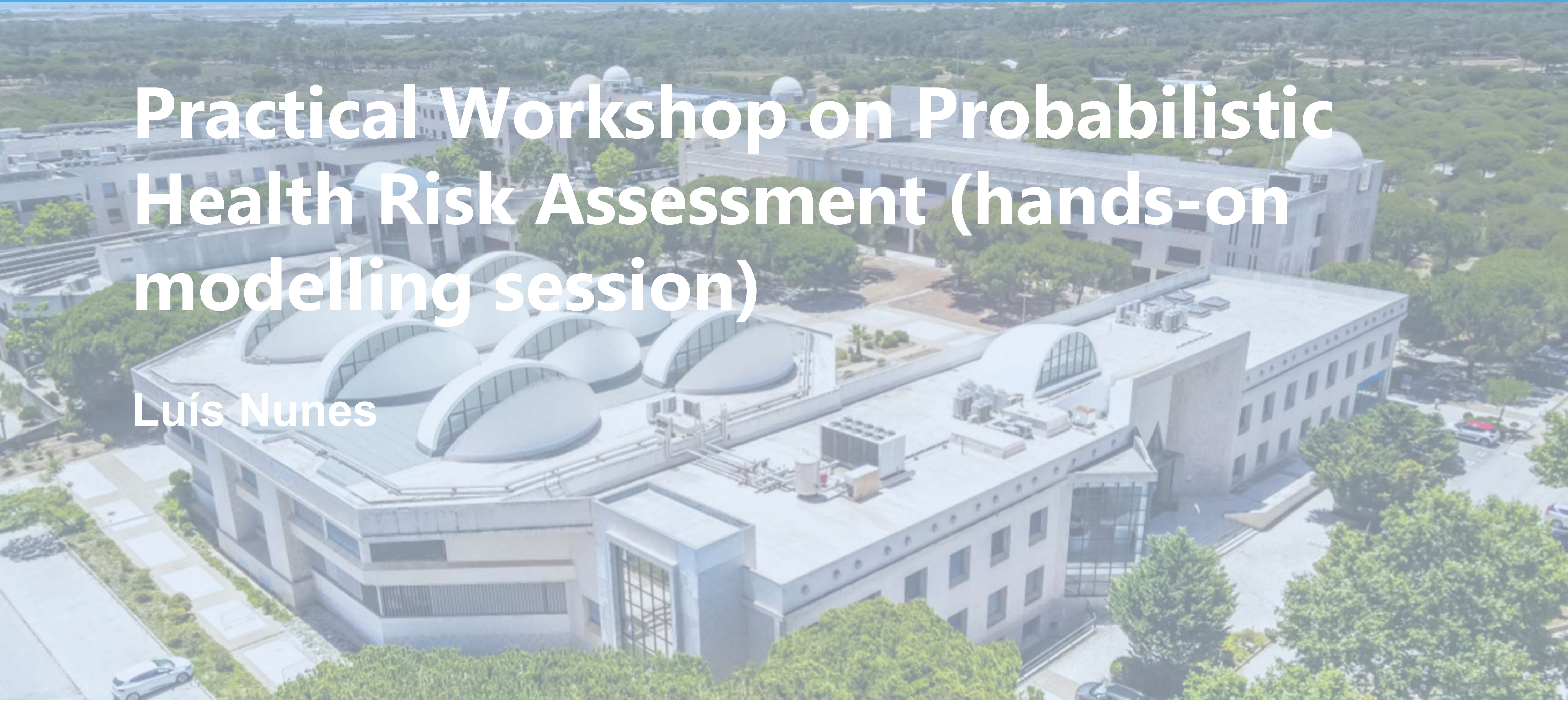
UAlg
UNIVERSIDADE DO ALGARVE

Practical Workshop on Probabilistic Health Risk Assessment (hands-on modelling session)

Luís Nunes



Objetive of the workshop

To provide an overview of the environmental risk assessment methodology, including deterministic and probabilistic solutions.

Have an hand-on experience.

Planning

1. Introduction
2. Environmental risk assessment methodology
3. Practical work 1 – Health risk due to exposure to arsenic in the diet
4. Practical work 2 - Health risk due to exposure to Cd in cosmetics (lipstick)

1. INTRODUCTION

Why do we need 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/ResponsePage.aspx?id=MQkPE_aguUSuhbnxbImtgnkngR0sCxpJhcC88DOeBh1UNVBNR1VLTlJIQzU1SFhESVBTS0UwN1QzWS4u

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

Environmental Risk Assessment

Lifecycle Assessment

Main environmental management tools

Tool / Aspect	Environmental Impact Assessment (EIA)	Environmental Risk Assessment (ERA)	Life Cycle Assessment (LCA)
Primary Purpose	Evaluate potential environmental impacts of proposed projects/policies	Assess probability and consequences of environmental hazards	Analyze environmental impacts throughout product/service lifecycle
Scope	Project-specific, location-based	Hazard-specific, risk-based	Cradle-to-grave, product/service-based
Timing (when it should be done)	Before project implementation		Throughout product lifecycle
Methodology	Impact prediction, evaluation, mitigation	Hazard identification, dose-response, exposure assessment	Inventory analysis, impact assessment, interpretation
Regulatory Framework	Legally mandated in most countries	Often regulatory requirement	Voluntary, ISO 14040/14044 standards
Spatial Scale		Local to global	Global supply chain
Temporal Scale	Project lifetime	Exposure duration	
Output/Results	Impact significance, mitigation measures	Risk levels, management strategies	Environmental hotspots, improvement opportunities

Main environmental management tools

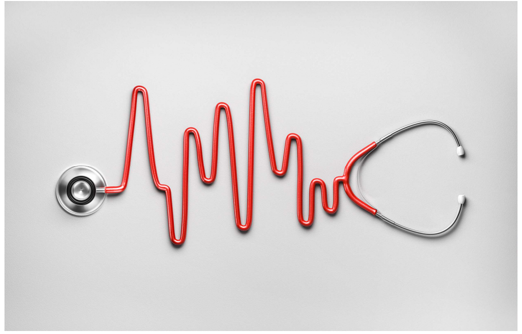
Introduction to EIA, ERA and LCA

EIA

https://www.youtube.com/watch?v=N7MpIVS8dQs

(3.53 min)

ERA



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

(5.28 min)

LCA

https://www.youtube.com/watch?v=ScY_Yb1V8AY

(5.48 min)

Please follow the videos and continue the quiz.

What s the purpose 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

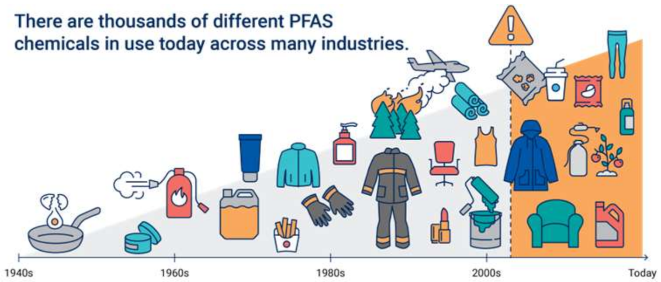
Pharmaceuticals and personal care products

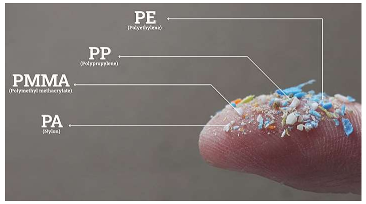
Per- and polyfluoroalkyl substances

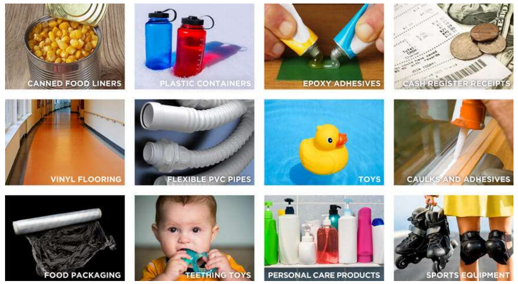
Microplastics

Endocrine disrupting chemicals

Uses/ origin







Effects

Antibiotic resistant bactéria, endocrine disruption.

Toxic to wildlife, behavioral changes in wildlife

Cancer, immune system suppression.

Wildlife reproductive impairment, high bioacumulation and bioamplification.

Imphlammatory responses, toxicity from additives

Intestinal blockages and malnutrition, ecosystem alteration.

Reproductive disorders, diabetes and obesity.

Severe reproductive impairment in wildlife.

Use of ERA

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

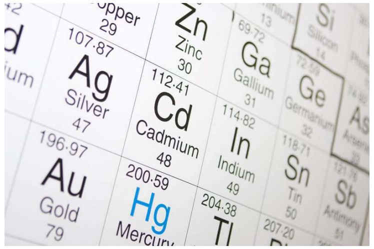
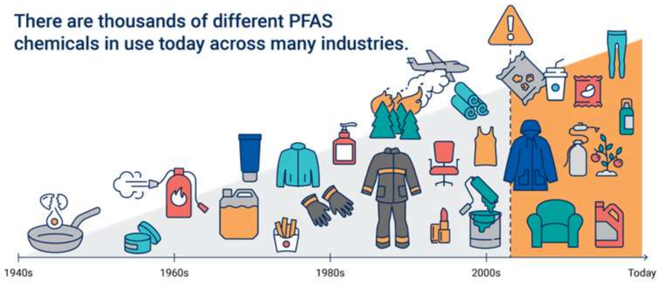
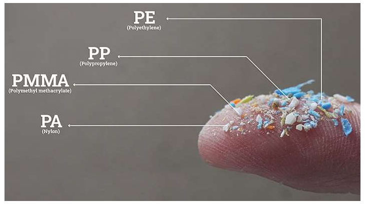
Heavy metals: e.g., Lead, mercury, cadmium, chromium, arsenic

Persistent organic pollutants (POPs): e.g., DDT, PCBs, dioxins, furans

Petroleum hydrocarbons: e.g., Benzene, toluene, xylene, PAHs (polycyclic aromatic hydrocarbons)

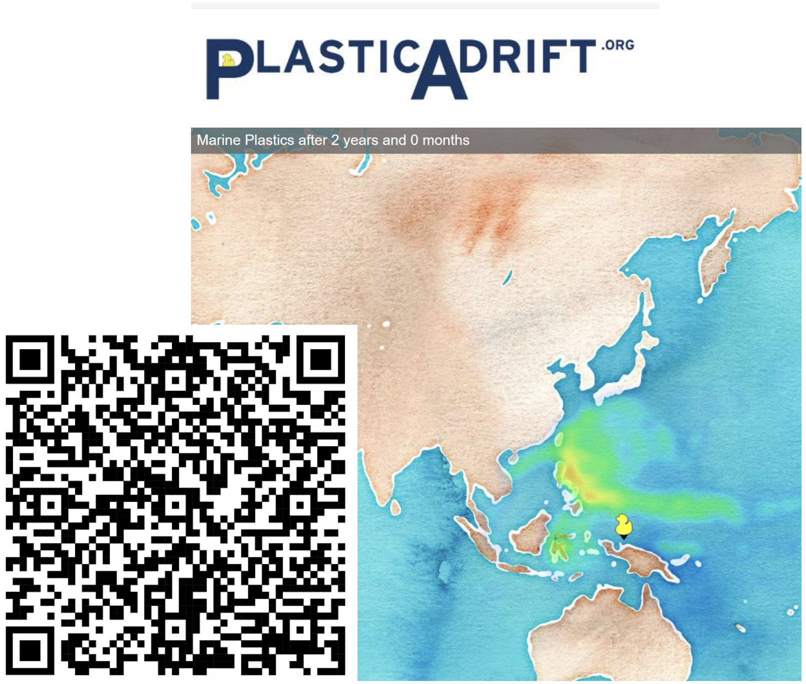
PCBs: Polychlorinated biphenyls; DDT: Dichlorodiphenyltrichloroethane; PAHs: Polycyclic aromatic hydrocarbons.

Examples of legacy contaminants

	Heavy metals	Persistent organic pollutants	Petroleum hydrocarbons
Uses/ origin			
Effects	e.g., cancer, neurological and cardiovascular diseases. Poisonous to wildlife.	e.g., cancer, neurological, cardiovascular diseases, reproductive effects. e.g., wildlife reproductive decrease and failure, community structure changes.	e.g., cancer, neurological and organ failure. Poisonous to wildlife, habitat degradation.

Use of ERA

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

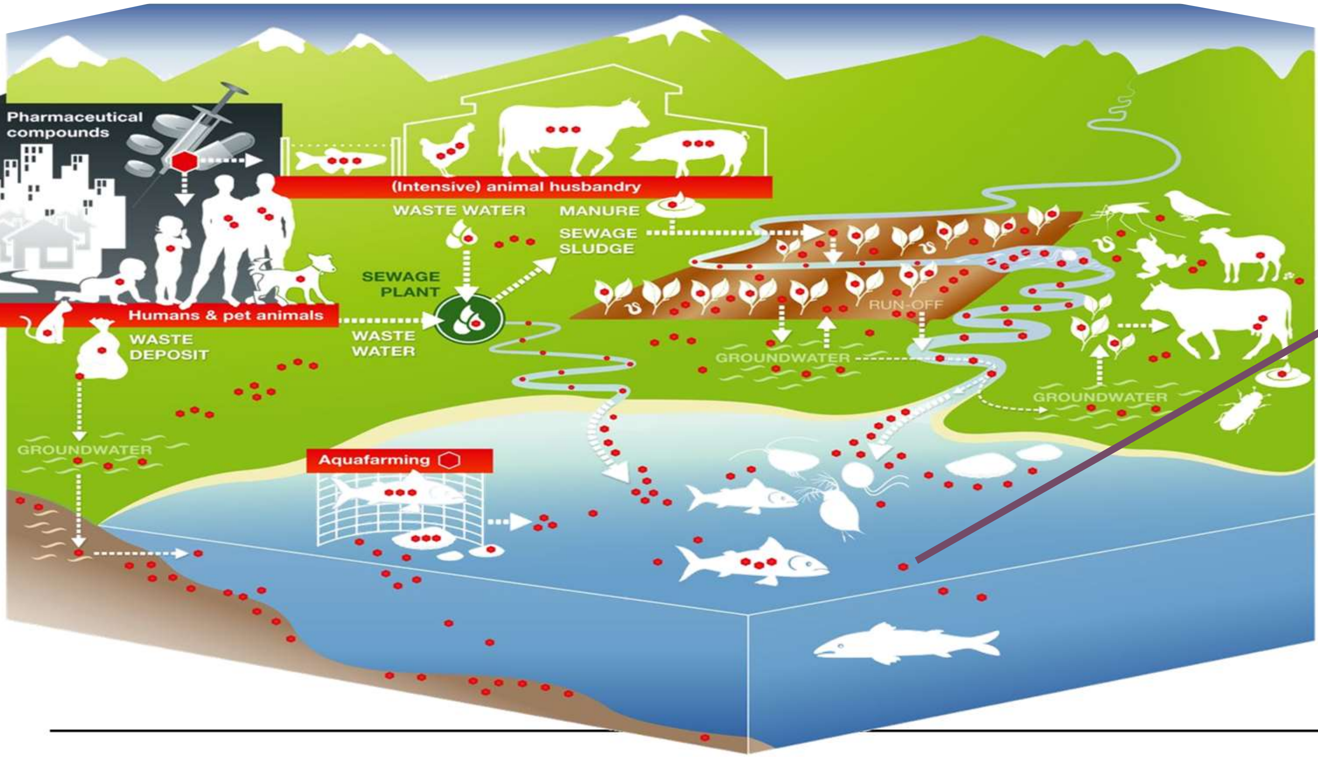


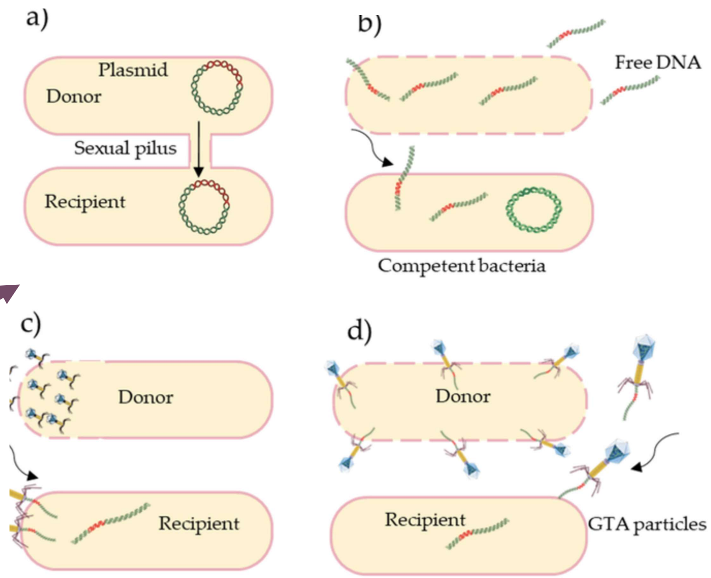
https://aqicn.org/forecast/model/silam-asia/jp/#!city:osaka

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

Use of ERA

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

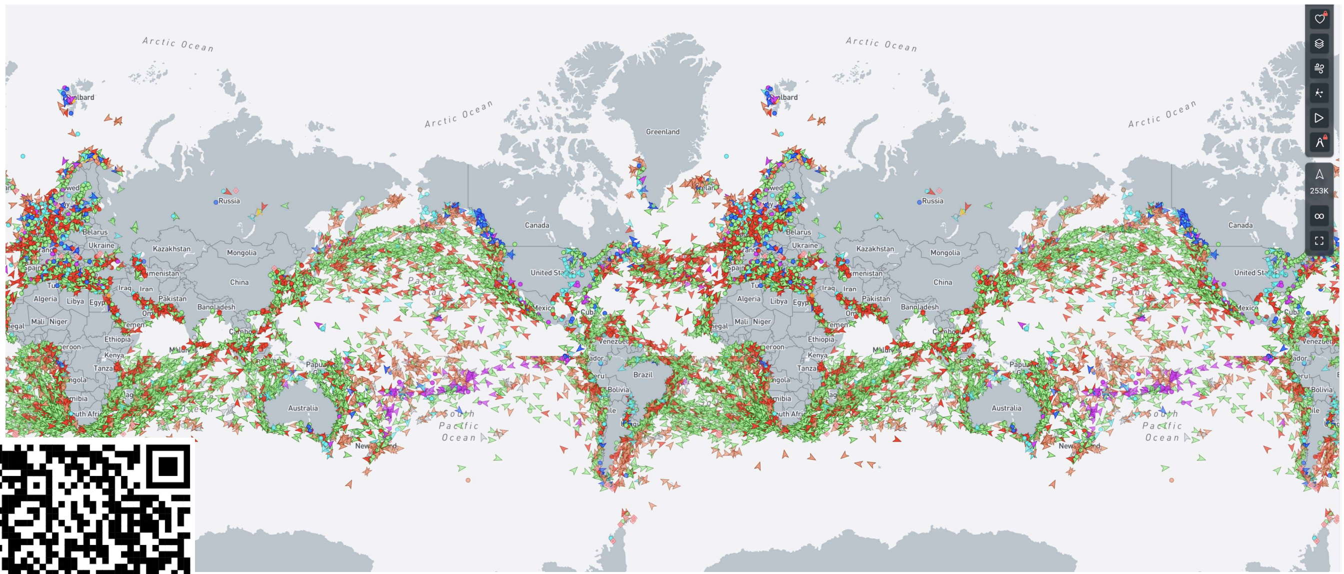




Antibiotic resistance transport mechanisms; (a) ϙ) Transformation, (c) Transduction, and (d) Gene ene transfer agents (GTAs), (adapted from [34]).

