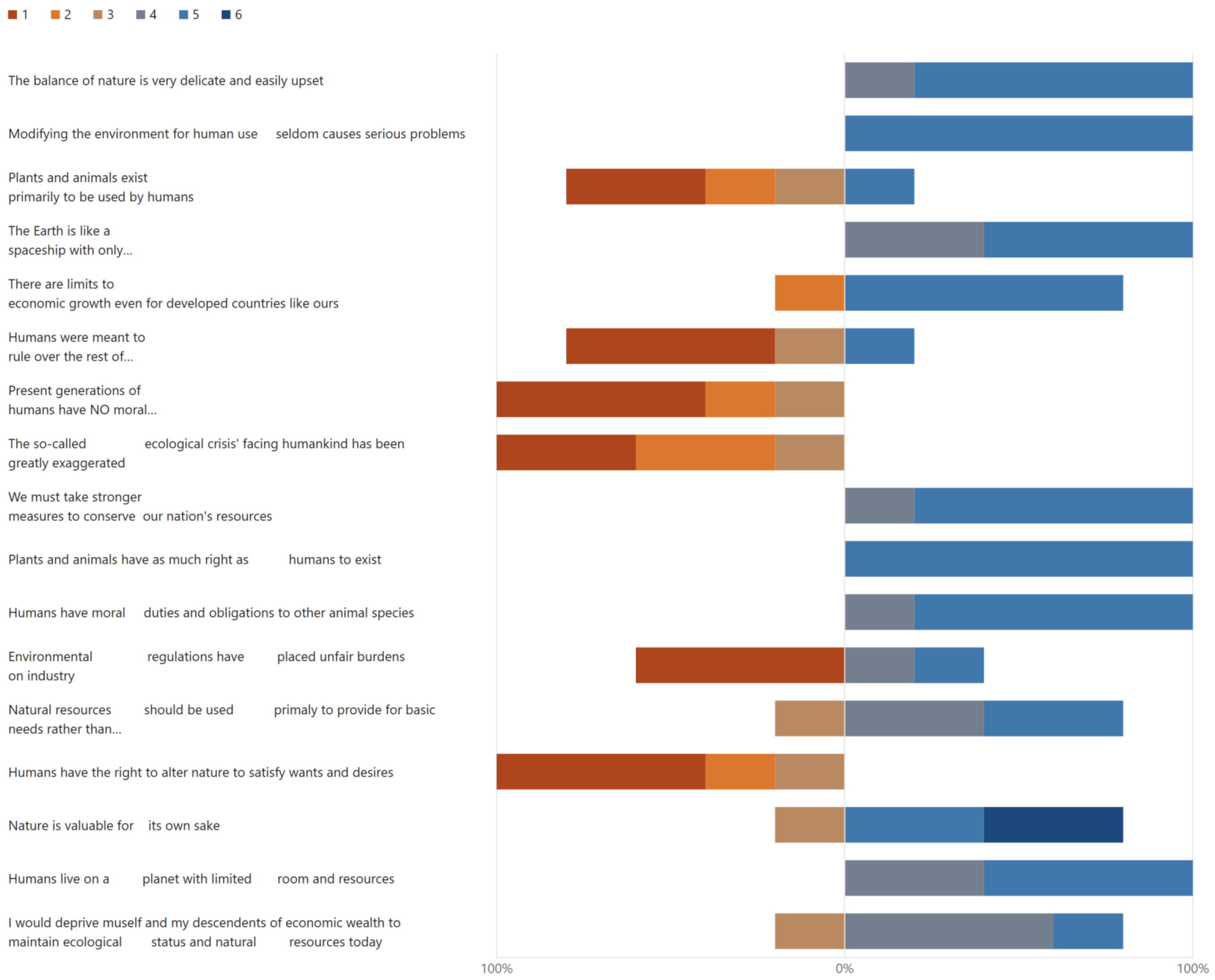
Environmental ethics:

Here is an example from a study done with my students of the BSc in Marine and Coastal Management.

They show different environmental ethics.

Their decisions as citizens and professionals will be based on that.

Wich means they may not agree on the management strategies to attain sustainable growth...



If people cannot agree on a strategy solely based on qualitative assessment, then the effects of strategic decisions need to be quantitatively assessed.

Hence the need to use tools such as the

Environmental Impact Assessment

Lifecycle Assessment

Environmental Risk Assessment

Main environmental management tools

Introduction to EIA, ERA and LCA

EIA

https://www.youtube.com/watch?v=V7W3l1Qgj-0

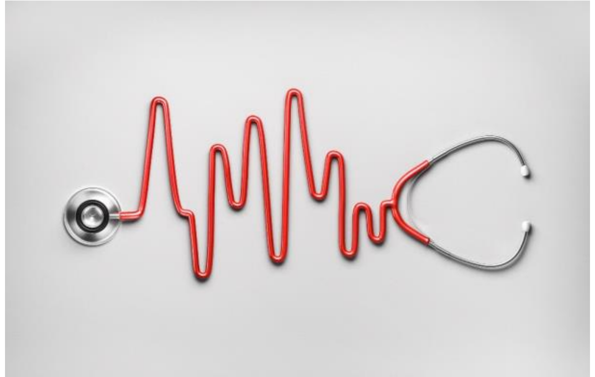
(1.28 min)

LCA

https://www.youtube.com/watch?v=SMnioyRxWNk

(1.50 min)

ERA



https://www.youtube.com/watch?v=kEinQtKEzwc

(3.00 min; start at 0.37)

Use of ERA

Presently, one of the main applications of ERA is assessing the **effects of chemical substances** produced by the chemical and pharmaceutical industries.

Every year, about **1.5 million new chemicals** are produced of which about **1000 enter the market.**

Between **50 and 100 new pharmaceuticals** are introduced in the market every year.

Between **10 and 20 new agrochemicals** are introduced in the market every year.

Data from:
CAS: Chemical Abstracts Service
REACH: EU Registration, Evaluation, Authorisation and Restriction of Chemicals
TSCA: EUA Toxic Substances Control Act of 1976

Use of ERA

The new chemicals may become **Emerging Contaminants** if they can pose risk.

Examples of emerging contaminants include:

Pharmaceuticals: e.g., Antibiotics, hormones, analgesics

Personal care products: containing, e.g., triclosan (antibiotic), parabens (preservatives), UV filters.

Per- and poly-fluoroalkyl substances (PFAS): e.g., PFOA, PFOS, GenX chemicals

Microplastics: Plastic particles <5mm from various sources

Endocrine disrupting chemicals: e.g., Bisphenol A (BPA), phthalates

PFOA: perfluorooctanoic acid; PFOS: perfluorooctanesulfonic acid; GenX: specific type of PFAS with very high environmental half-life.

Examples of emerging contaminants

Uses/ origin

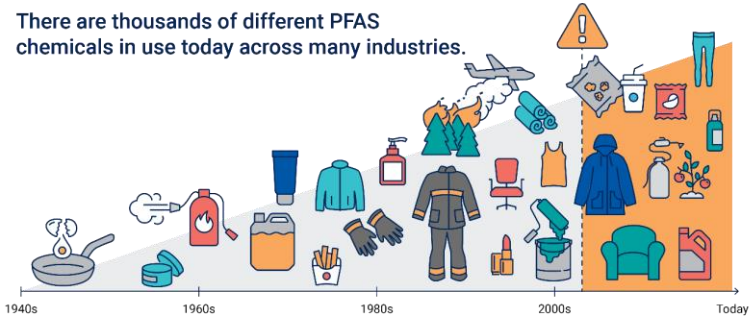
Effects

Pharmaceuticals and personal care products

Antibiotic resistant bactéria, endocrine disruption.

Toxic to wildlife, behavioral changes in wildlife

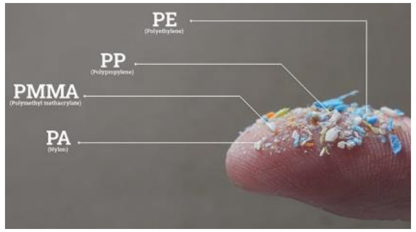
Per- and polyfluoroalkyl substances



Cancer, immune system suppression.

Wildlife reproductive impairment, high bioacumulation and bioamplification.

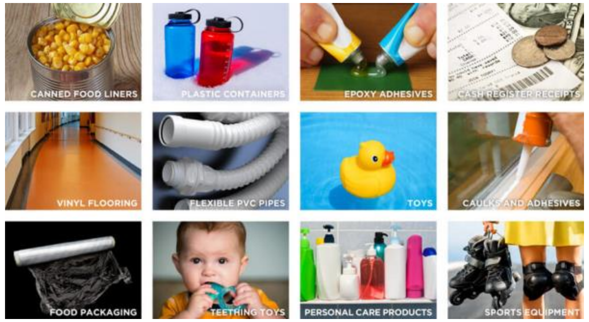
Microplastics



Imphlammatory responses, toxicity from additives

Intestinal blockages and malnutrition, ecosystem alteration.

Endocrine disrupting chemicals



Reproductive disorders, diabetes and obesity.

Severe reproductive impairment in wildlife.

Use of ERA

The **Traditional/Legacy contaminants** have been regulated for decades. These include:

- Heavy metals: e.g., Lead, mercury, cadmium, chromium, arsenic
- Persistent organic pollutants (POPs): e.g., DDT, PCBs, dioxins, furans
- Petroleum hydrocarbons: e.g., Benzene, toluene, xylene, PAHs (polycyclic aromatic hydrocarbons)

PCBs: Polychlorinated biphenyls; DDT: Dichlorodiphenyltrichloroethane; PAHs: Polycyclic aromatic hydrocarbons.

Examples of legacy contaminants

Uses/ origin

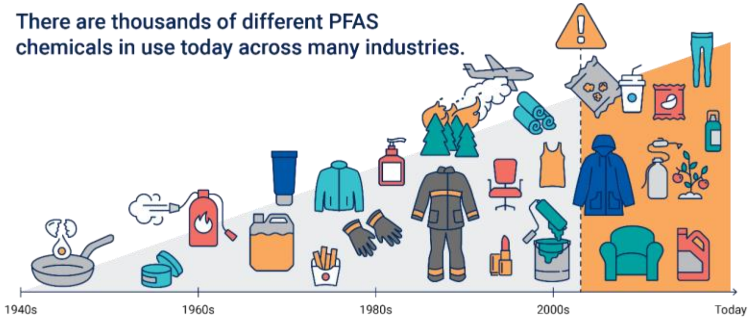
Effects

Heavy metals

e.g., cancer, neurological and cardiovascular diseases.

Poisonous to wildlife.

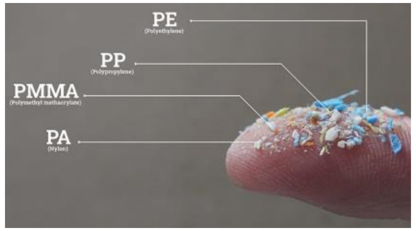
Persistent organic pollutants



e.g., cancer, neurological, cardiovascular diseases, reproductive effects.

e.g., wildlife reproductive decrease and failure, community structure changes.

Petroleum hydrocarbons

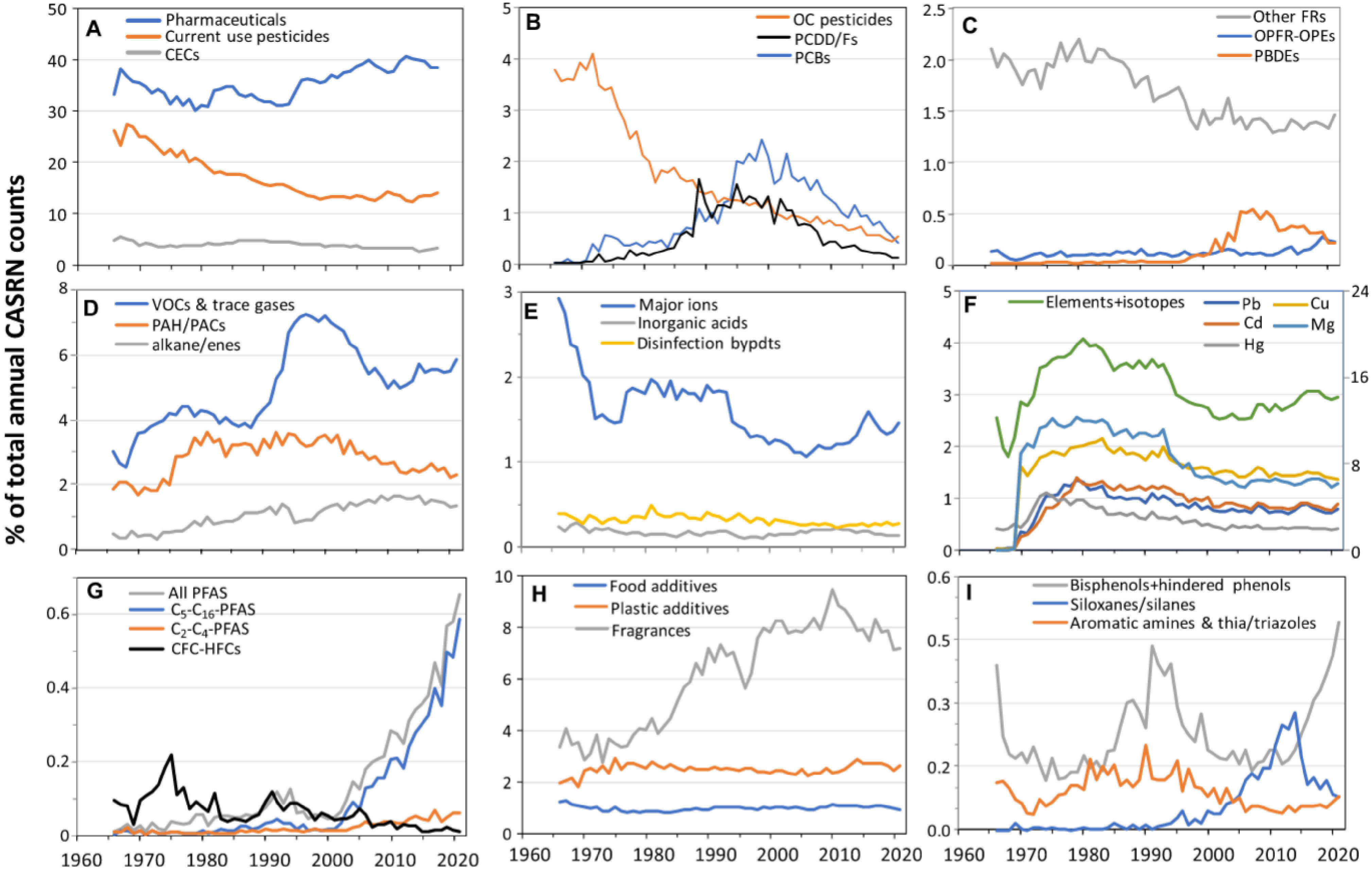


e.g., cancer, neurological and organ failure.

Poisonous to wildlife, habitat degradation.

Risk studies are lacking

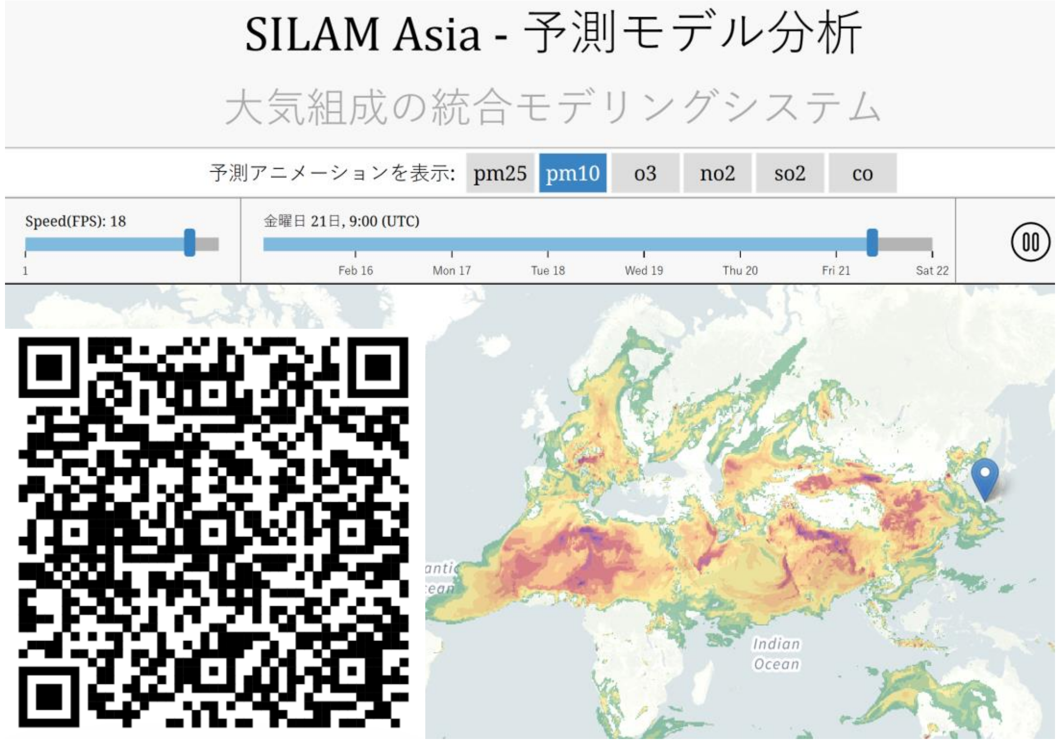
Only a very small fraction of the substances in the market undergone risk analysis

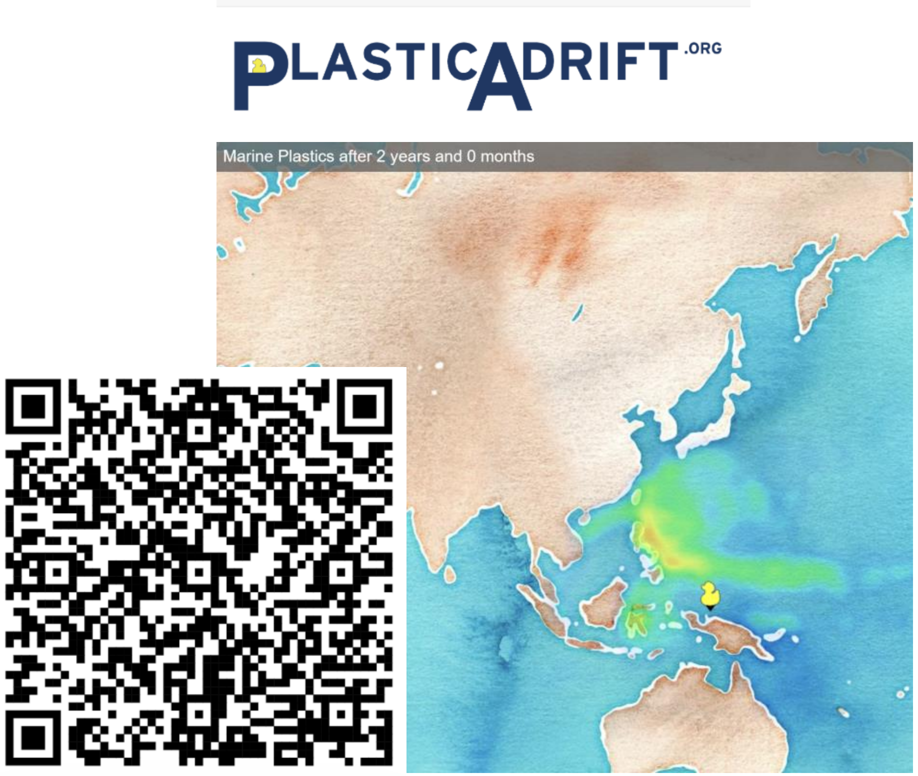


Lei, J., Ma, Q., Ding, X., Pang, Y., Liu, Q., Wu, J., Zhang, H., Zhang, T., 2024. Microplastic environmental behavior and health risk assessment: a review. Environ Chem Lett 22, 2913–2941.

Use of ERA

When contaminants enter the environment (water, air, soil, biota) they will undergo dispersion and physic-chemical alteration:



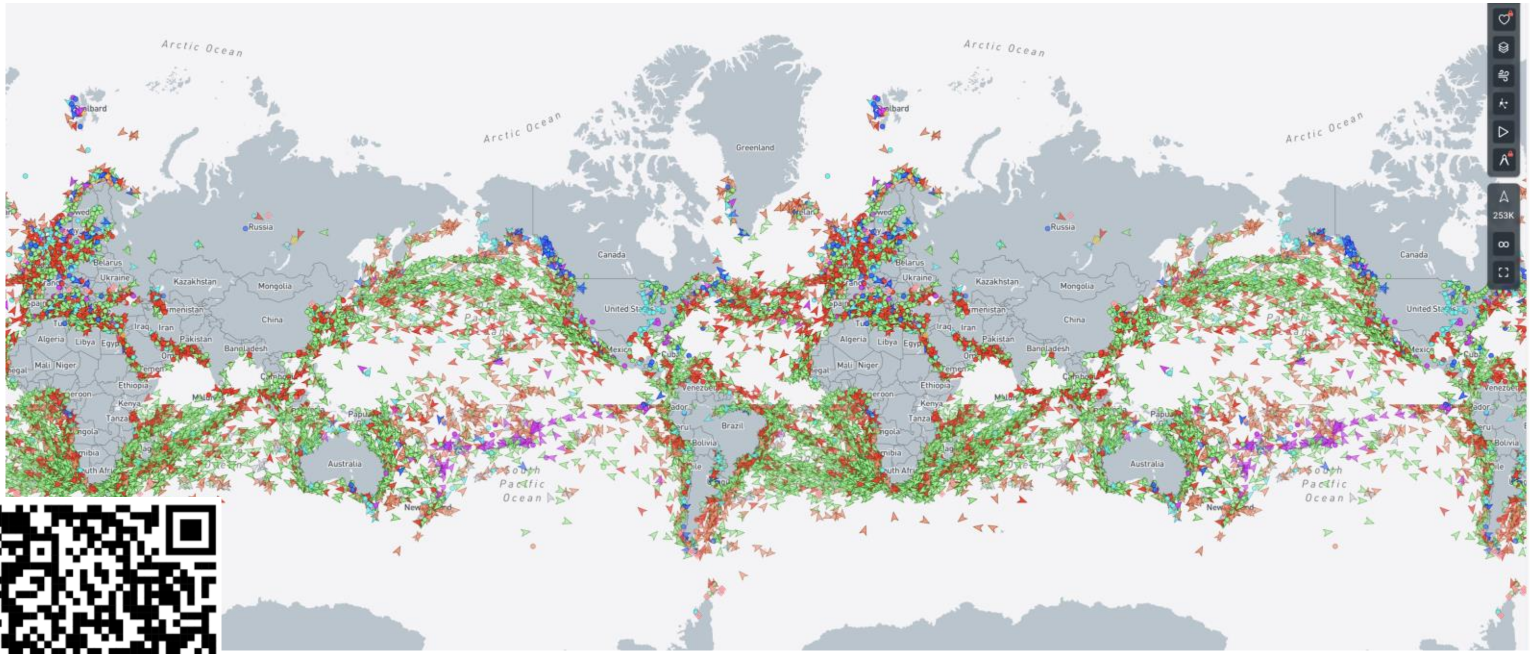


https://aqicn.org/forecast/model/silam-asia/jp/#!city:osaka

https://plasticadrift.org/?lat=-0.3&lng=136.9&center=12.1&startmon=jan&direction=fwd

Use of ERA

Antibiotic resistant microorganisms, as well as many other chemical pollutants and organisms are dispersed globally by ocean currents. But the fastest dispersing mechanisms is maritime transport due to the discharge of ballast water.



https://www.marinetraffic.com/en/ais/home/centerx:-28.5/centery:-0.0/zoom:2

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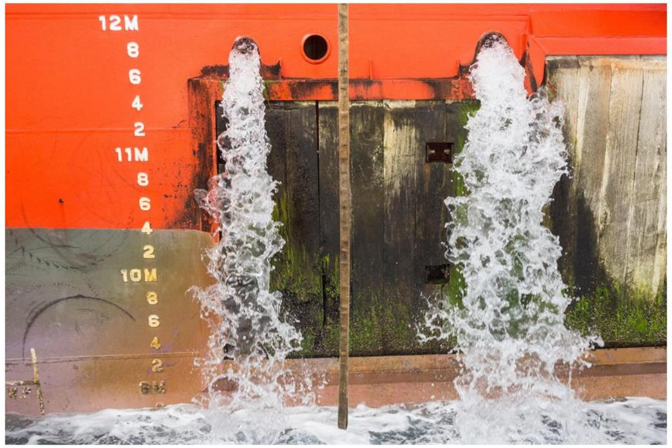
DAILY NEWS 20 April 2018