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

Some of these contaminants may be hazardous to human health and ecosystems, so we should assess the risks as soon as possible.

Example of the risks of legacy chemicals

DDT (Dichlorodiphenyltrichloroethane)

Historically used as an agricultural insecticide and in the fight against mosquitoes since the 1930s.

Studies made in the 1960s and early 1970s showed that it was highly persistent in the environment (half-life of decades) and toxic to human health and ecosystems.

- Carcinogenicity (girls exposed to DDT before puberty are five times more likely to develop breast cancer in middle age).
- Endocrine disruption (interferes with thyroid and reproductive hormones).
- Neurological damage, especially in children.
- Bioaccumulation in birds of prey, causing thinning of eggshells.
- Toxicity to fish and aquatic organisms.

Example of the risks of legacy chemicals

Its use was prohibited in Japan in 1970, in the USA in 1972 and in Portugal in 1988.

However, DDT degradation products were found in the blood of 99% of people tested in the USA recently, despite the use of DDT having been banned more than 50 years ago.

In Portugal, DDT degradation products were found in more than 56% of young students tested in 2023, despite it having been banned over two decades before they were born.

These results indicate that the effects of the chemical emissions of today will have impact for many generations.

In Japan DDT residues were found in the blood of adults living in:

Miyako, Okinawa

Saku, Nagano

Tottori, Tottori

Sapporo

Akita

Okinawa

Minh, T.B., et al. 2006. Human Blood Monitoring Program in Japan: Contamination and Bioaccumulation of Persistent Organochlorines in Japanese Residents. Arch Environ Contam Toxicol 51, 296–313.
https://doi.org/10.1007/s00244-004-0251-5

Despite these results, not everybody 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_aguUSuh
bnxbImtgnkngR0sCxpJhcC88DOeBh1UM0gxTkxaUkpUT1UwVlZGVk5FR0p
MWllMTC4u

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

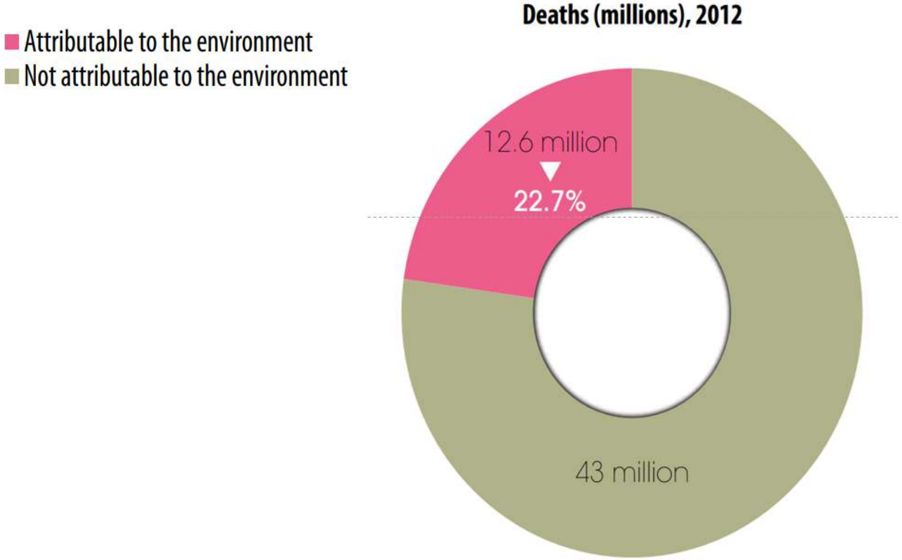
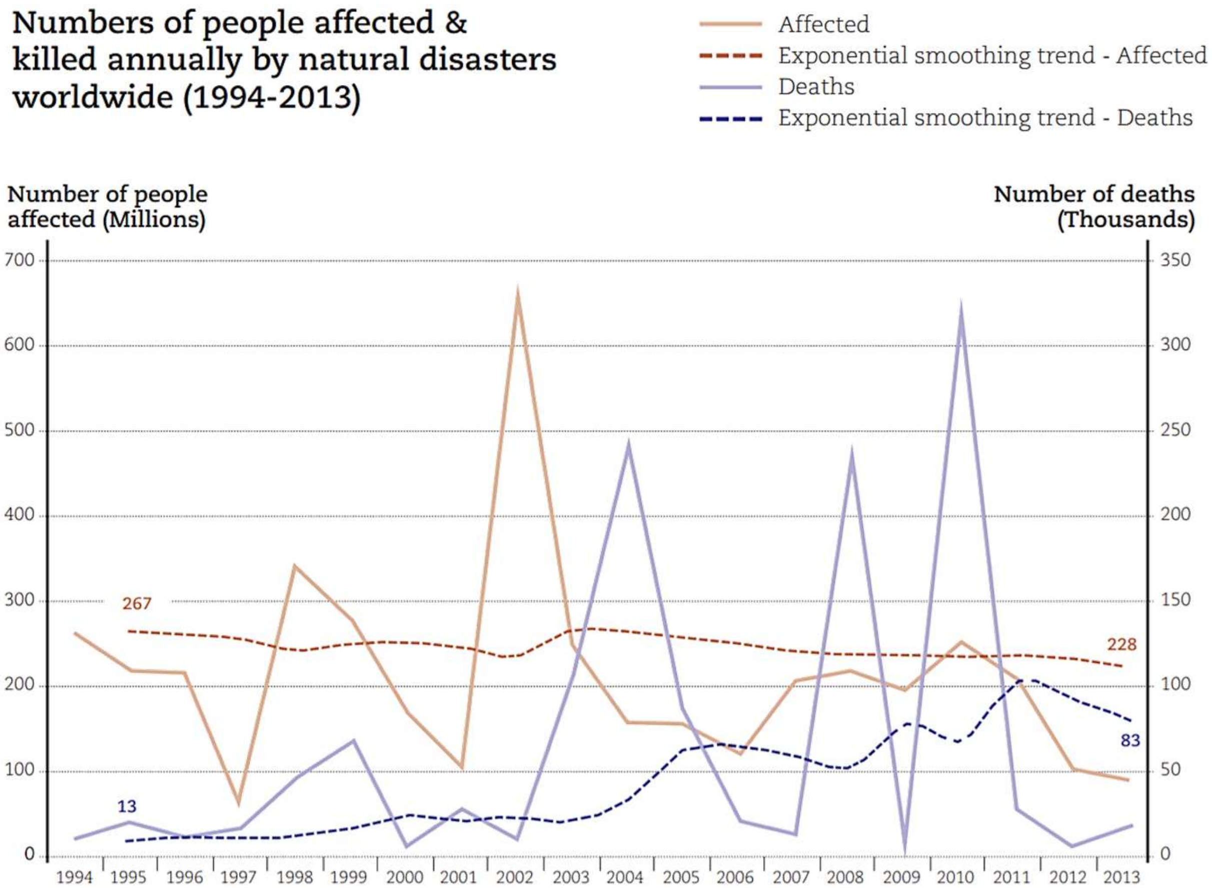


Table A2.3. Deaths attributable to the environment, by region, 2012

	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%

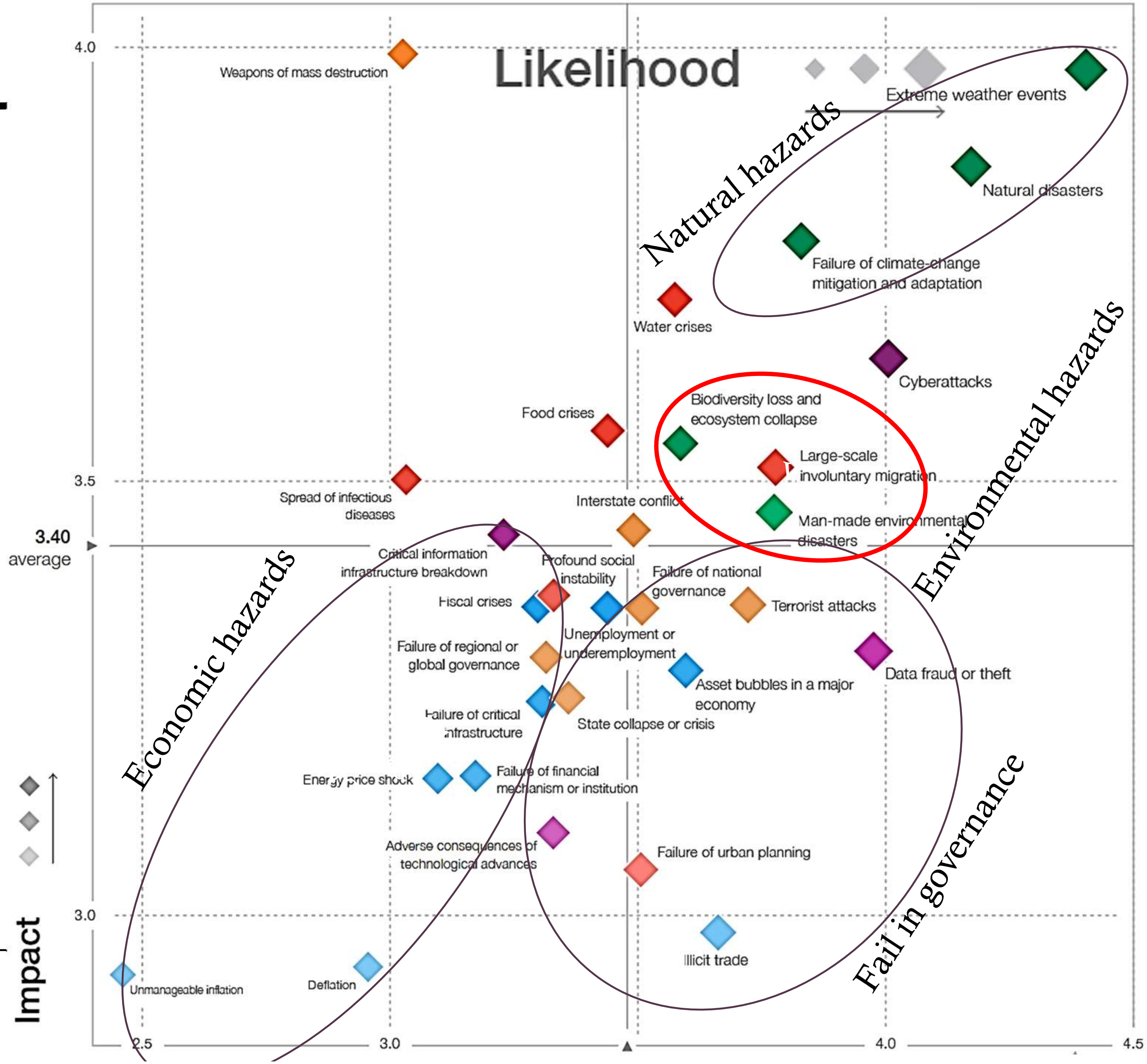
WHO (2016). Preventing disease through healthy environments: a global assessment of the burden of disease from environmental risks / Annette Prüss-Üstün … [et al]. World Health Organization, CH

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.

2. Methodology

Before we proceed:

Please follow this link to have access to all data and information:

https://sitesforprojects.wixsite.com/luismiguelnunes/copy-of-risk-management

Download file: MCS in practice.xlsx

WHY DO WE NEED PROBABILISTIC ERA METHODS?

We know from observation that nature is not deterministic (i.e., single possible outcome), and that every process will have many possible outcomes:

That is, for some set of input variables, the outcome will vary…

We can now study with a practical example.

Example exercise

“What is the estimated cost of a wardrobe for men in Japan (excluding underwear)?”

Assumptions:

- Prices are obtained exclusivey from online shops;
- Selection of shops and prices is random.
- The cost is calculated as the weighted sum of the prices of a set of apparels and accessories: headgear, sunglasses, t-shirts, shirts/blouses, pants, dresses/skirts, sneakers, shoes.
- The weights represent the percentage of use of that specific item (fraction of the apparel on the total number of pieces)

Example exercise

The cost model comes:

$$Cost = \sum w_j Price_j$$

With

j= {headgear, sunglasses, t-shirts, shirts/blouses, pants, dresses/skirts, sneakers, shoes}

Data (weights, as obtained from market search):

Japan

Piece	Percent use (w_j)	Price per piece (Yen)
Headgear (hat, cap, parasol)	F: 33.0% M: 24.8%	
Sunglasses	<10%	
T-shirt	F: 12.0% M: 12.0%	
Shirt/blouse	F: 58.0% M: 88.0%	
Pants	F: 70.0% M: 100%	
Skirt/dress	F: 30.0% M: 0.0%	
Sneakers	F and M: 2.8%	
Shoes	F and M: 97.2%	

Germany

Piece	Percent use	Cost per piece (Yen)
Headgear (hat, cap, parasol)	F: 12.9% M: 22.7%	Same as for Japan
Sunglasses	F: 59.0% M: 45.9%	Same as for Japan
T-shirt	F: 16.8% M: 28.6%	Same as for Japan
Shirt/blouse	F: 58.2% M: 71.4%	Same as for Japan
Pants	F: 75.0% M: 100%	Same as for Japan
Skirt/dress	F: 25.0% M: 0.0%	Same as for Japan
Sneakers	F and M: 35.4%	Same as for Japan
Shoes	F and M: 64.6%	Same as for Japan

Source of the data:

doi:10.1001/archdermatol.2011.236
doi.org/10.1111/jdv.14376
https://runrepeat.com/shoe-consumption-statistics#shoe-consumption-by-country
https://www.voguebusiness.com/consumers/germany-fashion-retail-market-gap-ganni
STATISTA: www.statista.com

Data (Prices):

We are going to collect this data now.

For that, I will ask you to:

1) enter the form following the link on the right;

2) Search online for prices of each apparel;

3) Upload the prices in the form

Piece	**Price per piece (Yen)**
Headgear (hat, cap, parasol)	
Sunglasses	
T-shirt	
Shirt/blouse	
Pants	
Skirt/dress	
Sneakers	
Shoes	

https://forms.office.com/Pages/ResponsePage.aspx?id=MQkPE_aguUSuhbnxbImtgnkngR0sCxpJhcC88DOeBh1UMFFIUkc5VjNNQTQ5OFMzRDlWOFczS1RZSi4u

Results

I will need now a few minutes to retrieve your data and plot share it…

When I tell you, please download the file "Updated price data.xlsx".

#	PRICES								COST
	Headgear	Sunglasses	T-shirt	Shirt/blouse	Pants	Skirt/dress	Sneakers	Shoes	COST
1	3.0	0.1	1.5	1.3	2.0	2.1	0.8	1.7	5.8
2	15.0	9.6	11.6	14.3	0.2	10.6	4.5	10.8	29.4
3	342.0	232.4	283.9	242.5	100.3	131.8	308.5	272.7	724.9
4	223.0	28.3	168.4	136.2	9.4	34.5	149.3	76.5	285.5
5	45.0	27.7	14.4	26.3	10.8	32.3	9.6	22.5	71.2
6	57.0	18.9	39.7	26.9	0.7	40.3	1.7	33.7	77.7
7	8.0	0.4	0.7	2.0	4.8	0.2	5.3	5.4	14.0
8	19.0	4.2	11.6	16.9	6.0	13.0	14.6	16.2	43.6
9	4.0	0.2	1.7	3.1	1.2	0.5	0.4	2.0	7.1
10	23.0	16.6	17.7	9.8	0.4	5.7	11.5	15.5	33.6
11	24.0	15.4	8.6	3.5	5.0	3.9	23.8	12.1	28.8
12	35.0	11.2	20.7	21.3	0.6	24.4	0.0	16.4	47.4
13	67.0	3.9	7.9	42.4	32.6	54.1	46.4	32.1	120.3
14	83.0	24.4	61.7	76.9	66.9	6.4	33.1	28.0	192.6
15	90.0	45.5	51.1	66.7	62.9	85.5	41.9	73.1	225.9
16	90.0	87.0	38.6	54.1	5.3	27.0	88.0	20.5	109.2
17	97.0	57.3	20.1	55.2	19.2	71.0	46.0	96.7	194.0
18	93.0	70.4	54.0	7.4	67.7	26.4	27.3	27.8	137.2
19	4.0	1.3	1.6	0.4	1.1	0.4	3.6	1.8	4.6
20	2.0	0.5	0.4	1.5	1.4	1.2	0.9	1.3	4.6
21	3.0	2.6	0.8	2.3	1.7	1.4	0.8	1.3	6.1
22	4.0	1.3	1.0	1.0	0.1	3.2	3.5	2.8	5.0
23	5.0	0.8	4.6	4.4	4.8	4.3	1.4	2.0	12.5
24	6.0	3.7	2.2	3.8	1.5	1.1	5.0	4.3	11.2
25	7.0	1.6	1.3	0.5	4.3	7.0	2.2	6.7	13.3
26	50.0	7.5	5.6	34.7	11.8	39.9	48.0	18.4	75.3
27	48.0	17.1	5.8	29.6	24.5	26.5	21.5	21.5	86.0
28	49.0	13.8	38.0	38.9	11.3	45.4	30.0	32.9	96.1
29	47.0	14.1	24.1	31.2	42.6	8.6	3.0	36.9	121.7
30	47.0	25.5	10.6	21.1	7.5	27.3	17.5	43.3	83.6
31	44.0	10.2	15.8	37.5	28.8	3.4	27.0	1.7	77.8

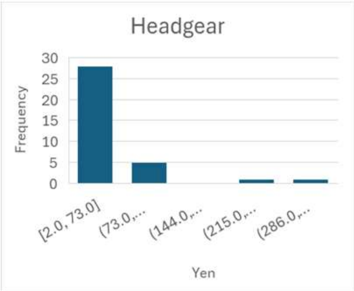
Replace these data with the one in "Updated price data.xlsx"

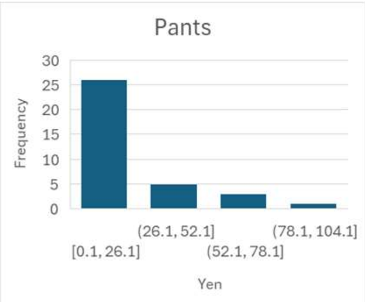
MCS in practice | Data from price search | MCS with software) | Sensitivity analysis | Table outup | Gra

The results shown in these slides are for demonstration.

Results (coming directly from the data):

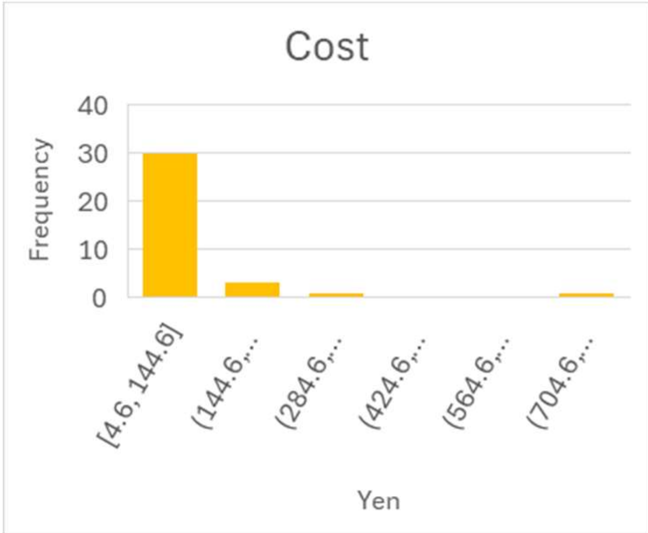
Prices per apparel





$$Cost = \sum w_j Price_j$$

Estimated cost



Etc.

Results (cost):

Why are the costs different?

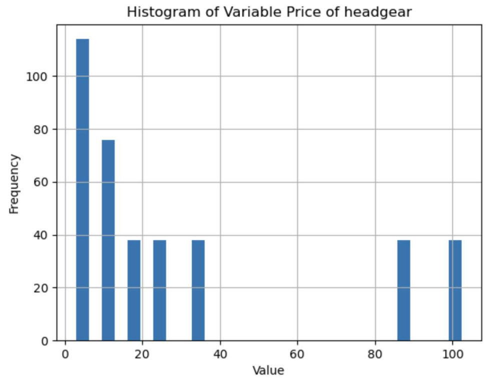
- prices were collected by different people.

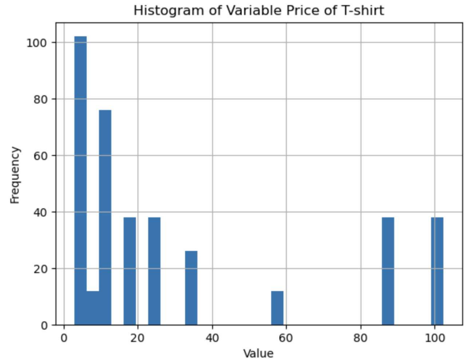
Each person will choose different criteria to find the prices, e.g., personal taste, searching engine, price range, etc.

- Each one of these criteria are sources of (**epistemic uncertainty** – i.e, dependent on the method).

- As we cannot sample all prices, there is here another source of **epistemic uncertainty** because statistics are estimated from the data.

Aleatoric uncertainty reflect the true variability of the prices. It cannot be reduced, and is unknown in most cases...





Results (cost):

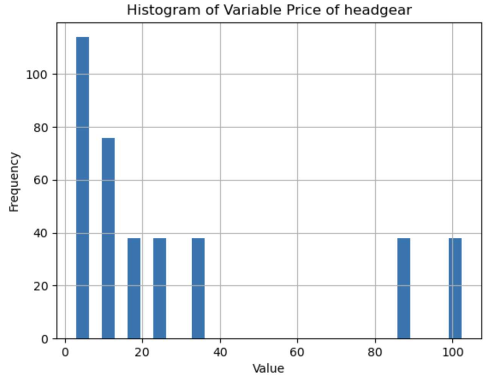
The **epistemic and aleatoric uncertainty** of each input variable will impact the uncertainty of the forecast.

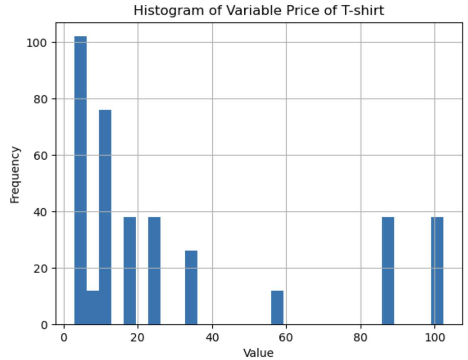
Monte Carlo Simulations is a method that allows the study of the **propagation of input uncertainty through the model** and its impact on the forecast.

Results include:

1) The estimate of forecast uncertainty (histogram and statistics);

2) The contribution of each individual variable to the uncertainty found in the forecast (sensitivity analysis)





Uncertainty propagation through the model

Monte Carlo Simulations is the best know and most used method for studying the uncertainty propagation through the model.

It allows: :

- the estimation of the **probabilistic risk level**,

- to quantifying the importance of each input variable to the variability of the estimate (**sensitivity analysis**)

The Monte Carlo simulations method

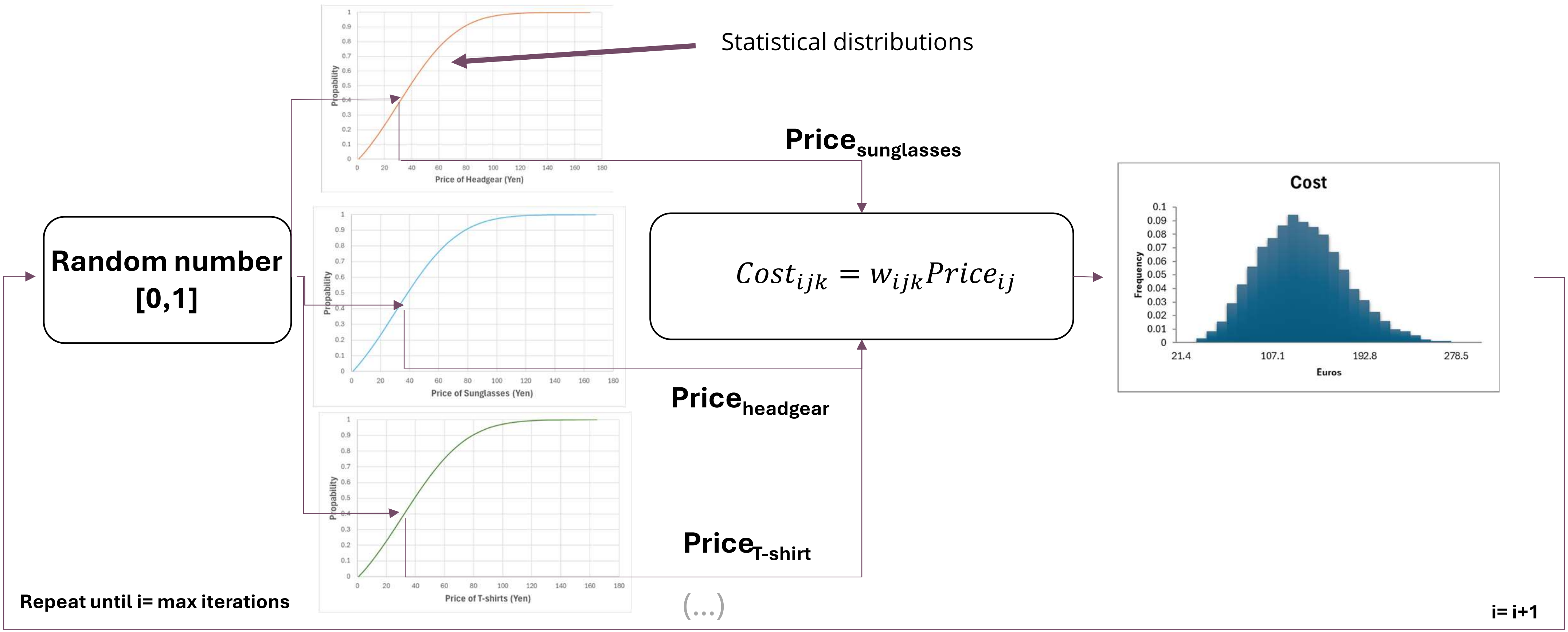
Monte Carlo Simulation (MCS) is a computational technique that employs repeated random sampling to determine the probability distribution of various potential outcomes.

The methodology was developed by mathematicians John von Neumann and Stanislaw Ulam during World War II as a tool for enhancing decision-making processes in situations involving uncertainty.

It derives its name from Monte Carlo, the famous gambling district in Monaco, reflecting how chance and randomness are fundamental to this modeling approach.

MCS transforms complex problems with uncertain variables into manageable statistical analyses, providing comprehensive insights into the full spectrum of possible outcomes and their associated probabilities.

The Monte Carlo simulations method



Building a MCS algorithm

As shown in the previous slide, MCS demands that each variable be represented by a **specific statistical distribution** – which is obtained from the data.

This implies having to **fit the data to some chosen statistical distribution**:

	Continuous
Unbounded	Cauchy Error function Error F Generalized Extreme Value Hyperbolic Secant Johnson Unbounded Kernel Laplace Logistic Mixed Normal Normal Slash Skew Normal Student t 3 parameter Student t

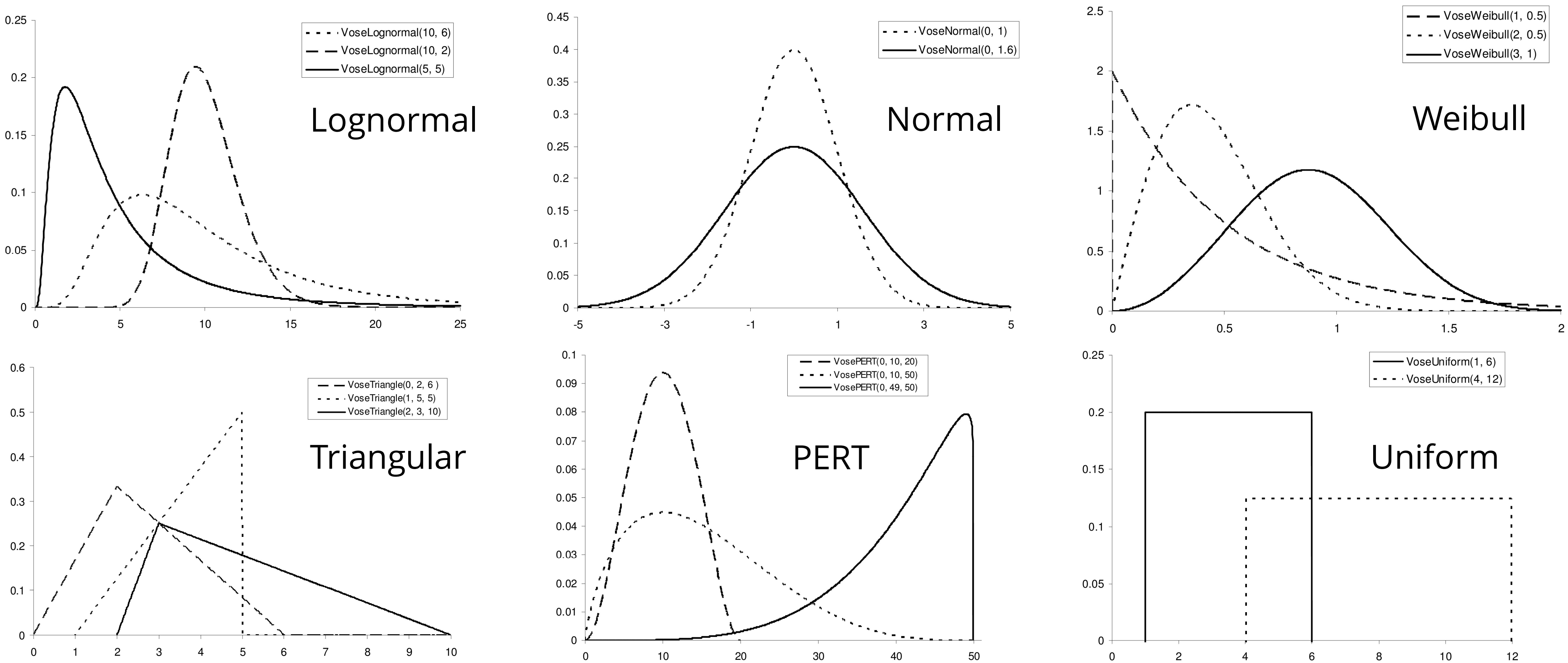
Left or right bounded	Bradford Burr Chi Chi Squared Dagum Erlang Exponential

(...)

	LogGamma LogLogistic LogLaplace Lognormal

Check an exhaustive list here:
Van Hauwermeiren, M., Vose, D., & Vanden Bossche, S. (2012). *A Compendium of Distributions* (2nd ed.) [E-book]. Vose Software. https://www.vosesoftware.com

Most ERA relly on a few distributions:



Van Hauwermeiren, M., Vose, D., & Vanden Bossche, S. (2012). *A Compendium of Distributions* (2nd ed.) [E-book]. Vose Software. https://www.vosesoftware.com

Building a MCS algorithm

Please check the Excel file “MCS in practice.xlsx”

We will build the MCS using:

1) Excel functions;

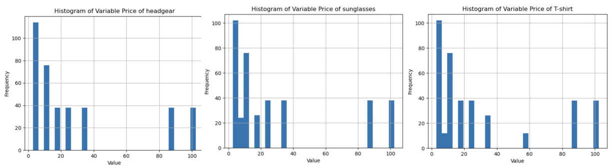
2) Repeat using an add-inn (Argo) to help in the process of inputing data and outputing results and sensitivity analysis.

Monte Carlo Simulations results

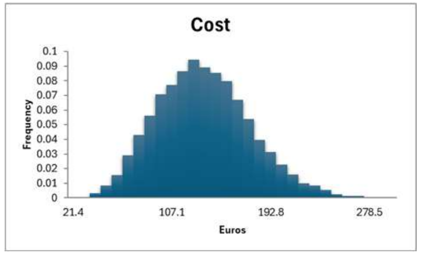
(the figures shown here are for demonstration only – we will obtain different ones once you provide the prices for the apparel.

Results:

We got a representation of the uncertainty of each input variable, and how they impact the forecast:



(...)



Uncertainty propagation through the model

Statistics	Values	Percentiles	Values
Mean	156.5	10.00%	95.3
Median	153.0	20.00%	113.5
Variance	2443.9	30.00%	127.8
Standard Deviation	49.4	40.00%	139.9
Coefficient of Variation	0.3	50.00%	153.0
Min	36.5	60.00%	165.7
Max	367.1	70.00%	179.9
Range	330.5	80.00%	197.0
Standard Error	0.5	90.00%	221.7
		100.00%	367.1

Sensitivity Analysis Using Correlation

Correlation-based sensitivity analysis measures the linear relationship between input parameters and model outputs using correlation coefficients. This approach is particularly useful for identifying which parameters have the strongest linear associations with model outcomes (more sensitive).