Antibiotic-resistant bacteria cross oceans hidden in cargo ships



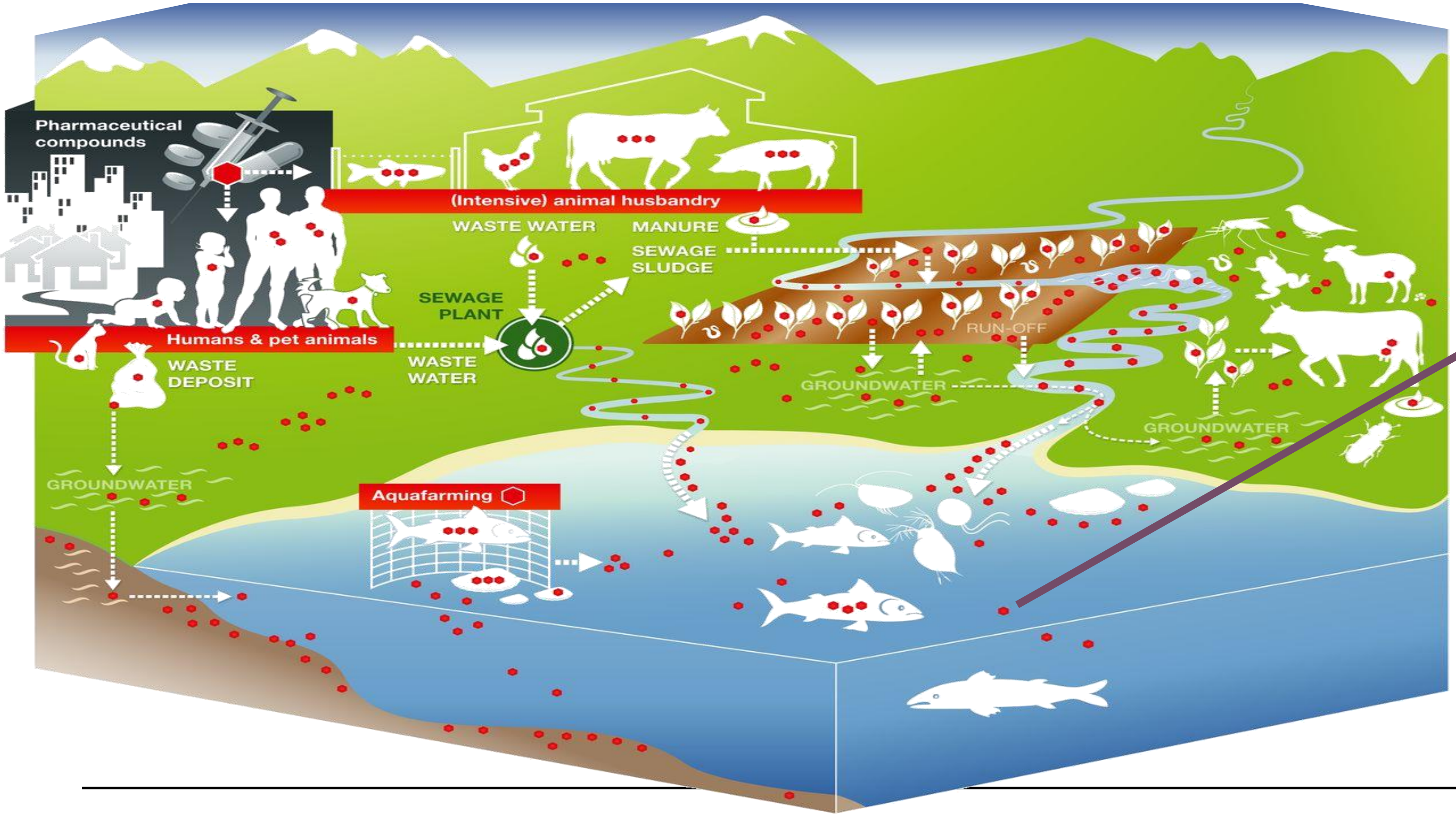
Secret passengers spread disease
Description:islandstock / Alamy Stock Photo

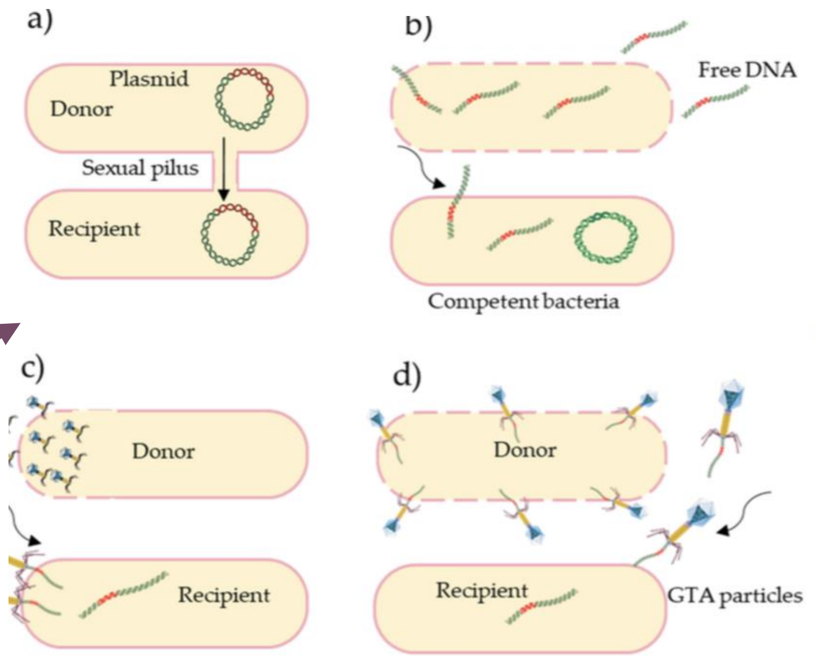
By Inga Vesper

Cargo ships are spreading antibiotic-resistant bacteria around the world by carrying dangerous pathogens in their ballast tanks and expelling them near harbours.

Use of ERA

And biologic alteration, of which the <u>antibiotic resistance</u> is one of the main concerns today.





Antibiotic resistance transport mechanisms; (a) ρ) Transformation, (c) Transduction, and (d) Gene transfer agents (GTAs), (adapted from [34]).

Not ecerybody is aware of the environmental risks…

Let’s check your perception of the risk. Please fill in the quiz:

https://forms.office.com/Pages/ResponsePage.aspx?id=MQkPE_aguUSuhbnxbImtgnkngR
0sCxpJhcC88DOeBh1UM0gxTkxaUkpUT1UwVlZGVk5FR0pMWlIMTC4u

Environmental risks are responsible for about one fourth of all deaths annualy: ca 12.6 million people.

Figure ES1. Fraction of deaths and DALYs attributable to the environment globally, 2012

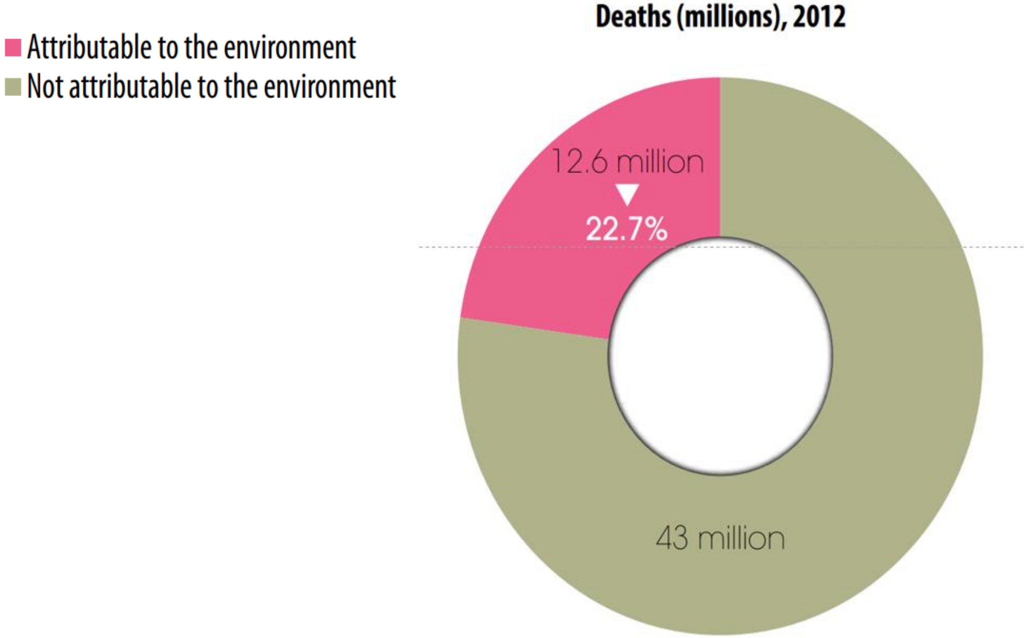
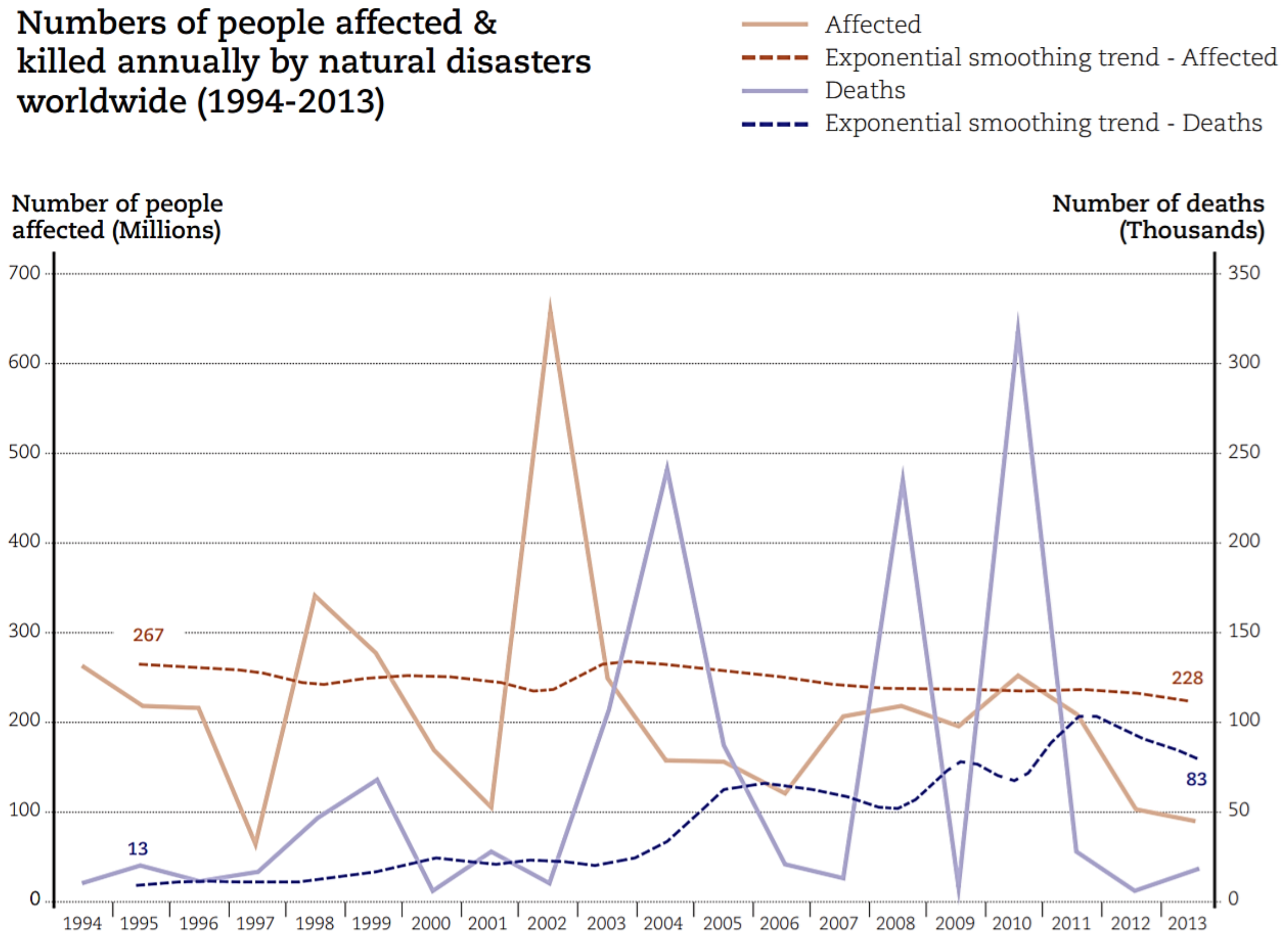