Sensitivity measures

Pearson Correlation Coefficient:

$r(X_i,Y) = Cov(X_i,Y)/[\sigma(X_i)\sigma(Y)] = \Sigma_{k=1}^N(x_{i_k} - \bar{x_i})(y_k - \bar{y})/\sqrt{[\Sigma_{k=1}^N(x_{i_k} - \bar{x_i})^2\Sigma_{k=1}^N(y_k - \bar{y})^2]}$

with:

x_{i_k} = k-th sample of parameter X_i

y_k = k-th model output

$\bar{x_i}$ = mean of parameter X_i

$\bar{y}$ = mean of output Y

Spearman Rank Correlation: $\rho_s(X_i,Y) = 1 - 6\Sigma_{k=1}^N d^2_k/[N(N^2-1)]$

Where $d_k = rank(x_{i_k}) - rank(y_k)$ is the difference in ranks.

Sensitivity Analysis Using One-Factor-at-a-Time

In *One-Factor-at-a-Time* (OFAT) analysis, each input parameter X_i is varied individually while all other parameters remain at their baseline values. For a model with output $Y = f(X_1, X_2, \ldots, X_n)$, the sensitivity is assessed by:

Base case calculation: $Y_0 = f(X_1^0, X_2^0, \ldots, X_n^0)$
Perturbed case for parameter i: $Y'_i = f(X_1^0, \ldots, X_i^0 \pm \boldsymbol{\Delta X_i}, \ldots, X_n^0)$

Examples of sensitivity metrics

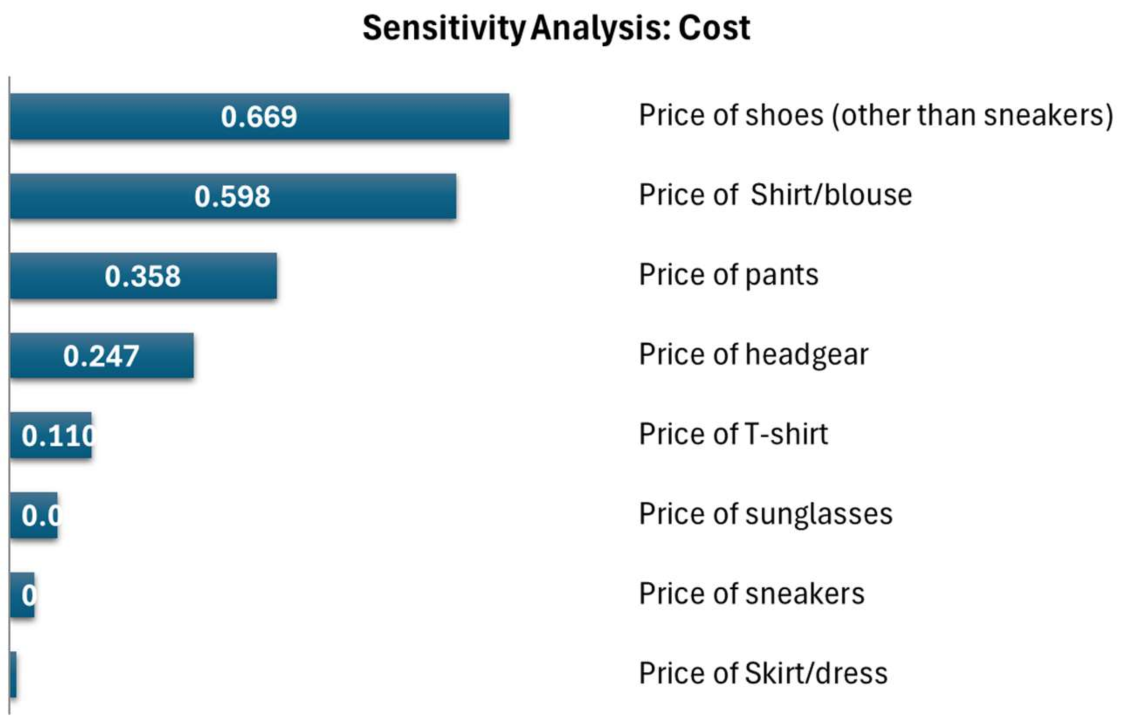
Absolute Sensitivity (AS): $AS_i = |Y'_i - Y_0|$

Relative Sensitivity (RS): $RS_i = (Y'_i - Y_0)/Y_0$

Normalized Sensitivity (NS): $NS_i = (\Delta Y/Y_0)/(\Delta X_i/X_i^0) = (Y'_i - Y_0)/Y_0 \times X_i^0/\Delta X_i$

Sensitivity Coefficient (SC): $SC_i = \partial Y/\partial X_i \approx (Y'_i - Y_0)/\Delta X_i$

Sensitivity Analysis, results using correlation. Average of relative sensitivity for 10 000 simulations



The model is most sensitive to the price of shoes, followed by the price of shirt/blouse…

Meaning that choosing less expensive shoesand shirts would be the smartest options if one wants to cut expenses!

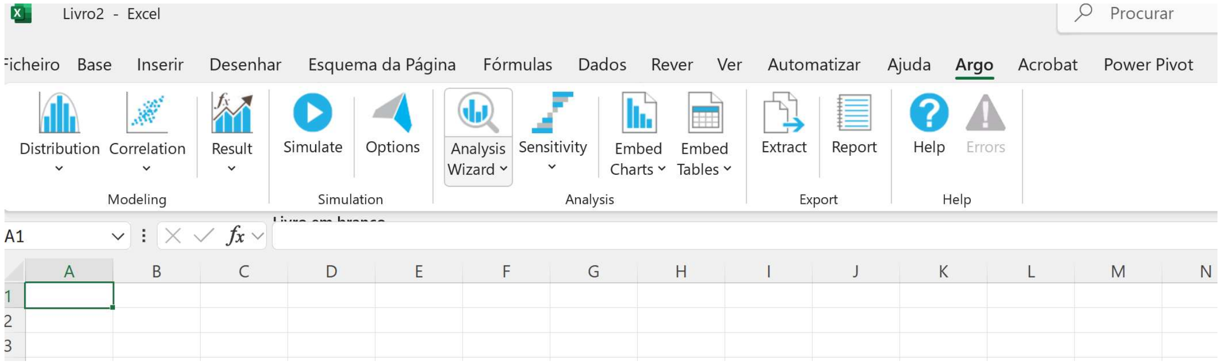
Working with Argo

Use software (Argo):

1. Start by downloading and installing Argo for Excel: https://boozallen.github.io/argo/

   Follow the instruction available on the site;

2. After installing you should see a dedicated menu:



Working with Argo

Distribution is the option for setting the statistical distributions for each variable.

Correlation allows to define the correlation coefficient between variables, if relevant. If correlation between variable is known, then it should be included to avoid underestimation of uncertainty.

Results cell(s) is where we set the function(s) to be modelled.

Simulate is the start button for the simulation.

Options allows the settings of some running alternatives.

Sensitivity allows the quantification of sensitivite measures (identify the variables with highest importance.

Embed charts and Embed Tables will create graphs and tabular outputs of the inputs and outputs.

Extract and Report will produce files with summary of results in PDF and in xlsx/csv format.

Working with Argo

Before starting using the software we need to **prepare the data** for each variable – dedicate one spreadsheet cell per variable:

1. Assumed (or modelled) statistical distribution
2. Mean
3. Standard deviation
4. Minimum and maximum
5. If necessary shape coefficients (e.g., k and λ of the Weibull distribution)
6. Model constants

Working with Argo

constants

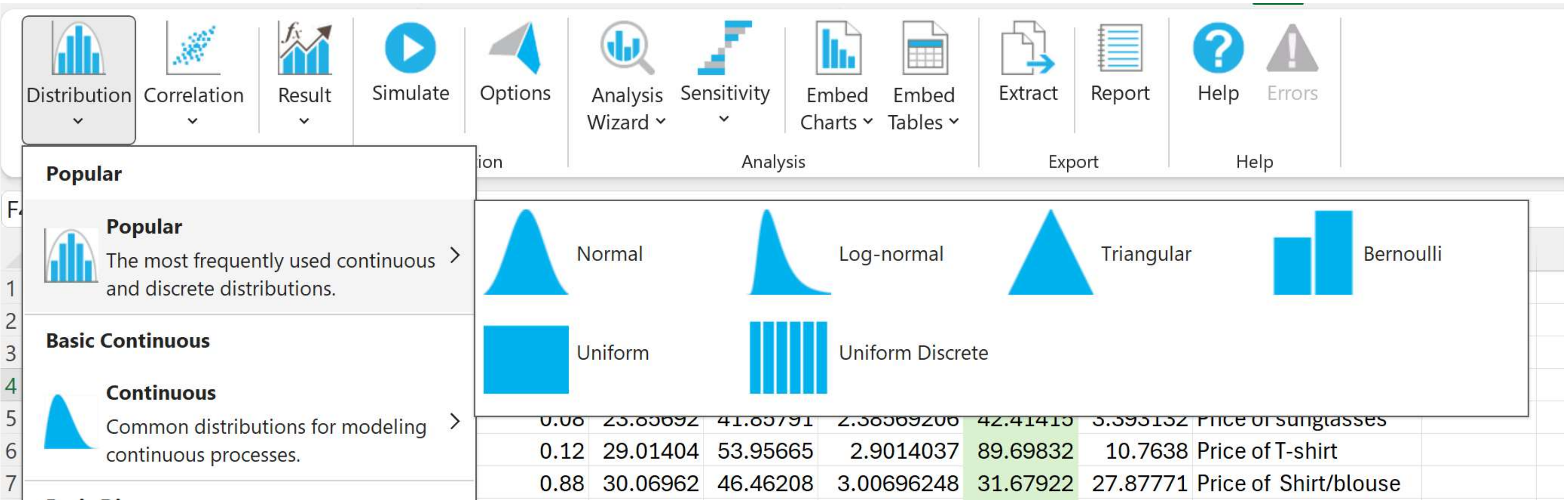
E.g.,

	Variable	Weigts	Mean	Std. Dev.	Min
4	Price of headgear	0.248	50.629	66.572	5.063
5	Price of sunglasses	0.08	23.857	41.858	2.386
6	Price of T-shirt	0.12	29.014	53.957	2.901
7	Price of Shirt/blouse	0.88	30.070	46.462	3.007
8	Price of pants	1	17.933	24.465	1.793
9	Price of Skirt/dress	0	23.424	28.319	2.342
10	Price of sneakers	0.028	30.683	56.633	3.068
11	Price of shoes (other than sneakers)	0.972	28.287	48.411	2.829

Working with Argo

To **set the statistical distribution** for a variable, click on a empty cell (preferably on the right side of the variable name) and then on “Distibution”.

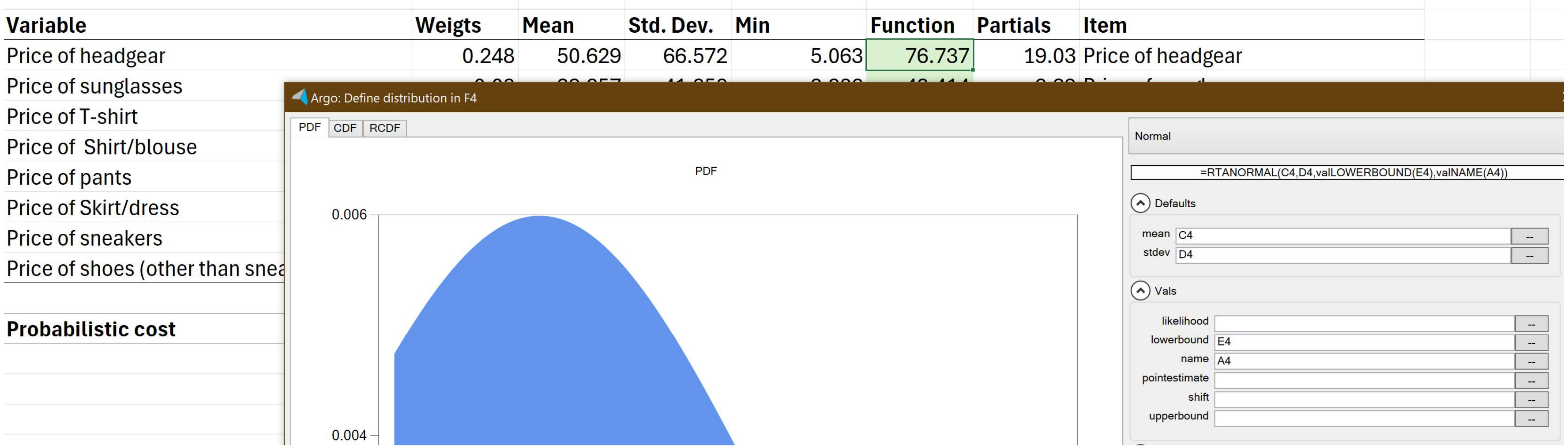
Choose the assumed distribution from the pop-down menu.



Working with Argo

Fill-in the data. The best is to click on the grey box and then on the spreadsheet cell containing the data.

For instance to fill-in the mean value, click on  and then on cell C4 (where the mean is).



Working with Argo

Next, we need to write the Model relating the variables.

Choose the cell where the formula will be calculated and write the Excell formula, linking each variable to the cell with the distributions.

In the following example I will compute the cost partials per apparel item and the compute the Cost by adding the partials.

We will have probabilistic results per partial and for the Cost.

Working with Argo

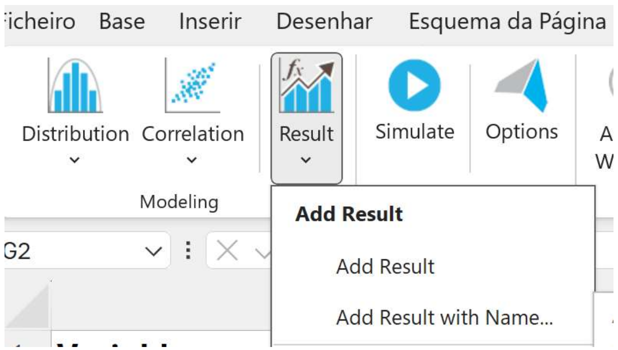
Each partial is the product of the Weight by the distribution Function:

=B2*F2

	A	B	C	D	E	F	G
1	**Variable**	**Weigts**	**Mean**	**Std. Dev.**	**Min**	**Function**	**Partials**
2	Price of headgear	0.248	50.629	66.572	5.063	76.737	19.03

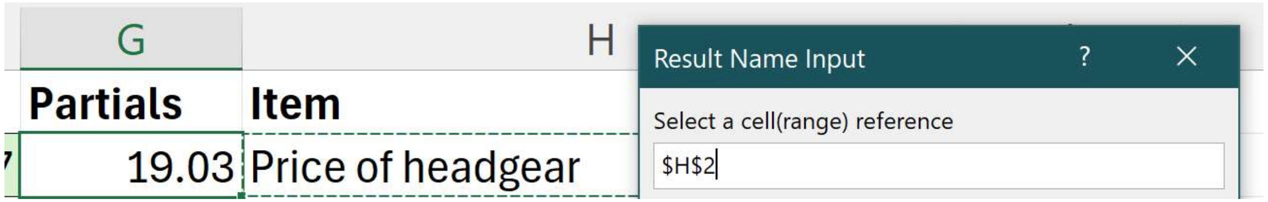
Now we set this Partial as a Result formula:

1. Click on the cell with the formula and then on Argo “Result” and choose “Add result with name”



Working with Argo

In the window **indicate the cell where the name of the partial is –** in this case it it the name of the variable.



Click **OK**

The following formula will show up:

=@RtaRESULT(B2*F2,H2)

Working with Argo

Repeat for all variables.

Here is the example with all variables and the final Cost

`=@RtaRESULT(G4+G5+G6+G7+G8+G9+G10+G11,A13)`

A	B	C	D	E	F	G
Variable	**Weigts**	**Mean**	**Std. Dev.**	**Min**	**Function**	**Partials**
Price of headgear	0.248	50.629	66.572	5.063	76.737	19.03
Price of sunglasses	0.08	23.857	41.858	2.386	42.414	3.39
Price of T-shirt	0.12	29.014	53.957	2.901	89.698	10.76
Price of Shirt/blouse	0.88	30.070	46.462	3.007	31.679	27.88
Price of pants	1	17.933	24.465	1.793	8.451	8.45
Price of Skirt/dress	0	23.424	28.319	2.342	39.090	0.00
Price of sneakers	0.028	30.683	56.633	3.068	39.366	1.10
Price of shoes (other than sneakers)	0.972	28.287	48.411	2.829	46.872	45.56
Probabilistic cost				Cost = Σ partials		**116.18**

Working with Argo

Now we can **prepare the simulations**:

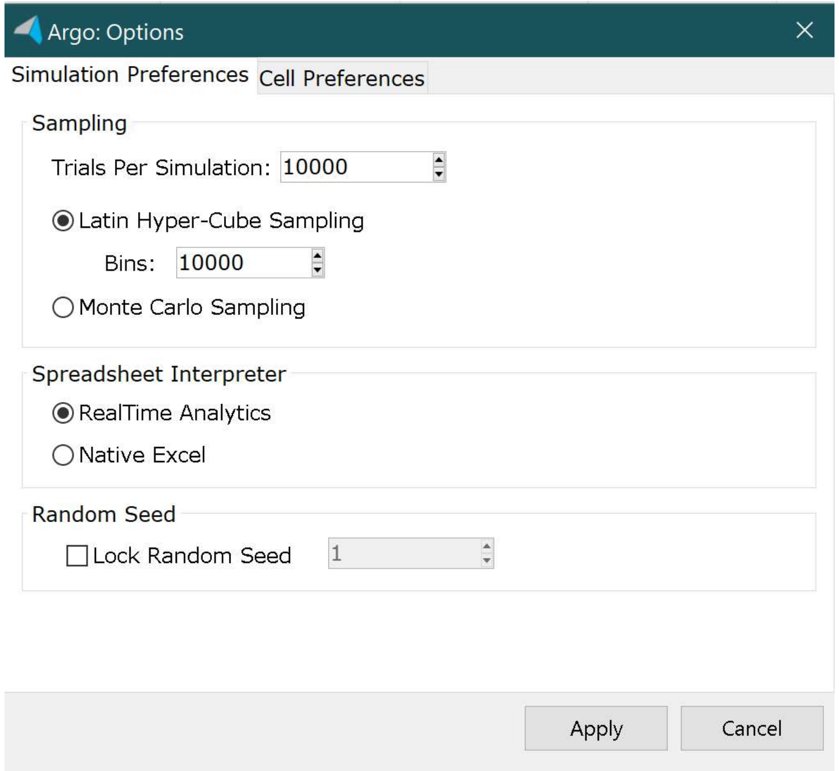
Click on "Options"

In "Sampling ", set:

1. Number of runs: set 10 000 (maximum allowed)

2. Method for searching the solution space: Latin Hypercube is best for small sample sizes; and MC when computing capacity is limited.

3. Interpreter for making the calculations: RealTime is the fastest and more stable.

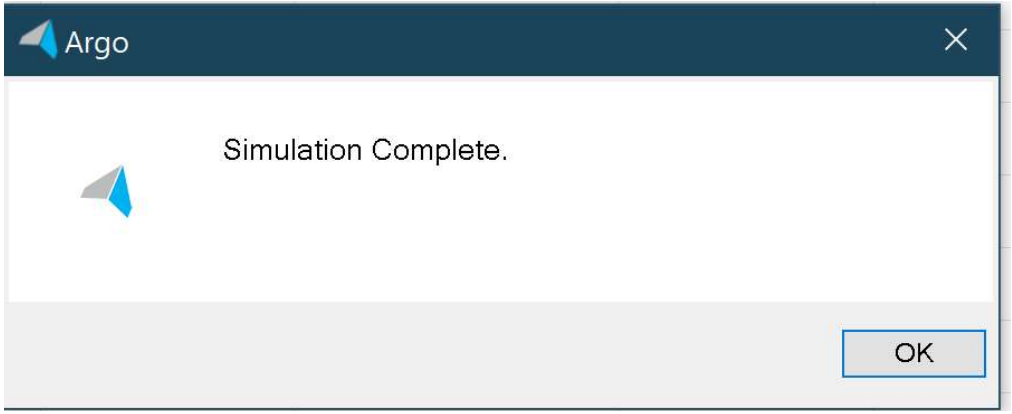


Working with Argo

Now we can **run the simulations**:

Click on "Simulate".

If this windows appears, then the run was successful:



Working with Argo

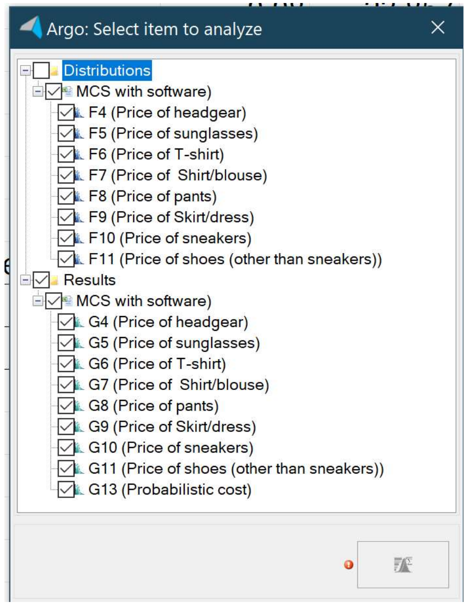
To see the results:

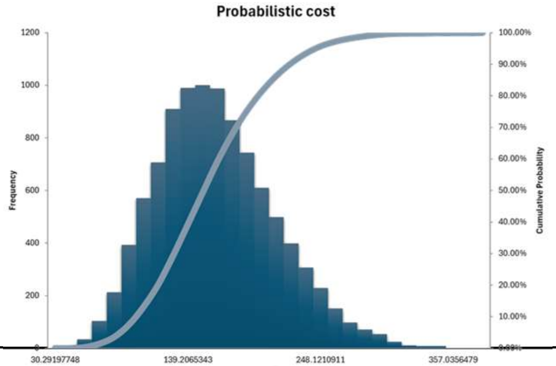
There are three options:

1. “Wizard” (“Choose distributions/results”) – shows graphs of imput and output distributions.

2. “Embed Charts” – shows graphs of imput and output distributions.

3. Embed Tables” – shows tables with statistical results.





Working with Argo

To see the **sensitivity analysis** results:

Choose “Sensitivity” and then “sensitivity analysis by correlation”.

In the window select: “Embed in Worksheet”.

Results show the sensitivity analysis based on Pearsons’ correlations, with the most correlated (sensitive) variables on top.

Working with Argo

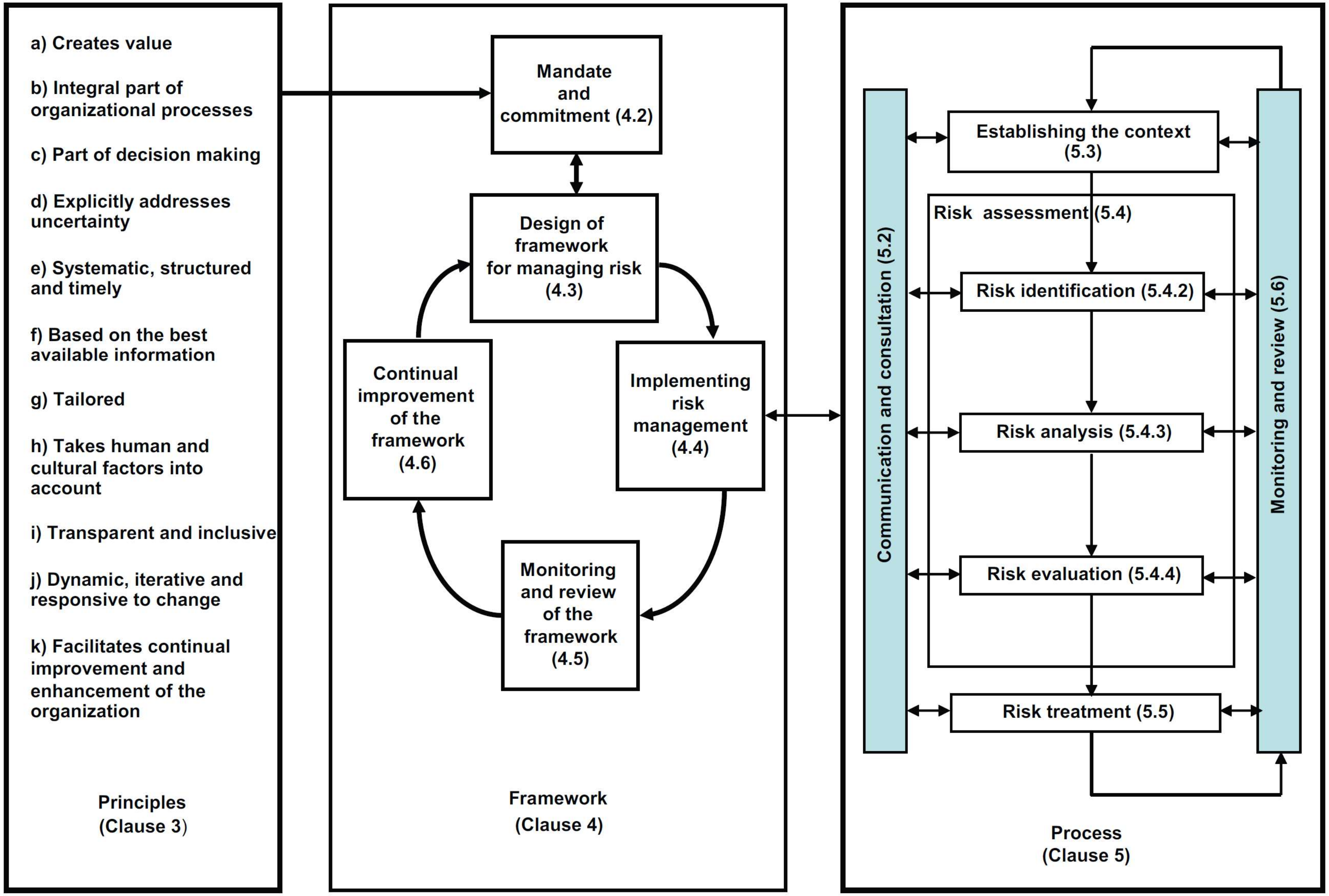
For the purpose of our analysis, we will want to check:

1. Mean and median of the estimate (Cost)
2. Percentiles of the estimate
3. Extremes of the estimate
4. Shape of the distribution functions (long tails, jagged histograms (irregular inputs or sampling) / smooth (inputs and sampling).
5. Sensitivity analysis

GENERAL ENVIRONMENTAL RISK ASSESSMENT METHOD

ISO 31000 (2018) sets the International Standard with principles and generic guidelines on risk management.

Figure 1 — Relationships between the risk management principles, framework and process



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

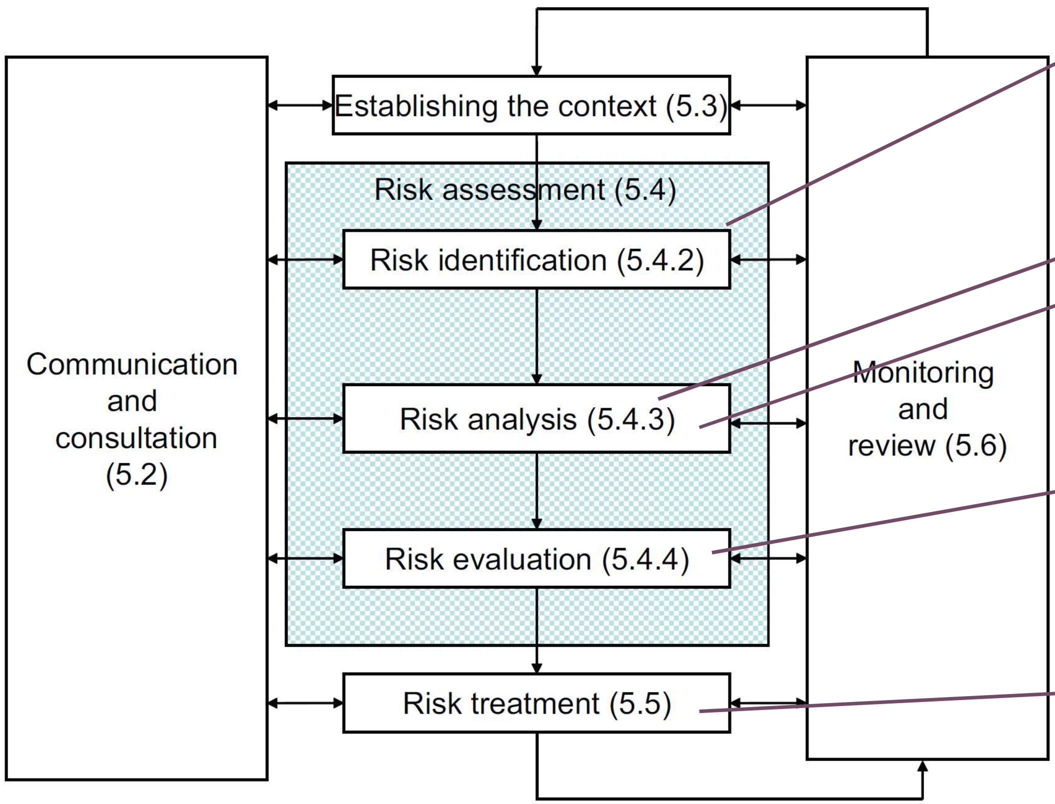
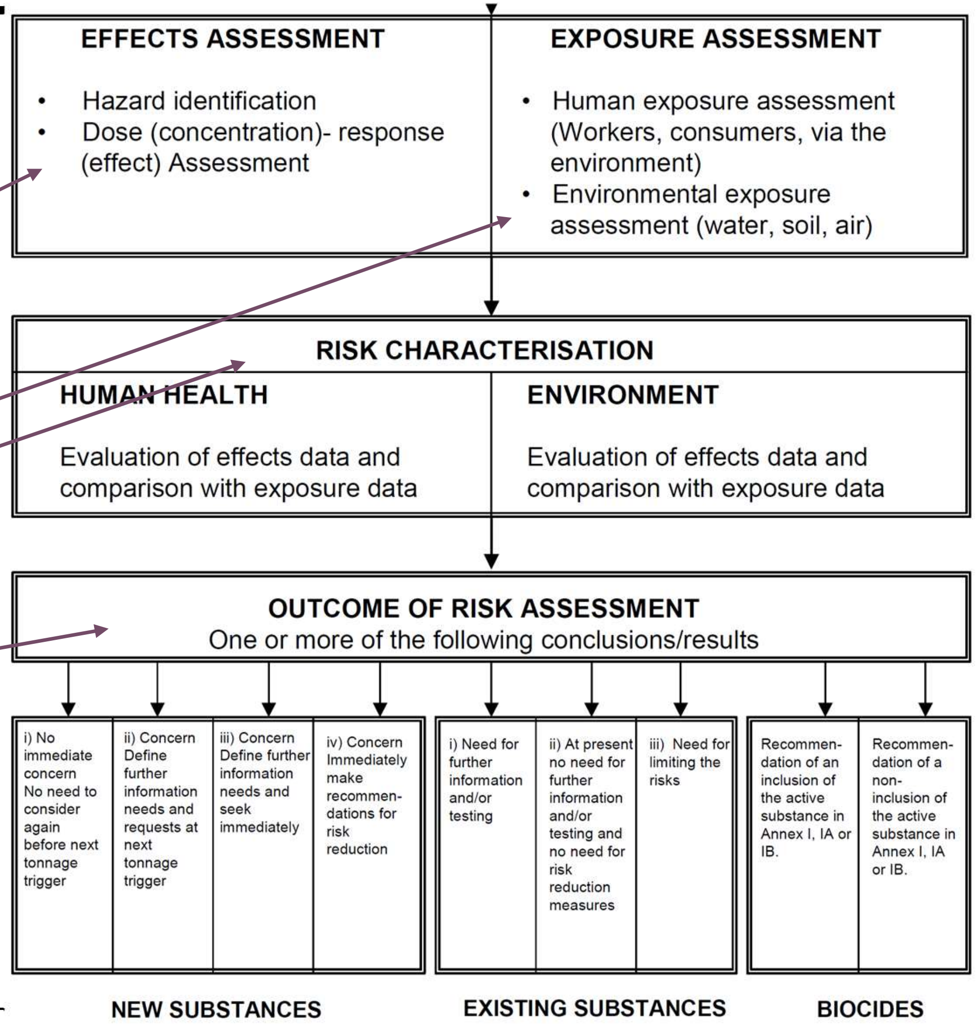


Figure 3 — Risk management process

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

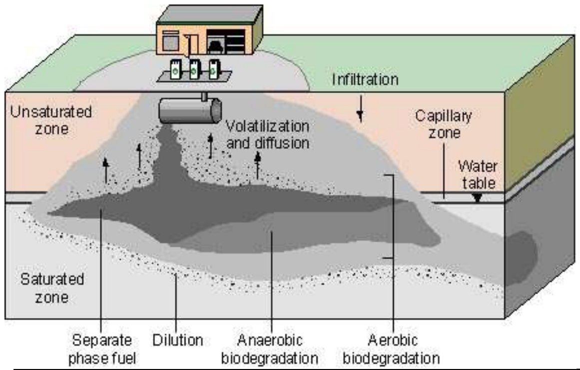
Consequence = ***g***(*toxicological effects*; *vulnerability of receptors*).

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.