Table A2.3. Deaths attributable to the environment, by region, 2012

	World Total	World Children 0–4 years	Africa[a] Sub-Saharan	Americas HIC OECD	Americas Non-OECD	Eastern Mediterranean
Population	7 044 272 076	651 316 807	903 366 628	369 808 057	586 970 922	601 534 755
Total deaths	55 656 266	6 550 241	9 400 673	2 999 179	3 435 168	3 870 847
Total environmental deaths	12 624 495	1 709 860	2 176 353	320 135	526 754	854 396
Burden attributable to the environment	22.7%	26%	23%	11%	15%	22%

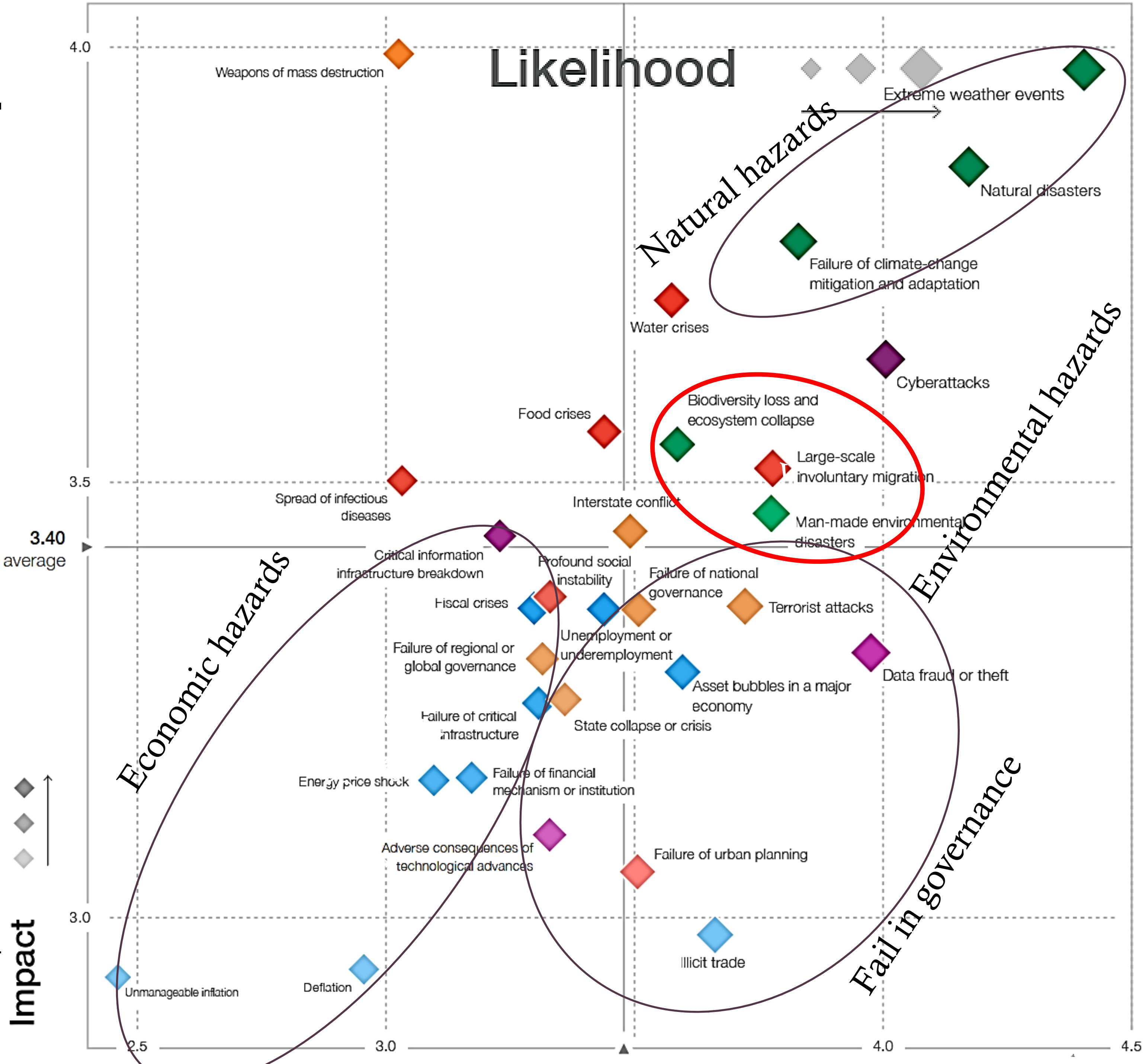
WHO (2016). Preventing disease through healthy environments: a global assessment of the burden of disease from environmental risks / Annette Prüss-Üstün … [et al]. World Health Organization, CH

By comparison, the deaths caused by natural hazards are less than 3% of the total victims caused by environmental risks



CRED (2015). The Human cost of Natural Disasters. Centre for Research on the Epidemiology of Disasters. France. https://unesdoc.unesco.org/ark:/48223/pf0000181793

However, risk perception is at odds with the actual facts...



Source: World Economic Forum Global Risks Perception Survey 2017–2018.
Note: Survey respondents were asked to assess the likelihood of the individual global risk on a scale of 1 to 5, 1 representing a risk that is very unlikely to happen and 5 a risk that is very likely to occur. They also assess the impact on each global risk on a scale of 1 to 5 (1: minimal impact, 2: minor impact, 3: moderate impact, 4: severe impact and 5: catastrophic impact). See Appendix B for more details. To ensure legibility, the names of the global risks are abbreviated; see Appendix A for the full name and description.

The Global Risks Report 2018, 13th Edition. World Economic Forum. CH.

https://unesdoc.unesco.org/ark:/48223/pf0000181793

The ERA studies provide objective quantitative measures of the risks, avoiding the problems raised by risk preconceptions, therefore allowing unbiased decision-making and public support and engagement.

Example of ERA:

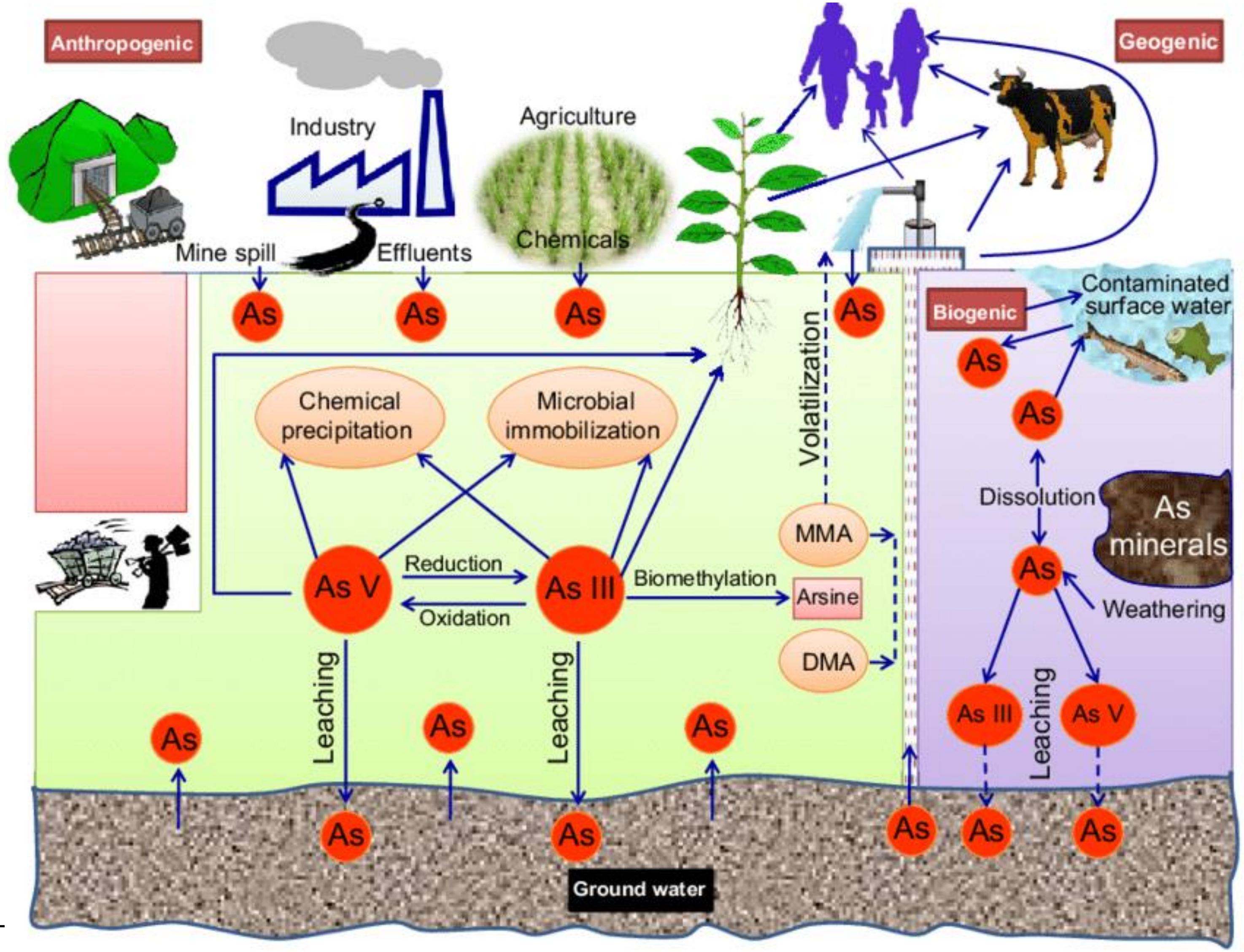
Risk characterization: working example

Increased lifetime risk for the **Japanese men** due to exposure to **inorganic arsenic** in **white rice**

Human **exposure** occurs through ingestion of contaminated water and food, inhalation of contaminated air, and dermal contact.

Skin, bladder, and lung cancer and skin lesions are accepted hazard outcomes for iAs.

Arsenic in the environment



Hasanuzzaman, M., Nahar, K., Hakeem, K.R., Öztürk, M., Fujita, M., 2015. Chapter 16 - Arsenic Toxicity in Plants and Possible Remediation, in: Hakeem, K.R., Sabir, M., Öztürk, M., Mermut, A.R. (Eds.), Soil Remediation and Plants. Academic Press, San Diego, pp. 433–501. https://doi.org/10.1016/B978-0-12-799937-1.00016-4

From ISO 31000 (2018) to Environmental Risk Assessment (ERA)