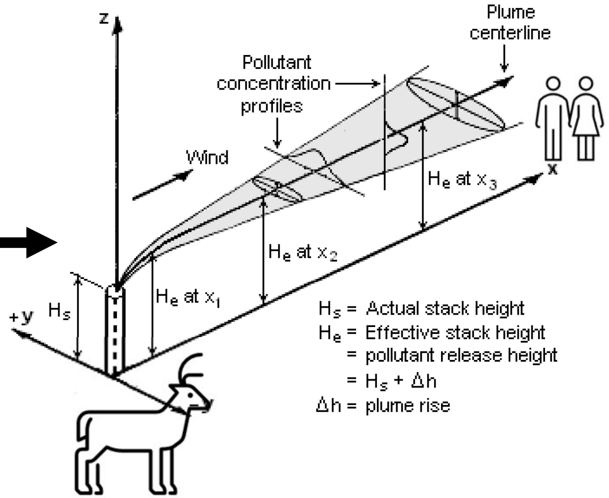
Concepts

Probability of a hazard

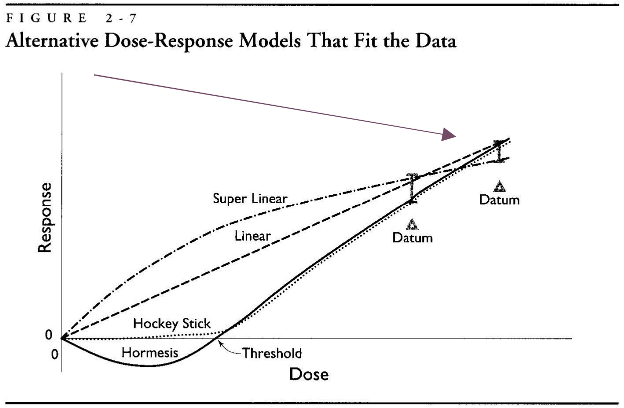
Probability of the event



Probability of exposure



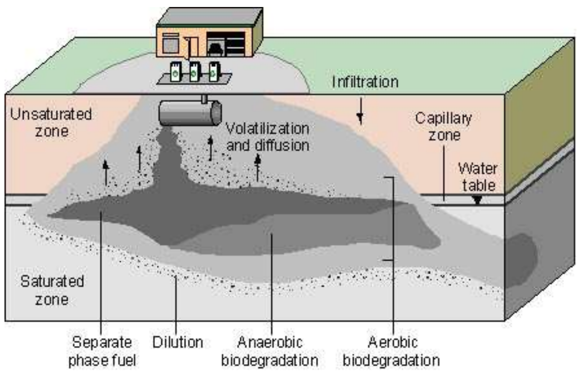
Consequence



Concepts

Probability of a hazard

Probability of the event



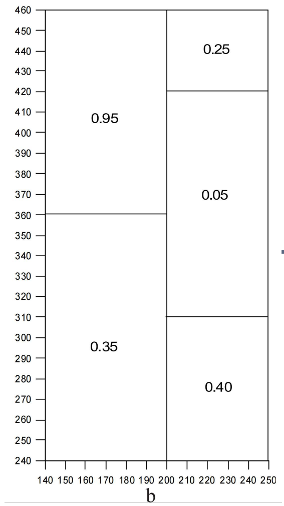


Table 2. Parameters for the estimation of emissions inside the industrial area.

	Sub-area, *i*													
Parameter	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)

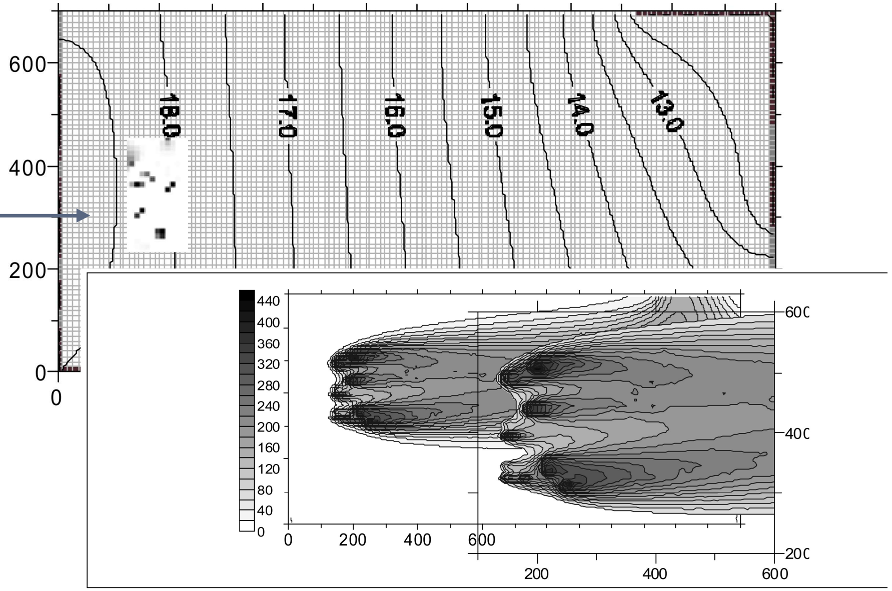


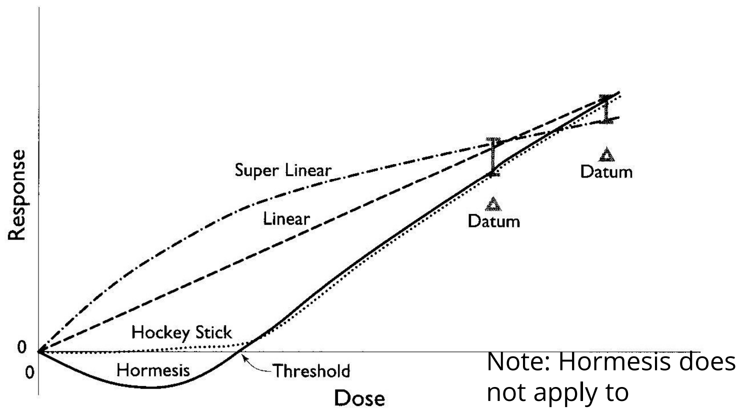
Figure 3. Example of a solute concentration plume after 7300 days (g/m3). Overlapping figure is a zoom in on the emission area.

Concepts

Consequence

Toxicological effects will increase with exposure (dose)

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



Note: Hormesis does not apply to contaminants

Dose – effect data comes from lab essays and epidemiological studies

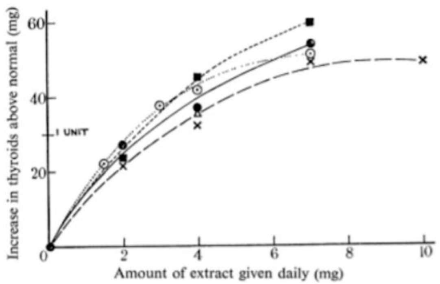
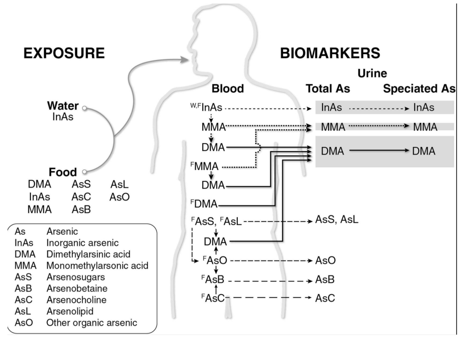


FIG. 1—Dose/response curves for various thyrotropic extracts. ●— AP15B; ···⊙ AP8B; Δ, AP14B; - - - ■ PR22; — — × T17B.



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.

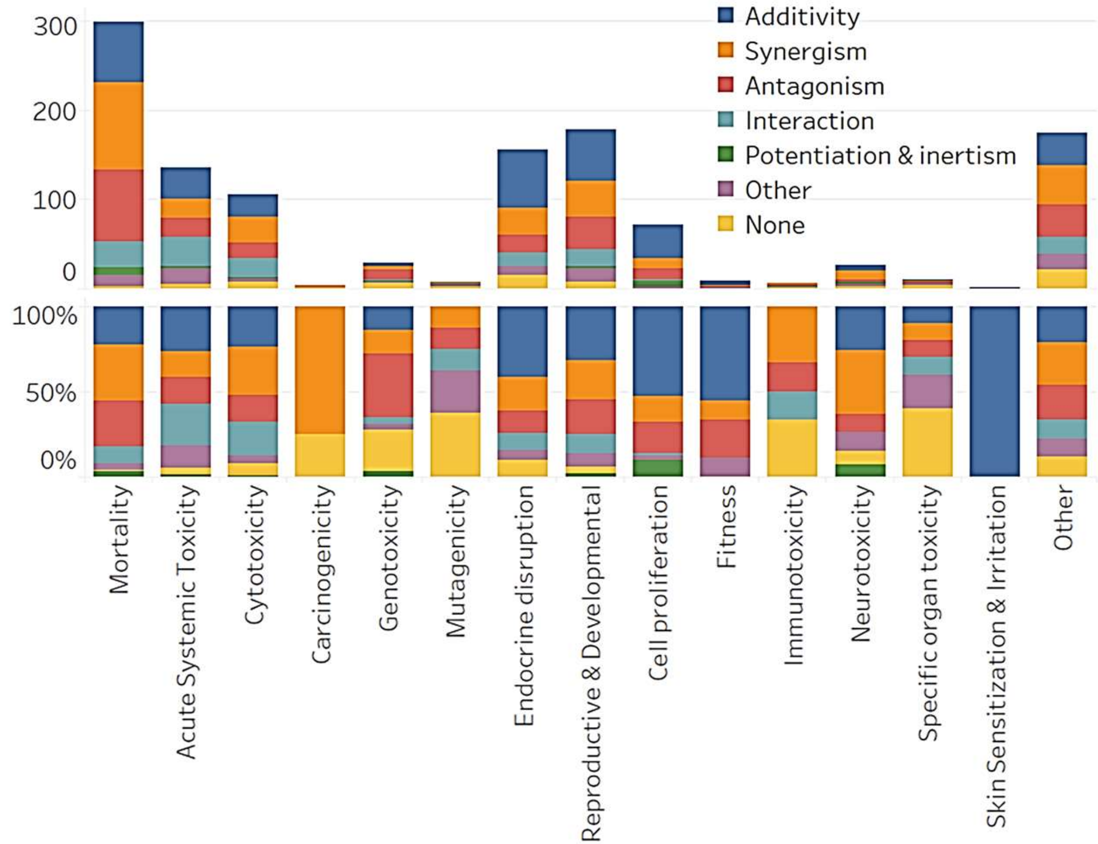
Introduced in the assessment by studying the risks for most sensitive populations.

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.

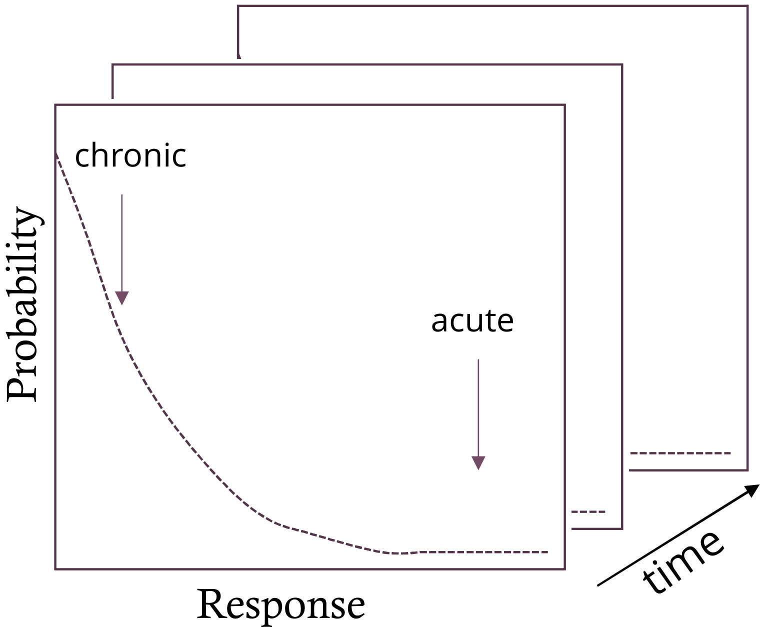
The figure shows examples of interactions for diferente endpoints when receptors are exposed to mixtures of contaminants.



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

Recalling the ERA model:

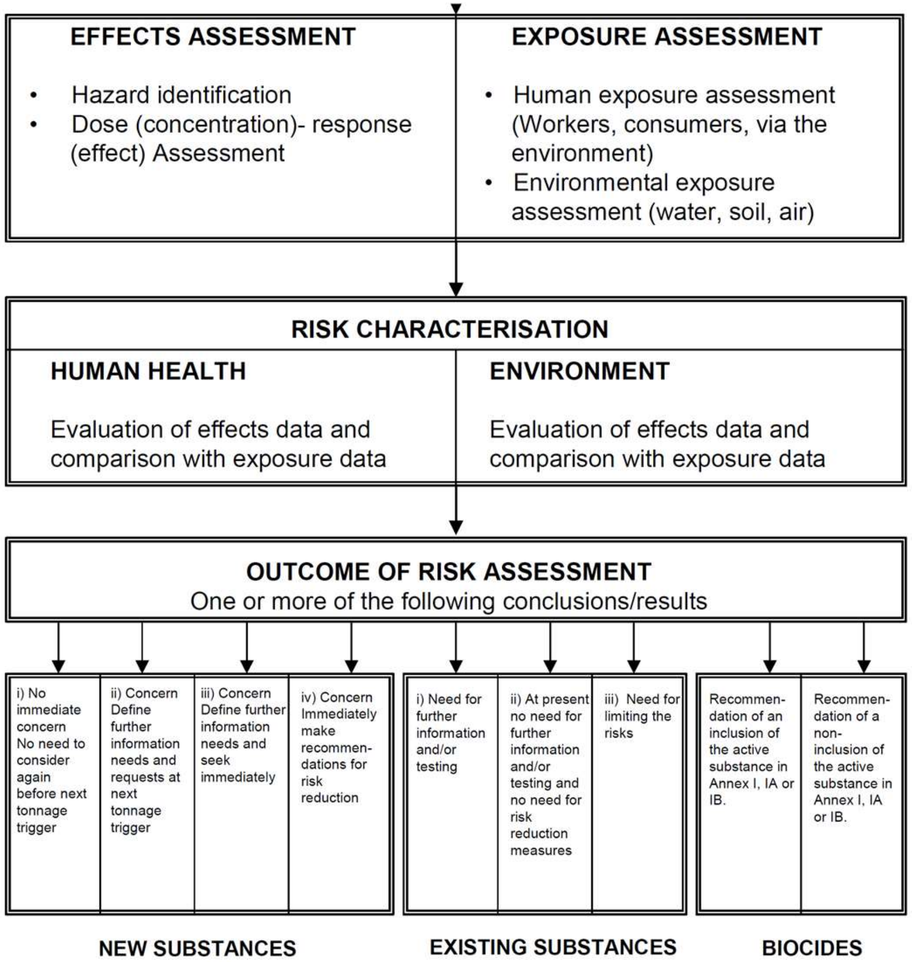
I will assume that the toxicological effects are known (i.e., can be obtained from databases), which is the case for the majority of real world cases.

Toxicological data can take decades to accumulate and is in permanent actualization.

Hence we need to explore:

Exposure assessment

Risk characterization



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

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)

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

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

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., 2×10^{-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.

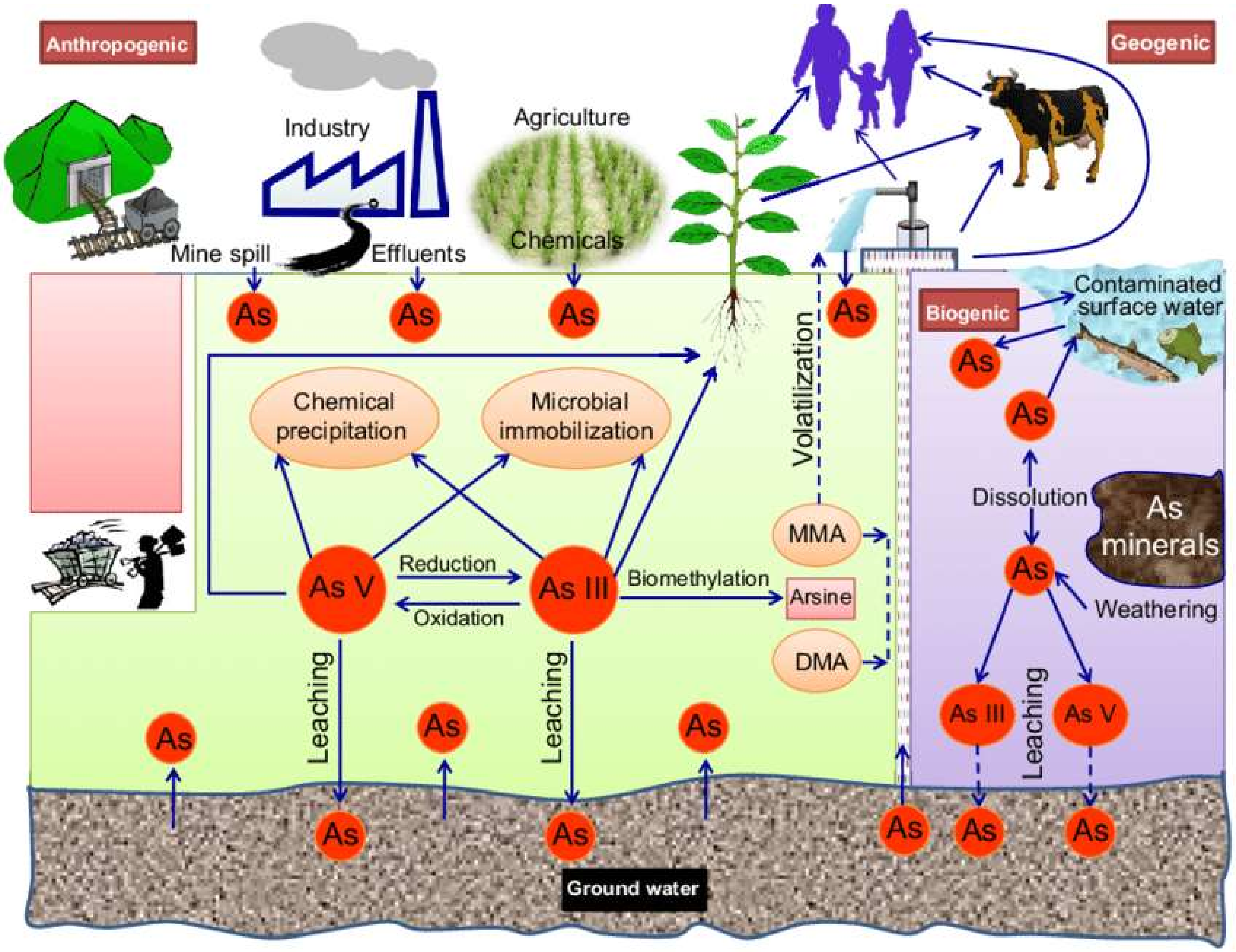
Note: that it suffices to establish the margin of safety level (e.g., 0.1, 0.001) to compute a reference dose once the ADI is known.