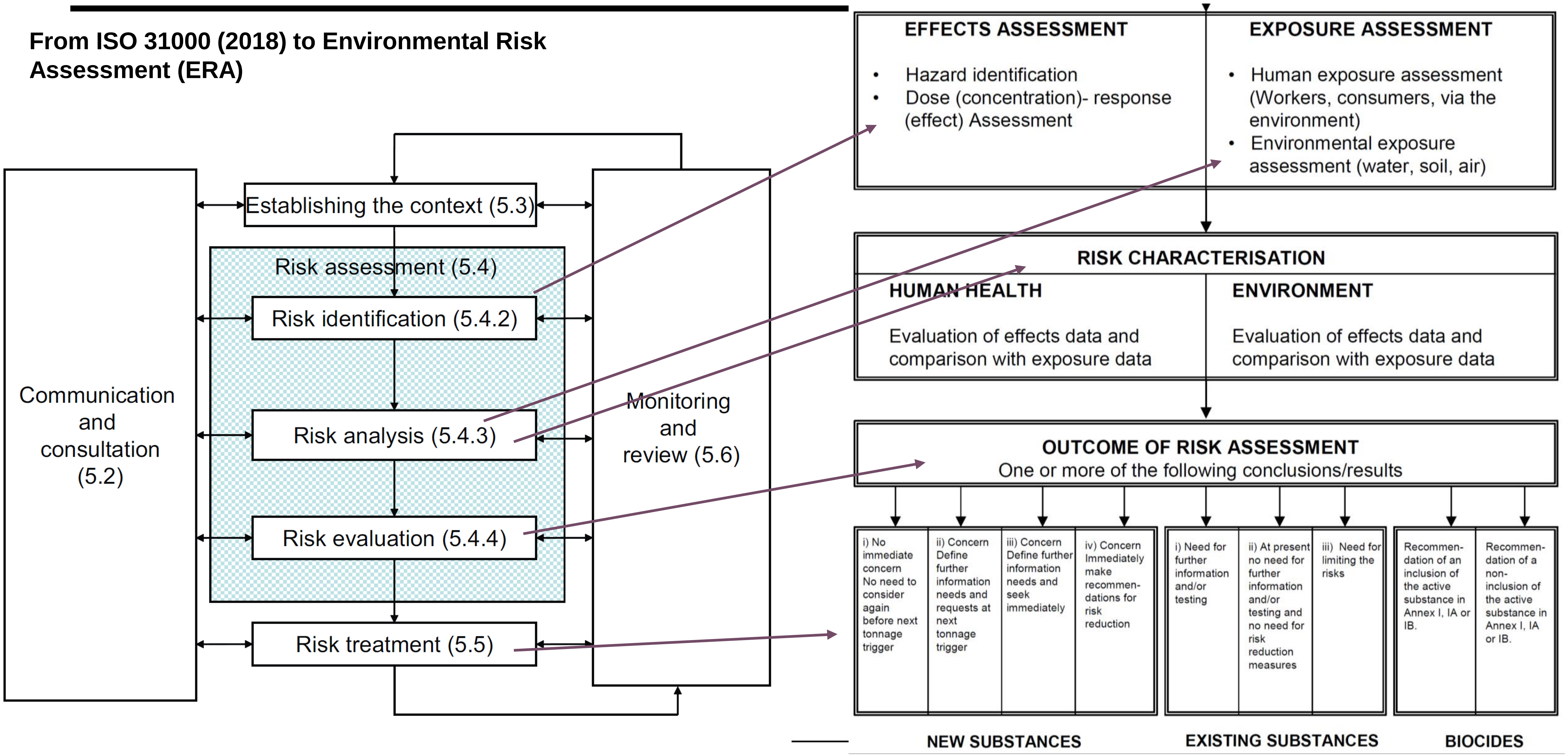


Figure 3 — Risk management process

ISO 31000 (2018)

European Chemical Bureau (2003). *Technical Guidance Document on Risk Assessment.* European Commission, Brussels.

Concepts

Risk = **Probability of a hazard** x **consequence**

Probability of a hazard = ***f***(*probability of the event*; *probability of exposure to the hazard*)

Probability of the event: e.g., of an accident or a leak

Probability of exposure: is related to questions such as who, when, for how long, to what concentration or dose

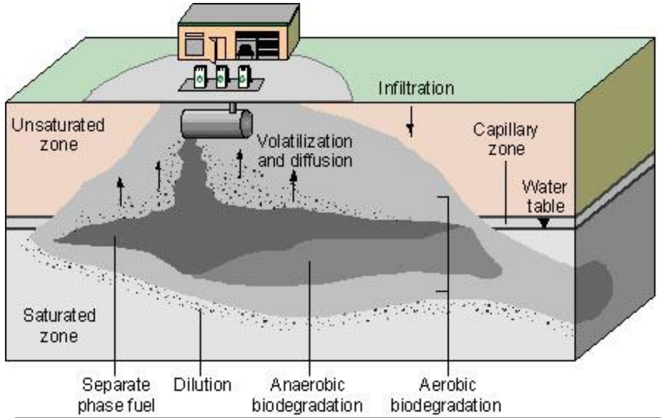
Consequence = ***g***(*toxicological effects*; *vulnerability of receptors*).

So, a substance may be hazardous, but have no risk to receptors if the likelyhood of exposure is very low or zero:
e.g., virus SARS-CoV-2 is very hazardous, but if one is in an isolated island, with zero exposure, then the risk is zero.

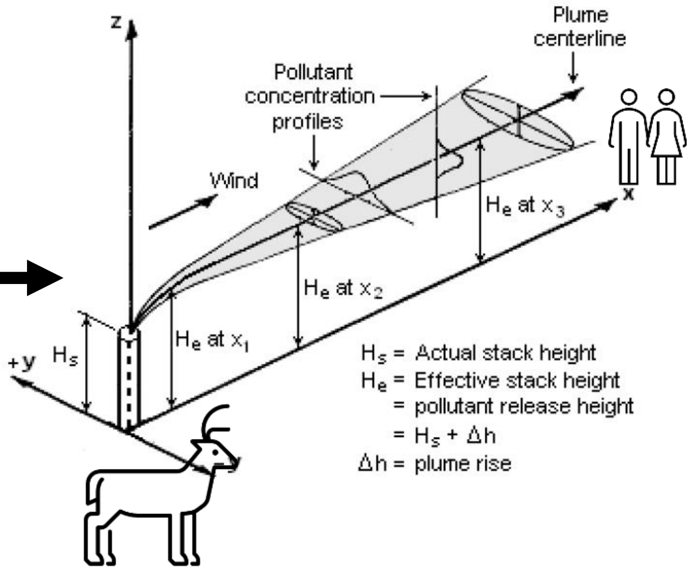
Concepts

Probability of a hazard

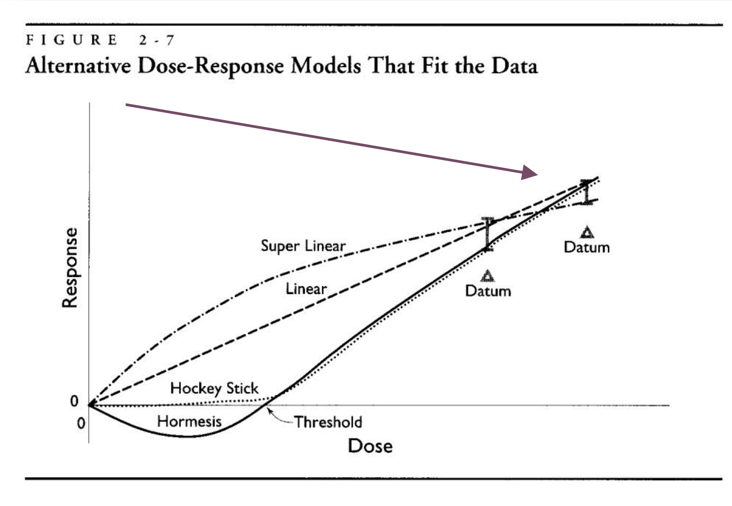
Probability of the event



Probability of exposure



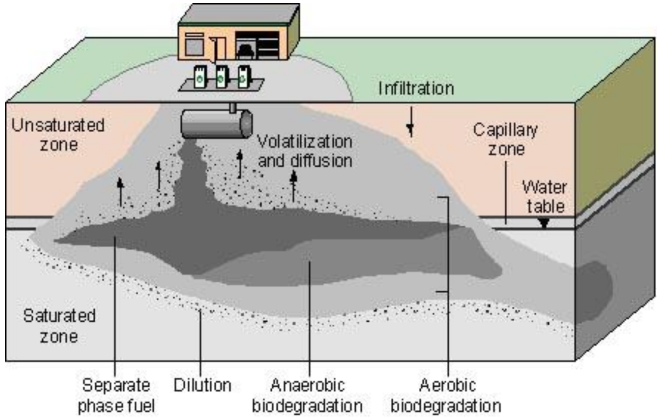
Consequence



Concepts

Probability of a hazard

Probability of the event



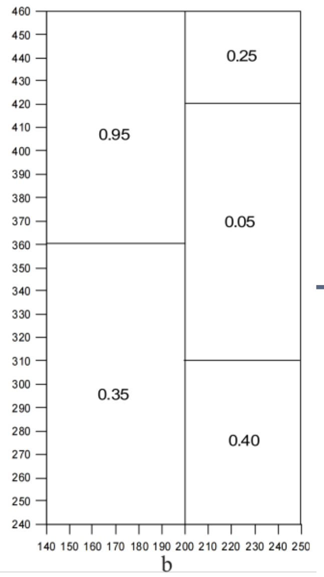


Table 2. Parameters for the estimation of emissions inside the industrial area.

Parameter	Sub-area, i 1	2	3	4	5	6	7	8	9	10	11	12	13	14
m_i (g/m^3)	1500	1200	50	1	10000	40	80	200	700	1100	900	300	20000	1000
δ_i	0.02	0.080	0.5	0.01	0.05	0.3	0.8	0.6	0.7	0.075	0.9	0.005	0.005	0.15

Probability of exposure (environmental concentrations)

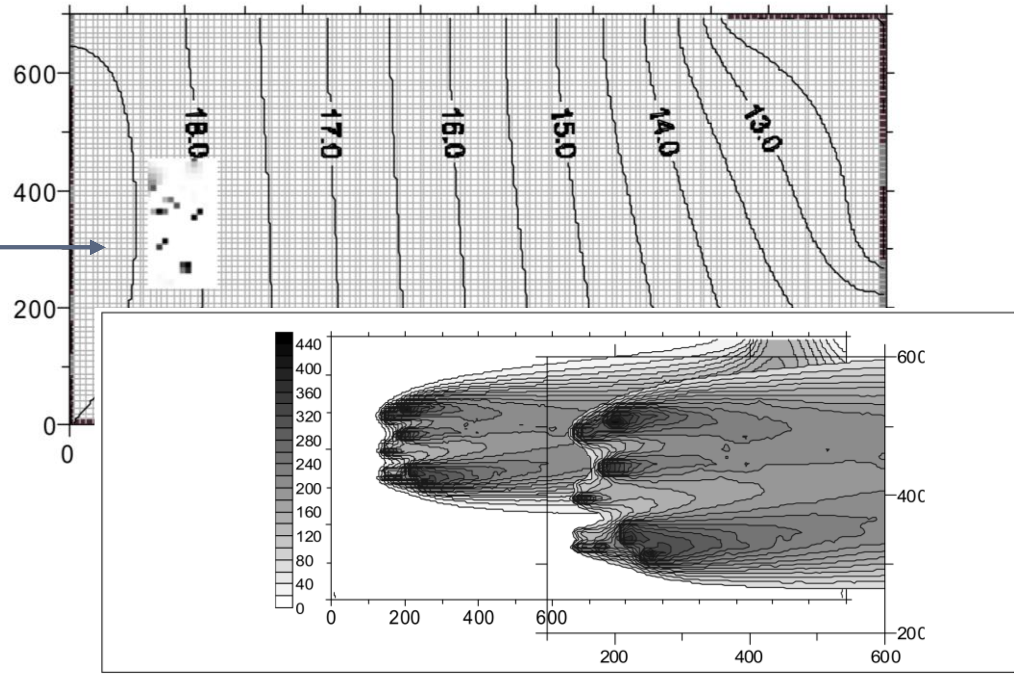


Figure 3. Example of a solute concentration plume after 7300 days (g/m3). Overlapping figure is a zoom in on the emission area.

Concepts

Consequence

Toxicological effects will increase with exposure (dose)

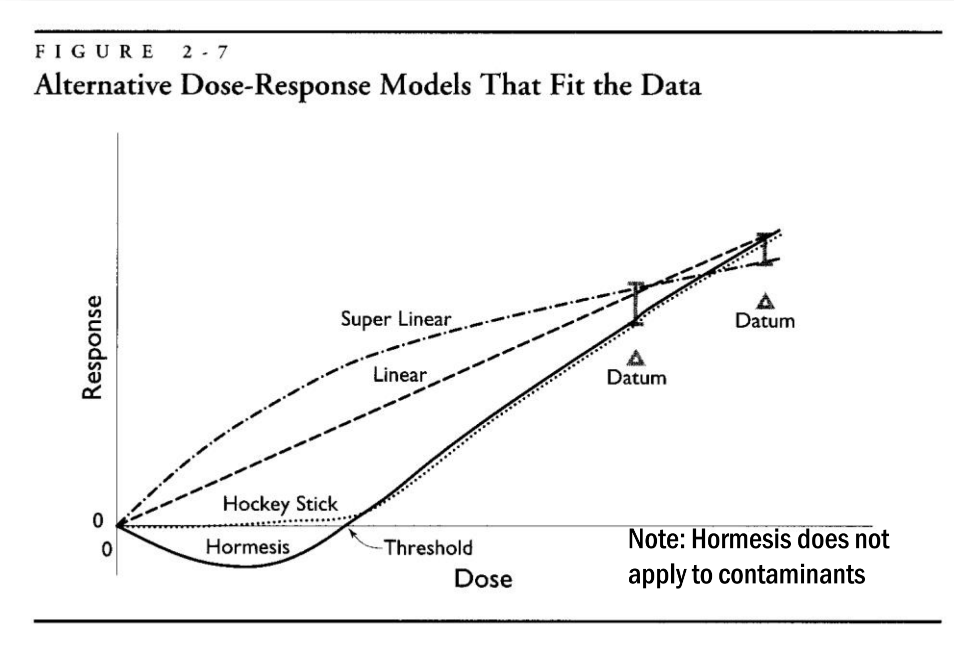


FIGURE 2-7
Alternative Dose-Response Models That Fit the Data

Dose – effect data comes from lab essays and epidemiological studies

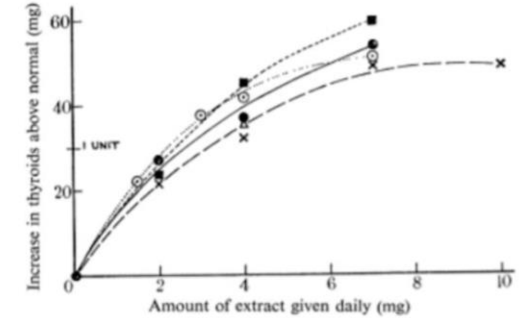
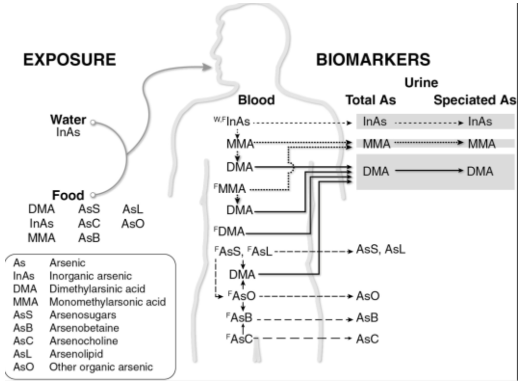


FIG. 1—Dose/response curves for various thyrotropic extracts. ●— AP15B; ···⊙ AP8B; Δ, AP14B; - - - ■ PR22; — — × T17B.



Concepts

Vulnerability (aka, sensitivity):

Is the level of resilience/susceptibility of the receptor to a given harm.

For example, nutritional unbalances may increase sensitivity to inorganic arsenic.

While diets rich in ascorbic acid, flavonoids, polyphenols, or selenium decrease the toxicity of arsenic in humans.

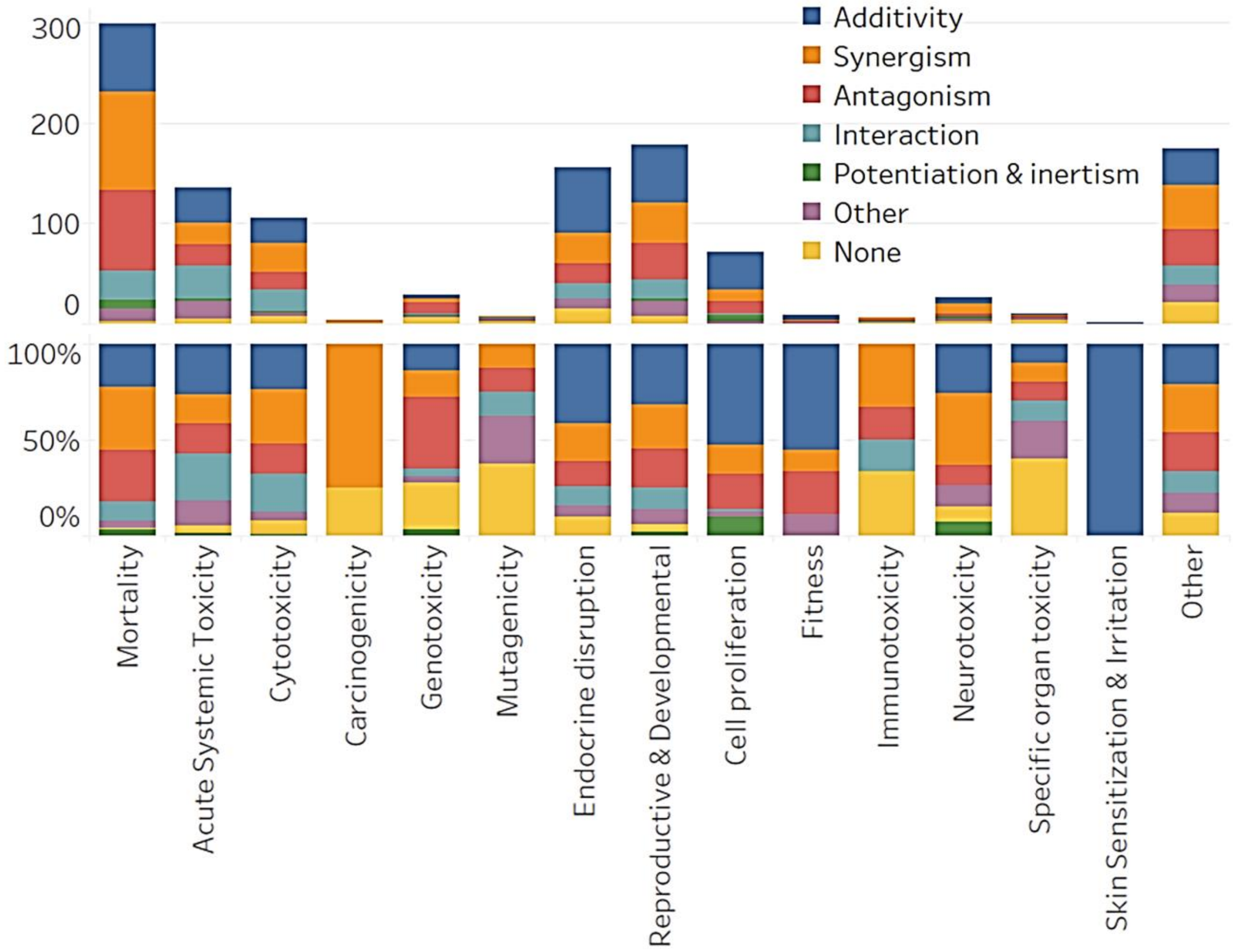
Introduced in the assessment by studying the risks for most sensitive populations.

Vahter, M.E., 2007. Interactions between arsenic-induced toxicity and nutrition in early life. J Nutr 137, 2798–2804. https://doi.org/137/12/2798 [pii]

Concepts

The *vulnerability* to a toxic may be affected by the simultaneous exposure to a mixture of substances.

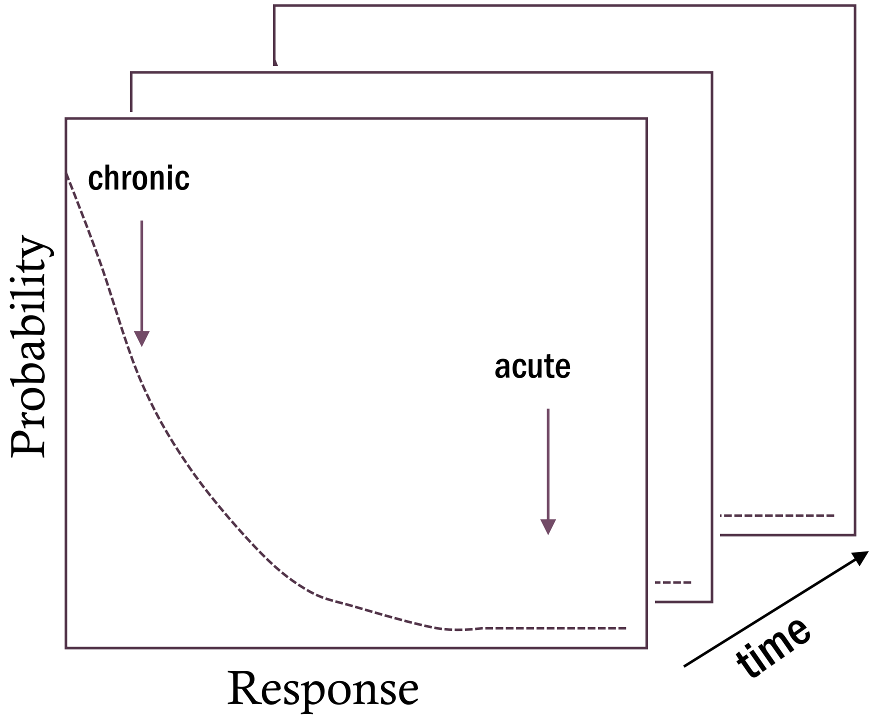
The figure shows examples of interactions for diferente endpoints when receptors are exposed to mixtures of contaminants.



Martin, O., Scholze, M., Ermler, S., McPhie, J., Bopp, S. K., Kienzler, A., Parissis, N., & Kortenkamp, A. (2021). Ten years of research on synergisms and antagonisms in chemical mixtures: A systematic review and quantitative reappraisal of mixture studies. *Environment International*, *146*(October 2020), 106206. https://doi.org/10.1016/j.envint.2020.106206

Concepts

Usually, hazards with high intensity of the response will have low probability of ocurring.



The Environmental Risk Assessment can focus in two distinctive regions of the Probability – Response curve:

A) Low response with high probability (**chronic effects**);

B) High response with low probability (**acute effects**).

In the following I will focus in A (chronic effects):

<u>Typical of environmental exposure to contaminants.</u>

Concepts

Exposure assessment

Exposure = environmental levels x **uptake**

Environmental levels = **f**(*probability of the event*; *probability of the exposure*):

They are obtained by monitoring, or estimated by modelling

Uptake = **g**(*exposure frequency*; *exposure duration*; *route of exposure*; *receptor characteristics*; *receptor activity*; *amount ingested*)

They are specific to each assessment scenario and define the conditions of exposure.

Concepts

Exposure assessment

Uptake = g(*exposure frequency*, *exposure duration*, *route of exposure*, *receptor characteristics*, *receptor activity*, *contact rate; environmental concentration*)

For instance, consider an ERA for lead in air in a city:

exposure frequency: daily
exposure duration: 24 h/day
route of exposure: inhalation
receptor characteristics: adult male, with moderate activity level (affects inhalation rate)
contact rate: inhalation rate (volume per unit time)

Concepts

Exposure assessment

Most of these parameteres are standardized in **Exposure Factor Handbooks.**

If not, then they have to be **collected by surveys** (this is a common practice in diet studies for specific populations)

Japanese Exposure Factors Handbook

Exposure Factors

Exposure Factors Sourcebook for European Populations (with Focus on UK Data)

Technical Report No. 79

ISSN -0773-8072-79

Brussels, June 2001

EXPOSURE FACTORS HANDBOOK: 2011 EDITION

EPA/600/R-09/052F
September 2011

National Center for Environmental Assessment
Office of Research and Development
U.S. Environmental Protection Agency
Washington, DC 20460

Exposure assessment (amount of the substance that is intaken)

Environmental levels (CF) Uptake

$$\text{Average Daily Intake (ADI)} = \frac{CF \times IR \times FI \times EF \times ED}{BW \times AT}$$

CF = Chemical Concentration (mg/kg)
IR = Ingestion Rate (kg/meal)
FI = Fraction Ingested from Contaminated Source (unitless)
EF = Exposure Frequency (days/year)
ED = Exposure Duration (years)
BW = Body Weight (kg)
AT = Averaging time (period over which exposure is averaged -- days)
(for carcinogenic substances is 70 years x 365 days/year = 25550 days)

[EFSA 2024, doil: 10.2903/j.efsa.2024.8488]

Risk characterization

For carcinogenic effects

Risk = Probability of a hazard x consequence

Increased Lifetime Risk (ILTR) = ADI x CSF

where:

ILTR = a unitless probability (e.g., 2 x 10^{-5}) of an individual developing cancer; Risk

CSF = slope factor, expressed in $(mg/kg\text{-}day)^{-1}$.

The slope factor is a plausible upper-bound estimate of the probability of a response per unit intake of chemical over a lifetime.

Risk characterization

For non-carcinogenic effects

Margin of Safety (MoF) = Tolerable Daily Intake / ADI

More common in the EU

Hazard Quotien (HQ) = ADI / Reference Dose

More common in the USA

The Tolerable Daily Intake (Reference Dose) is an estimate of a daily exposure level for the human population, including sensitive subpopulations, that is likely to be without an appreciable risk of deleterious effects for chronic exposures.

Note: that it suffices to establish the margin of safety level (e.g., 0.1, 0.001)
to compute a reference dose once the ADI is known.