3. Examples

Practical work 1 – Health risk due to exposure to arsenic in the diet (Japanese adult men)

Arsenic in the environment

Justification:



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

The world is precariously dependent on only a handful of staple food crops:

Corn (19.5% of production)
Rice (16.5%)
Wheat (15%),
Potato (5.3%),
Cassava and soybeans (4.7%)

Together they account for **> 75 % of total plant-derived energy intake** globally (FAO, 2023).

[FAO 2023, www.fao.org/cfs/cfs-hlpe/insights]

Rice is the staple food for more than half of the worlds population.

Its importance is increasing as production becomes more efficient in Asia.

The annual production amounts to 800 million tonnes.

Produced in an area that totals about 160 million hectars.

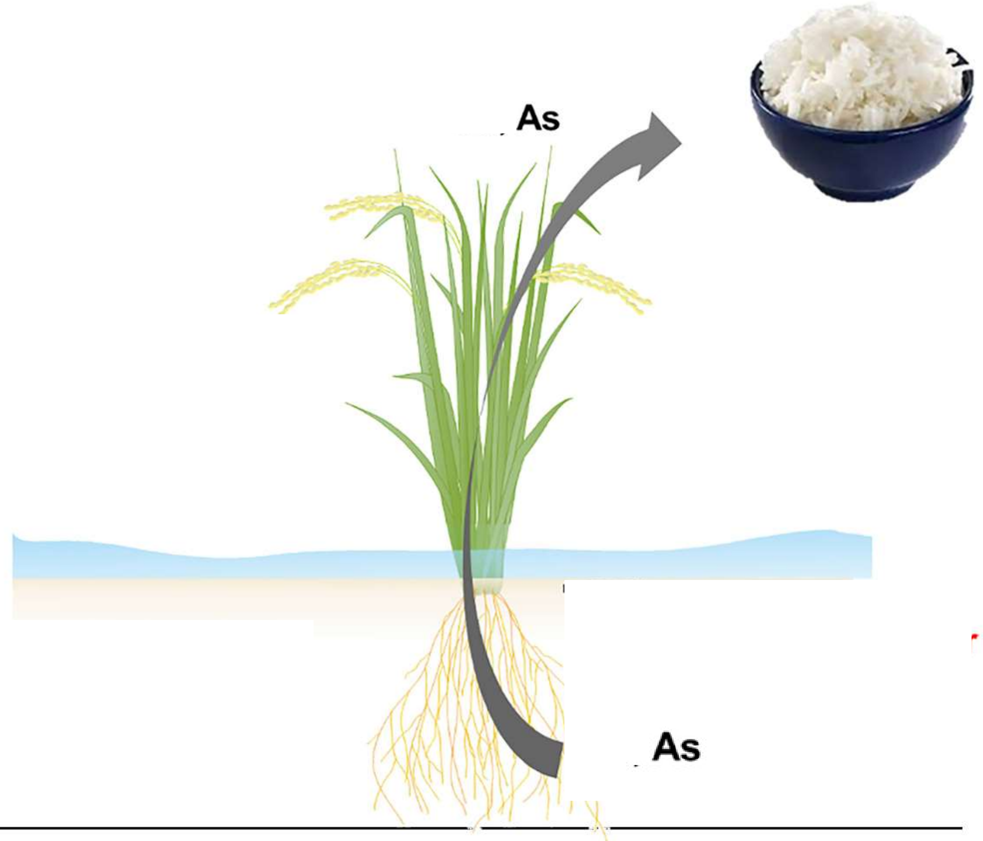
Arsenic is naturally present in soils and groundwater.

Antropogenic sources in paddy soils include industrial emissions and pest-control agrochemicals.

www.dreamstime.com

[FAO 2023, www.fao.org/cfs/cfs-hlpe/insights]

Rice is well-know for accumulating As in the grain up to toxic levels because the metal can surpass all natural barriers (solubility, translocation, and phytotoxicity) (Zhao and Wang 2020).



[Zhao and Wang 2020, doi.org/10.1007/s11104-019-04374-6]

In general, **paddy cultivation** for rice production **involves intermittent flooding** of paddy fields all along the growth of rice plants.

During the **non-flooding period**:

As(V) predominates, strongly sorbed or co-precipitated with amorphous /crystalline Fe(III) hydroxides present in the oxic soil (Dousova et al 2021; Voegelin et al 2007),

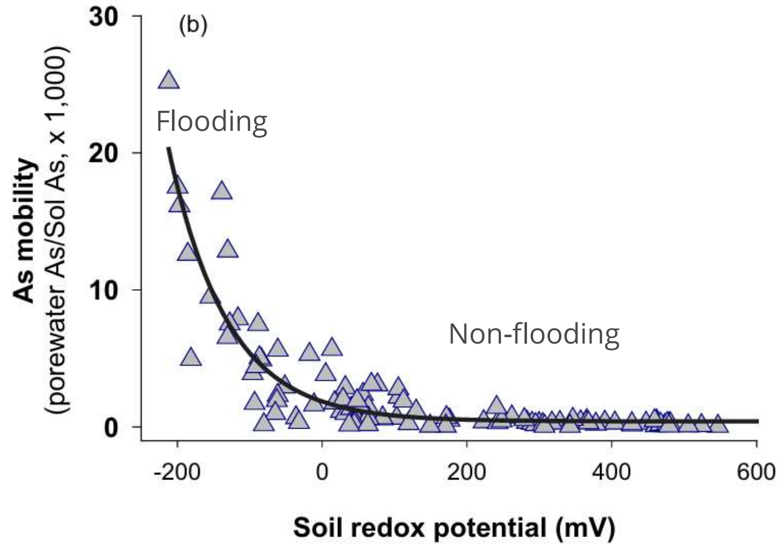
Arsenic bioavailability is low.

During the **flooding period**:

Paddy soil becomes anoxic, with low redox potential.

Significant **increase of dissolved As as** redox conditions leads to loss of sorption site and release of sorbed As into pore water (Xu et al., 2017; Zhang et al., 2018).

Arsenic bioavailability is high.

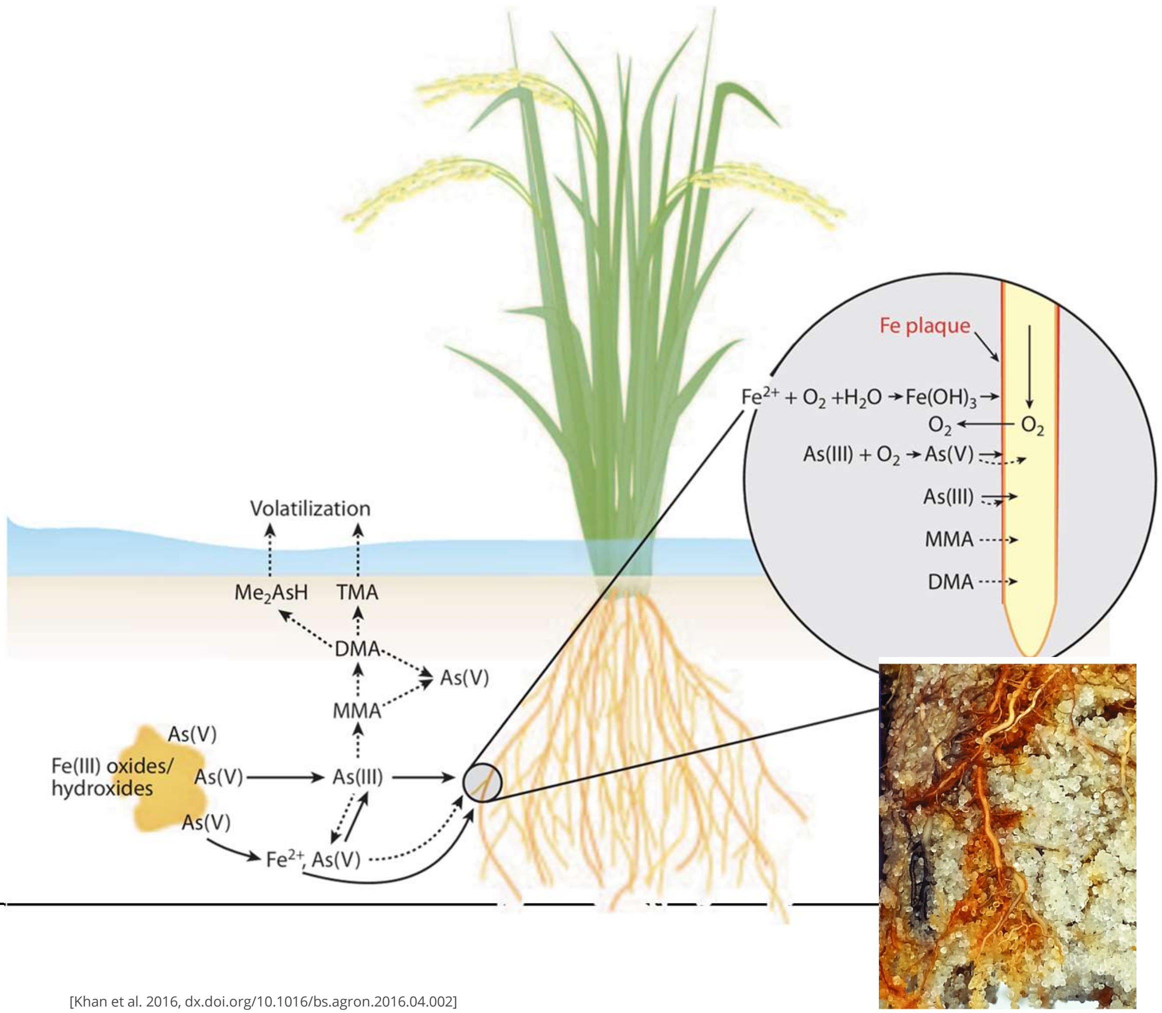


[Dousova et al. 2021, https://doi.org/10.1016/j.jhazmat.2021.125715; Voegelin et al. 2007, doi.org/10.1016/j.gca.2007.05.030; Xu et al. 20217, https://doi.org/10.1016/j.envpol.2017.07.084; Zhang et al. 2018, https://doi.org/10.1016/j.envpol.2018.01.092; Zhao and Wang, oi.org/10.1007/s11104-019-04374-6]

Hydrophyte plants have devised a way of detoxifying the environment around roots, by locally altering the geochemical conditions.

Radial oxygen loss (ROL) is the mechanism employed by hydrophytes to survive under anoxic conditions.

ROL changes the bio-physico-chemical properties of the rhizosphere that eventually make the hydrophyte tolerant to flooding and enable it to deal with soil toxicity.



[Khan et al. 2016, dx.doi.org/10.1016/bs.agron.2016.04.002]

Rice plants act as **As accumulators:**
bioconcentration factors (BCF) > 1

Bioconcentration factors (BCF) for the studied metals. Average ± standard deviation (sample size)

BCF	As *	Cd *	Cr *	Cu *	Ni *	Pb *	Zn *
Stem	1.6 ± 1.3 (8)	0.27 ± 0.57 (9)	5.3 ± 4.4 (8)	0.61 ± 0.94 (9)	0.56 ± 0.61 (9)	0.03 ± 0.02 (9)	18.7 ± 16.8 (9)
Leaf	1.7 ± 1.1 (8)	0.13 ± 0.07 (8)	8.0 ± 6.6 (8)	0.58 ± 0.18 (8)	0.49 ± 0.12 (8)	0.05 ± 0.02 (8)	9.2 ± 5.7 (8)
Grain	0.76 ± 0.44 (11)	0.18 ± 0.10 (11)	2.21 ± 2.35 (13)	0.55 ± 0.34 (13)	0.54 ± 0.45 (13)	0.08 ± 0.08 (13)	10.5 ± 8.3 (13)
Plant	1.31 ± 1.00 (min = 0.12; max = 4.64)	0.20 ± 0.30 (min = 0.05; max = 1.64)	4.52 ± 4.93 (min = 0.46; max = 22.0)	0.59 ± 0.55 (min = 0.17; max = 3.10)	0.54 ± 0.44 (min = 0.12; max = 2.14)	0.06 ± 0.06 (min = 0.01; max = 0.27)	12.78 ± 11.59 (min = 2.44; max = 55.8)

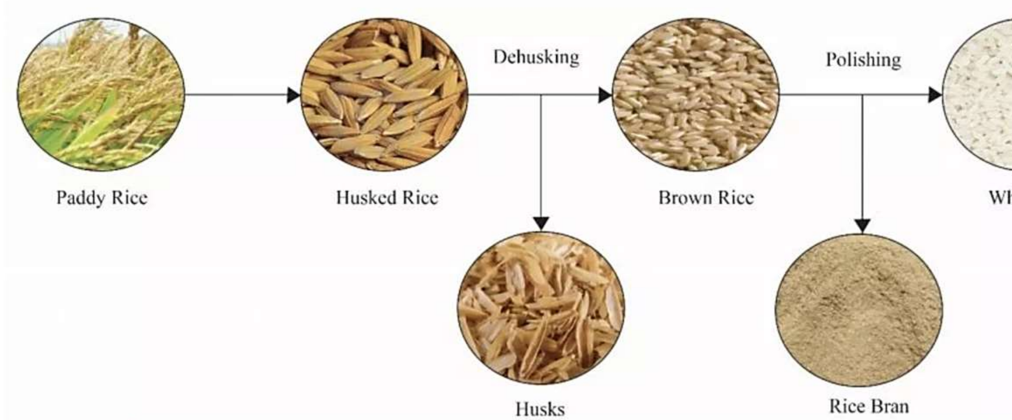
[Atiaga et al 2021, doi.org/10.3390/agronomy11081594]

Rice milling process and rice grain physiology

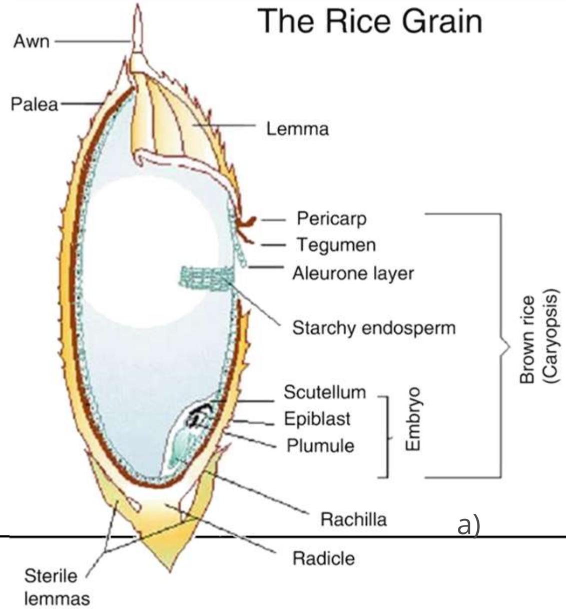
The edible part of the plant is the grain and when dehusked and polished it is known as **white rice.**

Dehusking removes the palea and lemmas.

Polishing removes the pericarp, tegumen and aleurone layer, together with the embryo.



b)



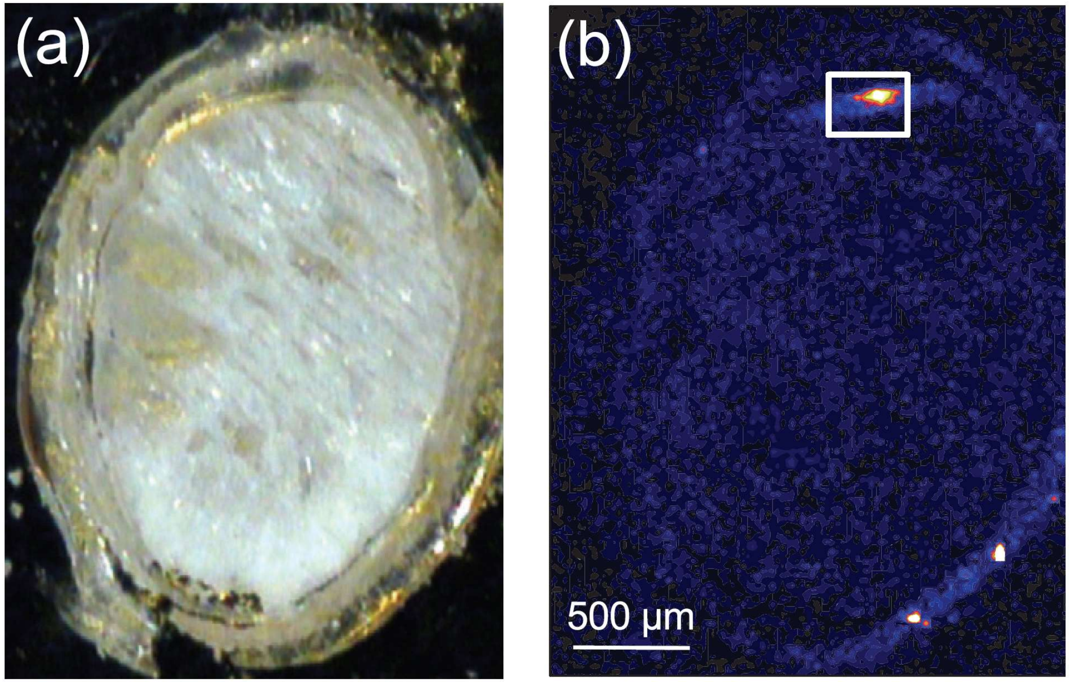
a)

[a) Mohapatra and Sahu, 2022, doi: 10.1007/978-3-030-67897-5_4; b) www.chinaricemill.com]

Arsenic concentrates mostly in the husk and pericarp, tegumen and aleurone layer.