Exposure assessment

$$\text{Average Daily Intake (ADI)} = \frac{CF \times IR \times FI \times EF \times ED}{BW \times AT}$$

CF = Chemical Concentration (mg/kg)
IR = Ingestion Rate (kg/meal)
FI = Fraction Ingested from Contaminated Source (unitless)
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(for carcinogenic substances is 70 years x 365 days/year = 25550 days)

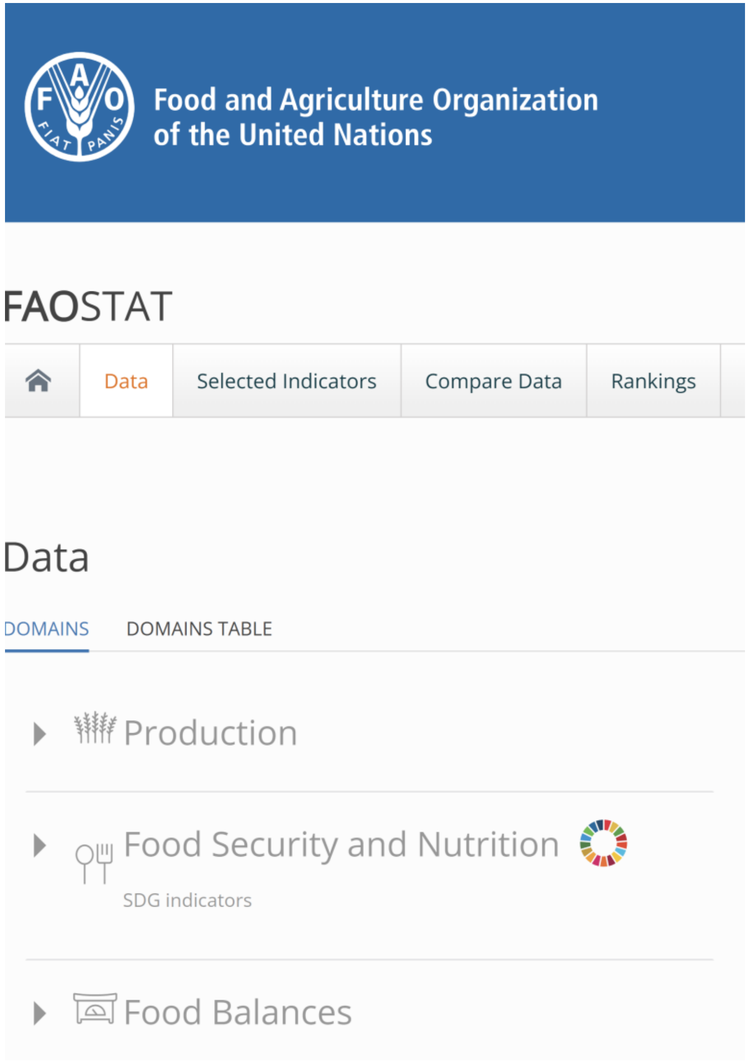
[EFSA 2024, doil: 10.2903/j.efsa.2024.8488]

Ingestion rate (rice consumption) (IR)

Rice consumption (kg/cap/d)	M	F
Mean	0.188	0.130
Standard deviation	0.014	0.010
Maximum	0.212	0.147
Minimum	0.162	0.112

Normal statistical distribution

https://www.fao.org/faostat/en/#data



Exposure duration (ED)

Human Body

Item	Representative value
Lifetime	Male: 77.72 yr Female: 84.60 yr

Japanese Exposure Factors Handbook

Exposure Factors

National Institute of Advanced Industrial Science and Technology AIST

https://unit.aist.go.jp/riss/crm/exposurefactors/english_summary.html

Concentration of inorganic arsenic in husked rice (CF)

Statistics	iAs (mg/kg)
Mean	0.089
St. Deviation	0.034
Geometric mean	0.082
Maximum	0.320
Minimum	0.010

Lognormal statistical distribution

Western Pacific Region,

inorganic rice,

rice (polished)

Raw rice

https://extranet.who.int/gemsfood/Search.aspx?Contaminant=Arsenic+(total)

Body weight (kg)

Body weight (kg)	M	F
Mean	66.3	52.2
Standard deviation	4.91	2.46
Maximum	72.8	55.6
Minimum	57.0	48.7

Normal statistical distribution

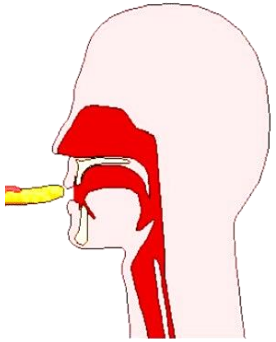
MHLW
Ministry of Health, Labour and Welfare of Japan

Handbook of Health and Welfare Statistics 2023

https://www.mhlw.go.jp/english/database/db-hh/2-1.html

Exposure level

Average Daily Intake (ADI) $= \frac{CF \times IR \times FI \times EF \times ED}{BW \times AT}$

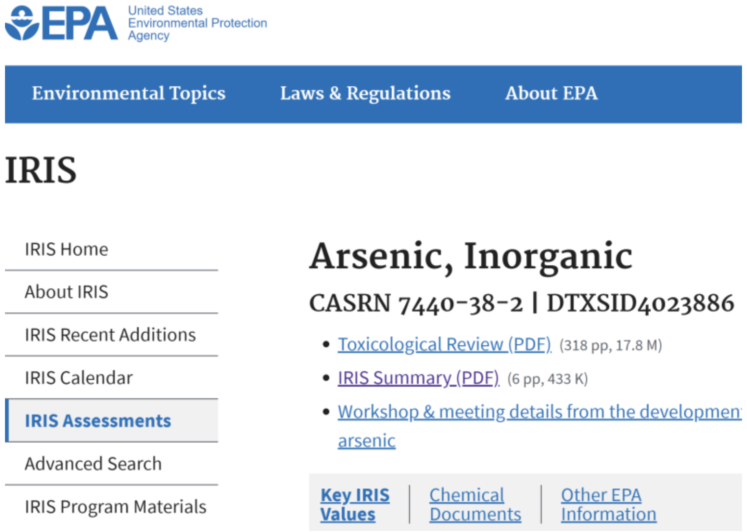


$\mathbf{ADI} = 2.8 \times 10^{-4}$ mg/kg.d

Effects assessment

We now need information about the <u>hazard</u> and the <u>dose – effects assessment</u> for inorganic arsenic.

These are available in, e.g., the U.S. EPA IRIS repository, or the European Chemical Agency

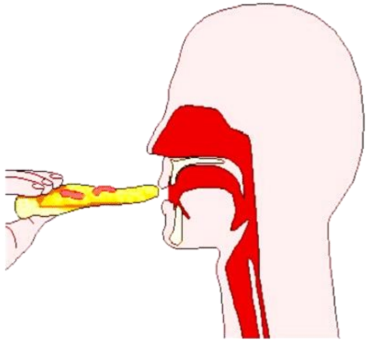


Quantitative Estimate of Carcinogenic Risk from Oral Exposure (PDF)

(6 pp, 433 K)

Oral Slope Factor: 32 per mg/kg-day

Deterministic estimation increased lifetime risk, ILTR



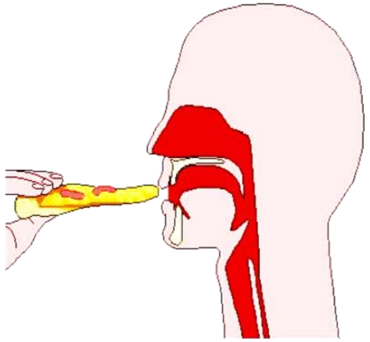
Replacing the CSF in the equation.

$$\textbf{ILTR} = \boldsymbol{ADI} \textbf{ x } \boldsymbol{CSF}$$

$$\textbf{ILTR} = 2.8 \text{ x } 10^{-4} \text{ x } 32 = \mathbf{9.0 \text{ x } 10^{-3}} \cong 1 \textbf{ x } \mathbf{10^{-2}}$$

Meaning that Japanese men are exposed to an increased **1% risk** of developing cancer throughout their lifetime (for an “average man”, only due to the ingestion of inorganic arsenic in white rice.

Deterministic estimation of increased lifetime risk, ILTR



$$\textbf{Increased lifetime health risk} \cong 1\%$$

Meaning that Japanese men are exposed to an increased **1% risk** of developing cancer throughout their lifetime, only due to the ingestion of inorganic arsenic in white rice.

To put this value into context:

- consider the ca. **15%** lifetime risk of developing lung cancer for **Japanese male smokers.**
- The World Health Organization considers a hazard to be safe if the risk is **< 0.0001%**
- Cancer prevalence in Japan is similar to other developed nations.

The risk value in perspective

The 1% risk level is similar to that of
Being president of USA or France…

Occupational Risks *(continued)*

Deaths per Year of Risky Activity (Disabling Injuries Not Included Except When Stated)

Occupation or Industry	Annual per Capita Risk per 100,000	Annual Trend per 100,000	Source Based On	Ref, #
Tractor fatalities	10	–1	1969–98	7
Police officers killed in line of duty				
Total	32	+0.5	1975–98	3#355
By felons	15	+0.3	1975–97	4, text
Railroad employees	15	–0.4	1975–00	9
Steel workers (accidents only)	28		1969–72	2
Assassination, murder, or battle injury				
President of United States	1,900		1789–2000	text
President of Egypt	1,900		1948–2000	text
President of France	1,400		1848–2000	text
King/Queen of England	430		1066–2000	text
Spouse of King/Queen	210		1066–2000	text
Government office worker	9		1997	text
Airline pilot (accidents only)	10		1997	text
Frequent flying professor (accident only)	3		2000	text
Astronaut Space launch (per launch):				
From direct data (Including Challenger)	4,000		1975–86	text
O-ring failure at 31°F	13,000			text
O-ring failure at 60°F	2,000			text
Fire fighters (buildings)	40	-0.7	1972-99	8
Wildfire fighters				
Total	21		2000	6, 8
Per 12 months work	100		2000	6, 8

Wilson, R. & Crouch E. A. C. (2001). Risk-benefit Analysis. Harvard University Press. USA

Some unaccounted **factors may alter (reduce)** exposure or arsenic toxicity, with significant impact on **risk estimates**:

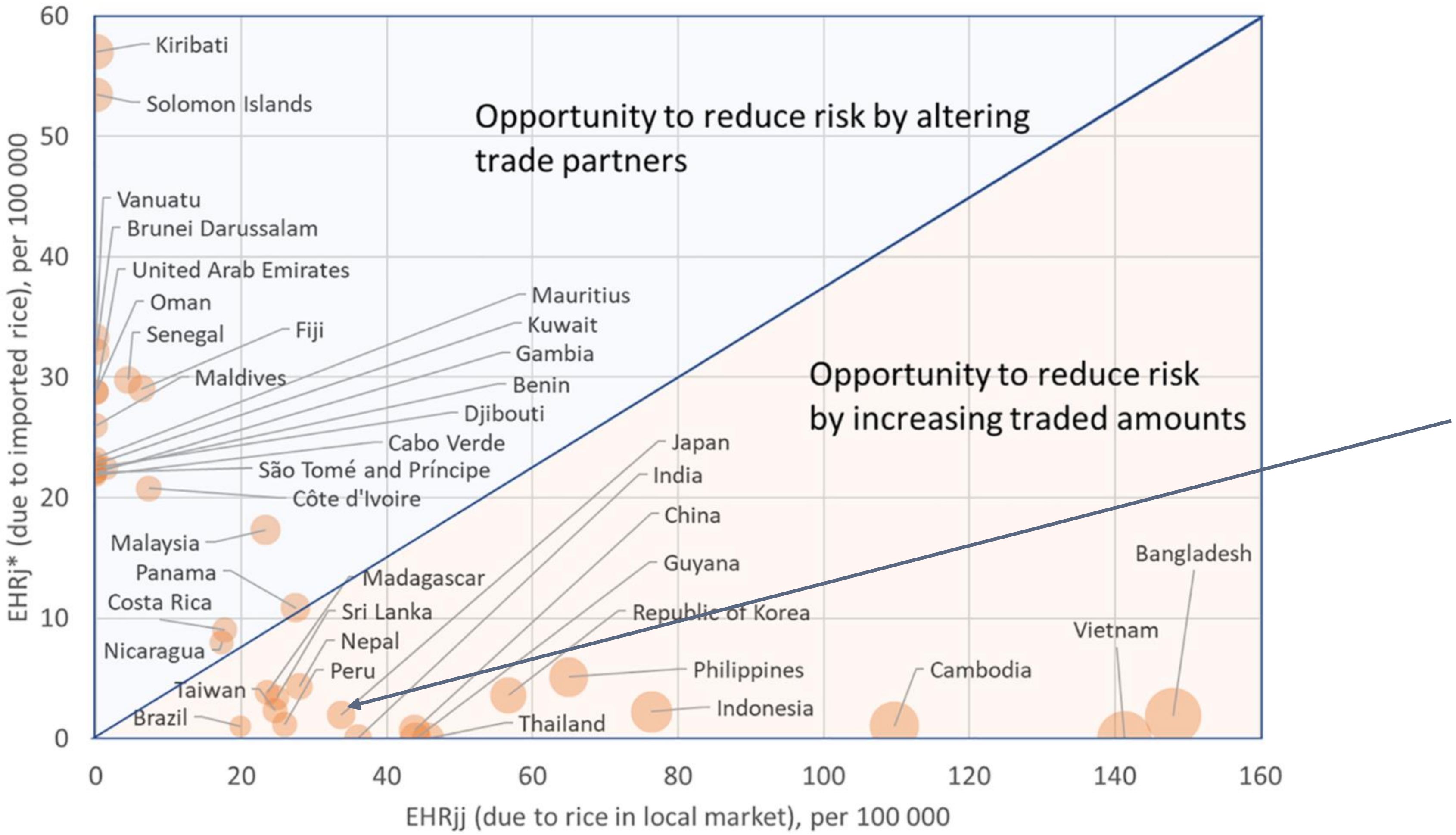
i) Cooking method

ii) Arsenic bioavailability

iii) Nutritional factors

iv) Combined effects (mixtures)

Deterministic estimation of increased lifetime risk, ILTR



Risk-based management (reduce the risk).

Japan can decrease the risk by:

- importing rice with lower inorganic arsenic content;
- reduce rice per capita consumption (alter the diet).

Nunes, L. M. Li, G.,; Chen, W.-Q.., Meharg, A., O'Connor, P., Zhu, Y.-G. (2022). Embedded health risk from arsenic in globally traded rice. E*nvironmental Science and Technology*, 56, 10, 6415–6425. https://doi.org/10.1021/acs.est.1c08238

Thank you for attending this session.

If you have any question, please ask.

Here is my contact:

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Some unaccounted **factors may alter** exposure or arsenic toxicity, with impact on **risk estimates**:

i) Cooking method

ii) Arsenic bioavailability

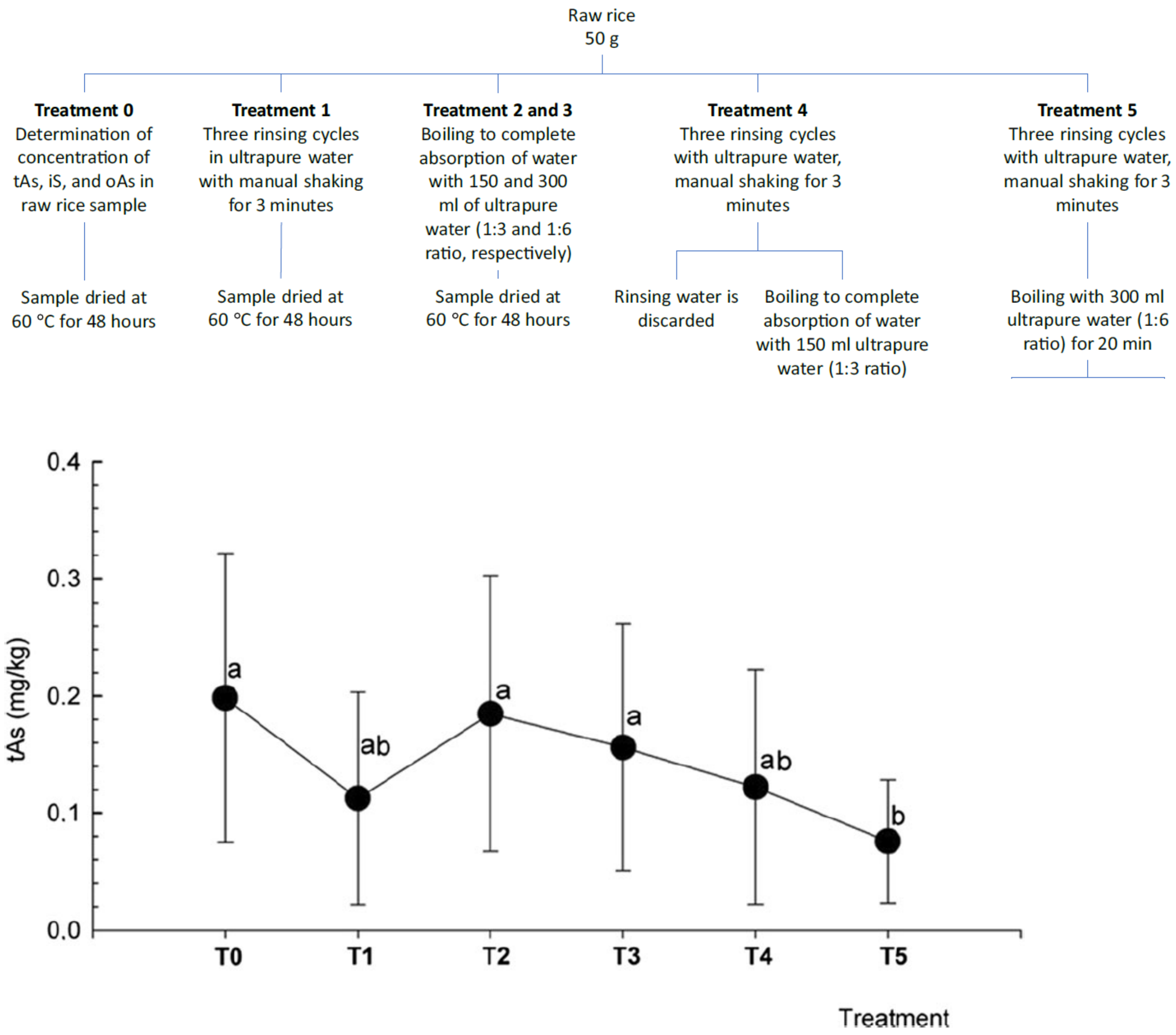
iii) Nutritional factors

iv) Combined effects (mixtures)

i) Cooking method

Simply **rinsing rice** grains before cooking can **reduce TEHR by 50%.**

Rinsing and cooking **discarding excess water**, can reduce TEHR by **over 80%** (Raab et al 2009; Atiaga et al 2020; Menon et al 2021)



[Atiaga et al 2020, doi:10.1007/s11356-019-07552-2; Menon et al 2021, doi: 10.1016/j.scitotenv.2020.143341; Raab et al 2009, doi: 10.1016/j.foodchem.2012.02.113]

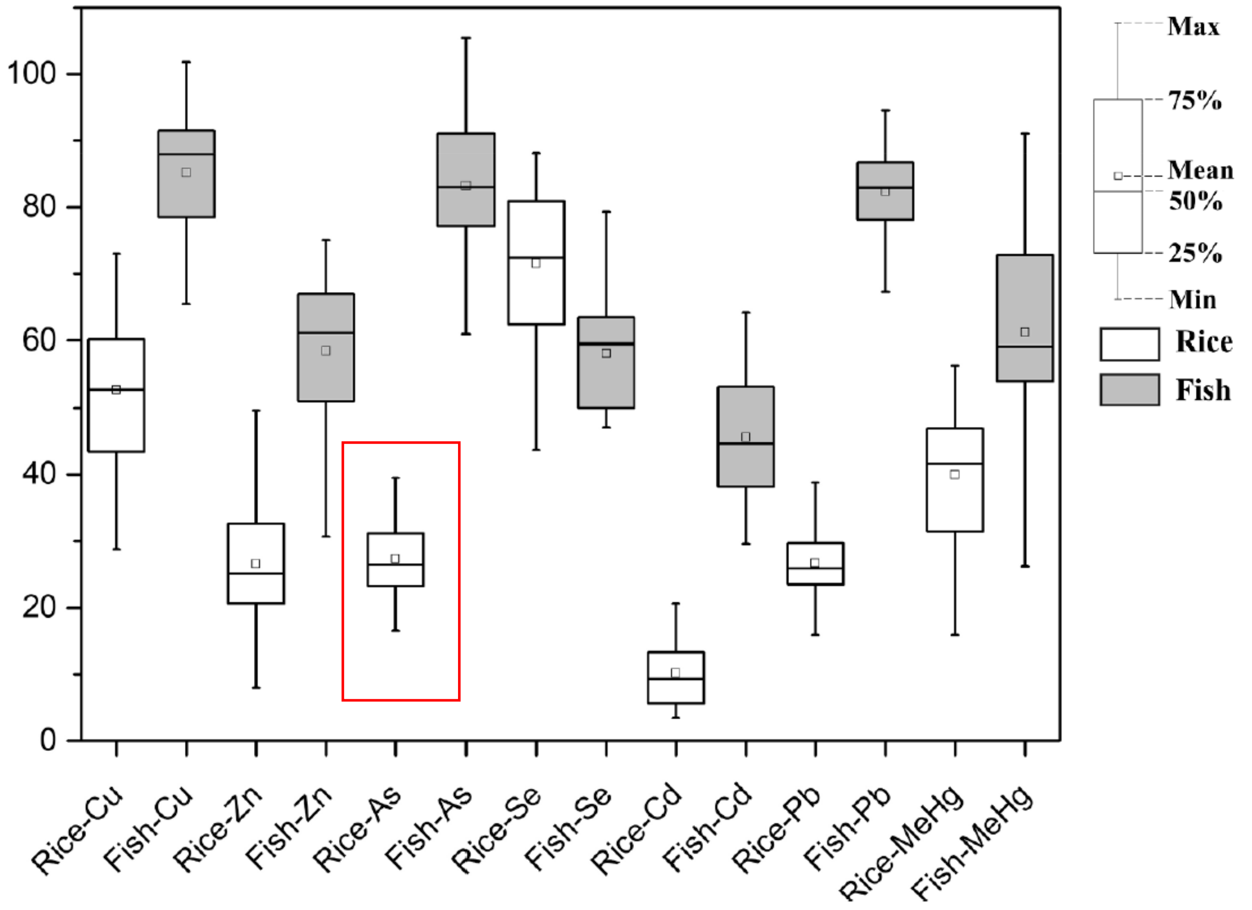
ii. Bioavailbility

Bioavailability tests simulate the human intestinal microbial ecosystem, pollutant characteristics (e.g., metal(loid) type) and matrices (e.g., food item), and digestion conditions in the gut.

It is the result of in vivo and in silico studies (Wang et al 2022) .

Bioavailability for iAs in rice **is low**, which indicates that **risk may be lower than** estimated.

Bioavailability of metal(oids) (%)



[Wang et al 2021, doi:10.1007/s11356-019-07552-2]

iii. Nutritional factors

There are several plausible mechanisms by which arsenic **toxicity can be affected by nutrition**:

- arsenic induces oxidative stress and arsenic-induced inhibition of several of the antioxidant systems. **Toxicity is decreased in diets rich in flavonoids, selenium, vitamins C and E** (Vahter 2007);
- arsenic is metabolized by a series of reduction and methylation reactions. **Toxicity is reduced in diets rich in calcium, animal protein, folate, and fiber** (Mitra et al 2004);
- arsenic exerts epigenetic effects, like many other environmental toxins. **Balanced diets and regular physical activity can reduce toxicity** (Voisin et al 2015; Choi and Friso 2010).

[Choi and Friso 2010, doi: 10.3945/an.110.1004; Mitra et al 2004, doi.org/10.1289/ehp.68; Vahter 2007, doi.org/10.1093/jn/137.12.2798; Voisin et al 2015, doi:10.1111/apha.12414]

iv. Combined effects (mixtures)

Arsenic (As) and selenium (Se) both induce and cure cancer.

- at low concentration, **Se can decrease As toxicity** (antagonistic effect);

- at high concentrations, **Se can enhance As toxicity** (synergistic effect) (Sun et al 2014).

When **As and flouride** are exposed in combination, they have a **synergistic effect** (Aydin and Orta-Yilmaz 2022)

[Sun et al 2014, doi.org/10.1016/j.envint.2014.04.019; Aydin and Orta-Yilmaz 2022, doi.org/10.1016/j.tox.2022.153241]

In conclusion:

A diversified and balanced diet is the best protection against the environmental hazards!

[Sun et al 2014, doi.org/10.1016/j.envint.2014.04.019; Aydin and Orta-Yilmaz 2022, doi.org/10.1016/j.tox.2022.153241]