Polishing removes a substantial part of the arsenic, which then accumulates in the bran.

Distribution of As in the rice grain using X-ray fluorescence.



[Lombi et al 2009, doi: 10.1111/j.1469-8137.2009.02912.x]

The brown rice, though more nutritive than the polished, contains higher concentrations of total arsenic.

Concentration of total As and forms of As (mg/kg) in commercial rice samples from different countries (mean ± SD)

Country	Type	As(III)	As(V)	$\sum$ inorg As	AsB	DMA	MMA	$\sum$oAs	TAs	iAs/tAs
Ecuador										
	Polished (n = 10)	0.037 ± 0.018	0.016 ± 0.012	0.053 ± 0.027	0.003 ± 0.001	0.031 ± 0.008	0.004 ± 0.008	0.038 ± 0.011	0.130 ± 0.034	0.70
	Brown (n = 3)	0.057 ± 0.003	0.049 ± 0.056	0.105 ± 0.052	0.010 ± 0.001	0.046 ± 0.009	< LD	0.056 ± 0.010	0.221 ± 0.014	0.72
	Parboiled (n = 3)	0.054 ± 0.030	0.036 ± 0.002	0.090 ± 0.031	0.004 ± 0.004	0.042 ± 0.020	0.009 ± 0.013	0.055 ± 0.018	0.156 ± 0.021	0.58
	Field samples (n = 8)	0.073 ± 0.017	0.033 ± 0.011	0.106 ± 0.014	0.002 ± 0.001	0.013 ± 0.007	0.007 ± 0.008	0.128 ± 0.012	0.138 ± 0.017	0.79
Brazil										
	Polished (n = 4)	0.067 ± 0.012	0.029 ± 0.008	0.096 ± 0.007	< LD-0.001	0.071 ± 0.021	0.002 ± 0.004	0.074 ± 0.020	0.166 ± 0.016	0.59
	Brown (n = 2)	0.113 ± 0.040	0.037 ± 0.001	0.150 ± 0.039	< LD	0.055 ± 0.053	0.012 ± 0.001	0.067 ± 0.054	0.220 ± 0.020	0.68
	Parboiled (n = 1)	0.075	0.034	0.110	0.002	0.061	0.029	0.092	0.160	0.69
Peru										
	Polished (n = 3)	0.069 ± 0.021	0.062 ± 0.005	0.131 ± 0.026	< LD-0.001	0.021 ± 0.005	0.005 ± 0.002	0.026 ± 0.006	0.138 ± 0.039	0.94
Iberian Peninsula										
	Polished (n = 9)	0.055 ± 0.027	0.025 ± 0.019	0.080 ± 0.042	0.001 ± 0.001	0.080 ± 0.046	0.012 ± 0.013	0.093 ± 0.054	0.191 ± 0.066	0.41
	Brown (n = 2)	0.091 ± 0.057	0.028 ± 0.014	0.118 ± 0.071	0.002 ± 0.003	0.081 ± 0.060	0.004 ± 0.002	0.087 ± 0.066	0.310 ± 0.128	0.35
	Parboiled (n = 1)	0.090	0.067	0.157	< LD	0.140	0.40	0.180	0.307	0.51

[EFSA 2009, doi:doi.org/10.2903/j.efsa.2009.1351]

[Otero et al 2020, doi:10.1007/s10653-020-00581-8]

Low to moderate exposure to iAs is associated to:

- cancers of the skin, bladder and lung;

- skin lesions other than skin cancer, spontaneous abortion, stillbirth, infant mortality, congenital heart disease, respiratory disease, chronic kidney disease, neurodevelopmental effects, ischemic heart disease, and carotid artery atherosclerosis.

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

Risk characterization

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.

We will study risk due to ingestion.

Risk characterization

Please download file:

“Session 2 ARSENIC MODEL.xlsx”

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)
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)

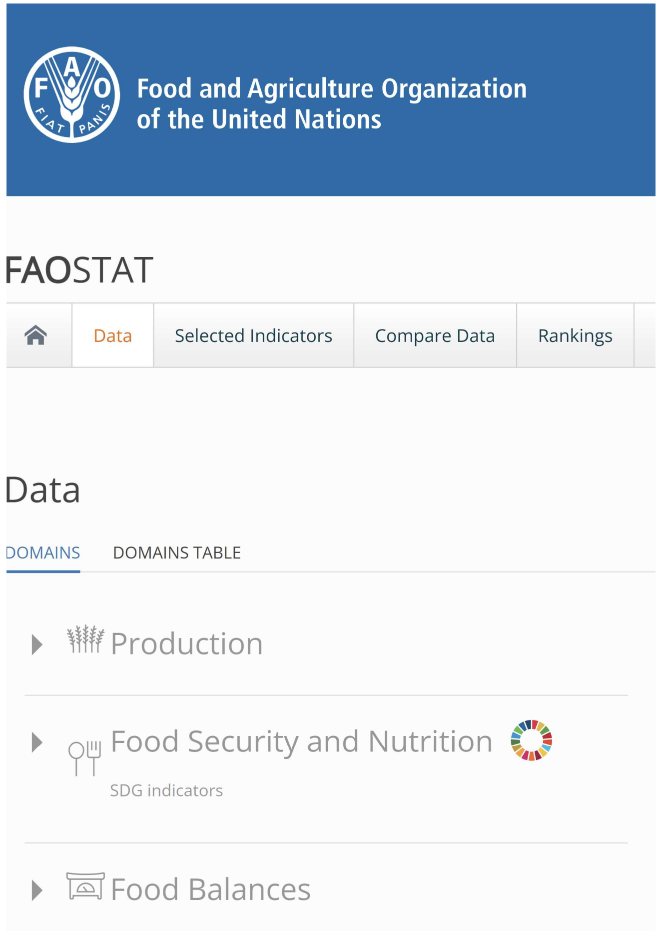
[EFSA 2024, doil: 10.2903/j.efsa.2024.8488]

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

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

Western Pacific Region,

inorganic rice,

rice (polished)

Raw rice

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

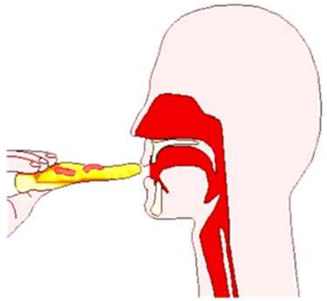
MHLW

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

Deterministic estimation of intake, ADI (mg/kg.d)



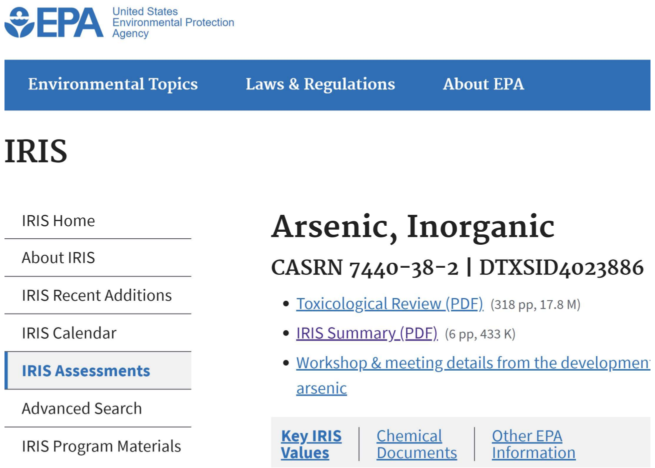
$$\mathbf{ADI} = \frac{\boldsymbol{CF} \text{ x } \boldsymbol{IR} \text{ x } \boldsymbol{FI} \text{ x } \boldsymbol{FE} \text{ x } \boldsymbol{ED}}{\boldsymbol{BW} \text{ x } \boldsymbol{AT}}$$

$$\mathbf{ADI} = \frac{0.088 \text{ x } 0.188 \text{ x } 1 \text{ x } 365 \text{ x } 77.72}{66.3 \text{ x } 25550} = \mathbf{2.8 \text{ x } 10^{-4}} \text{ mg iAs/kg.d}$$

Effects assessment

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

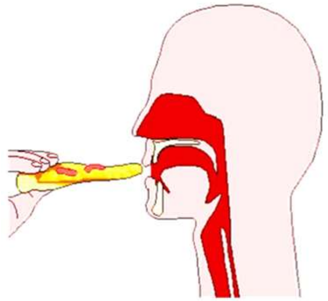
These are available in, e.g., the U.S. EPA IRIS repository, or the European Chemical Agency



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.

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

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

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.**

Let us repeat the assessment using a probabilistic estimation of intake, ADI (mg/kg.d)

The mathematical notation for the expression is:

$$\textbf{ADI} = \frac{\text{LN}(0.094, 0.034) \times N(0.189, 0.014) \times 1 \times 365 \times 77.72}{N(66.3, 4.91) \times 25550}$$

Which can be simplified as:

$$\textbf{ADI} = \frac{28359.8 \cdot X_1 \cdot X_2}{25550 \cdot X_3} = 1.11056 \cdot \frac{X_1 \cdot X_2}{X_3}$$

Where:

- $X_1 \sim \text{LN}(0.094, 0.034)$ $\quad f_{X_1}(x) = \frac{1}{x \cdot 0.034\sqrt{2\pi}} \exp\left(-\frac{(\ln x - 0.094}{2(0.034)^2}\right), \quad x > 0$
- $X_2 \sim N(0.189, 0.014)$ $\quad f_{X_2}(x) = \frac{1}{0.014\sqrt{2\pi}} \exp\left(-\frac{(x-0.189)^2}{2(0.014)^2}\right)$
- $X_3 \sim N(66.3, 4.91)$ $\quad f_{X_3}(x) = \frac{1}{4.91\sqrt{2\pi}} \exp\left(-\frac{(x-66.3)^2}{2(4.91)^2}\right)$

Estimation of intake, ADI (mg/kg.d)

The analytical derivation requires solving: **ADI** $=$

$$\int_{-\infty}^{\infty}\int_{-\infty}^{\infty}\int_{0}^{\infty} f_{X_1}(x_1) f_{X_2}(x_2) f_{X_3}(x_3)|x_3|\,\delta\left(adi - \frac{28359.8\cdot x_1 x_2}{25550\cdot x_3}\right) dx_1 dx_2 dx_3$$

This is analytically intractable.

Monte Carlo Simulations

Probabilitic assessment

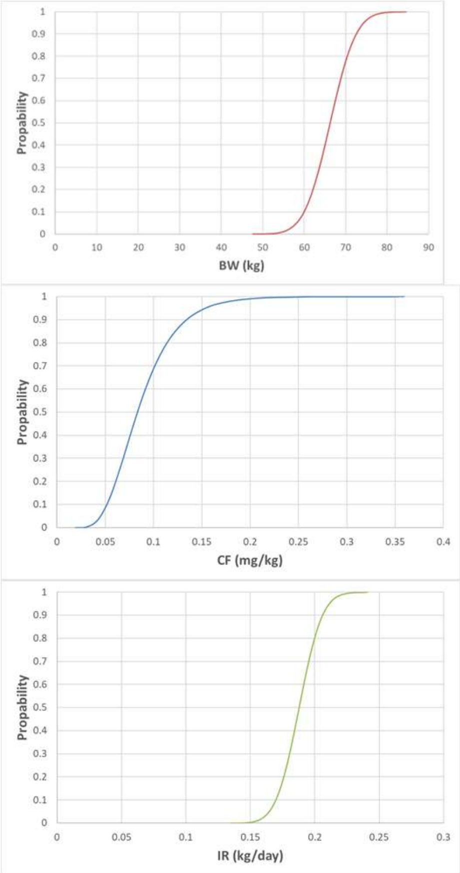
Use MCS to estimate the ILTR using Argo.

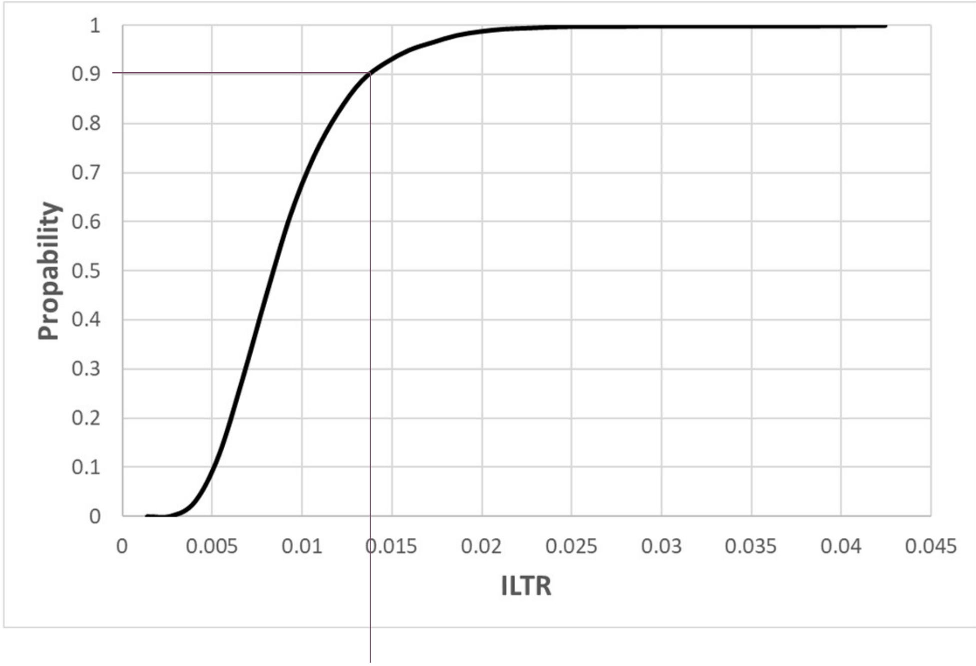
Estimate the increased lifetime risk (ILTR) with Monte Carlo Simulations

Data:

Abbreviation	Description	Unit	Mean	St. Deviation	Statistical distribution	Comment
CF	Concentration of iAs in rice	mg/kg	0.004	0.034	Lognormal	Assumed due to positive bias
CF (geometric mean)			0.088			
IR (men)	Ingestion rate for men	kg/d	0.188	0.014	Normal	Assumed
IR (women)	Ingestion rate for women	kg/d	0.130	0.010	Normal	Assumed
FI	Fraction ingested	-	1		constant	
EF	Exposure frequency	days/year	365		constant	Daily
ED (men)	Exposure duration for men	years	77.72		constant	Lifetime
ED (women)	Exposure duration for women	years	84.6		constant	Lifetime
BW (men)	Body weight for men	kg	66.3	4.91	Normal	Assumed
BW (women)	Body weight for women	kg	52.2	2.46	Normal	Assumed
AT	Averaging time for carcinogens	days	25550		constant	Assumed equal to 70 years
CSF	Cancer slope factor	1/(mg/kg.d)	32			From USEPA IRIS (https://iris.epa.gov/ChemicalLanding/&substance_nmbr=278)

Results of the probabilistic assessment:





P90 = 0.14
P95 = 0.16

Results of the probabilistic assessment:

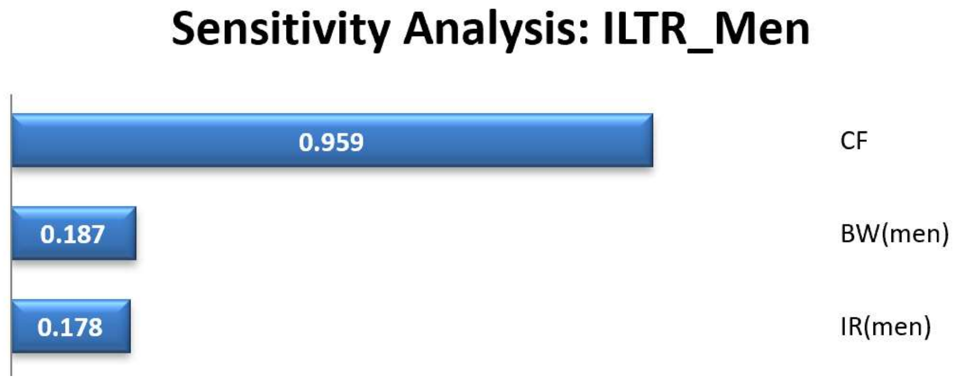
ILTR_Men			
Statistics	Values	Percentiles	Values
Mean	**1.0×10^{-2}**	10%	5.6×10^{-3}
Median	9.0×10^{-3}	20%	6.5×10^{-3}
Variance	1.3×10^{-5}	30%	7.3×10^{-3}
Standard Deviation	3.6×10^{-3}	40%	8.1×10^{-3}
Coefficient of Variation	3.8×10^{-1}	50%	8.9×10^{-3}
Min	2.0×10^{-3}	60%	9.7×10^{-3}
Max	3.3×10^{-2}	70%	1.1×10^{-2}
Range	**4.0×10^{-2}**	80%	1.2×10^{-2}
Standard Error	2.6×10^{-5}	**90%**	**1.4×10^{-2}**
		100%	3.3×10^{-2}

The estimated mean is equal to the deterministic value (ca. 1%), as expected.

The high percentiles, P90 (1.4%) and P95 (1.6%) are considered as more protective of high-end consumers, while avoiding outliers.

Results of the probabilistic assessment:

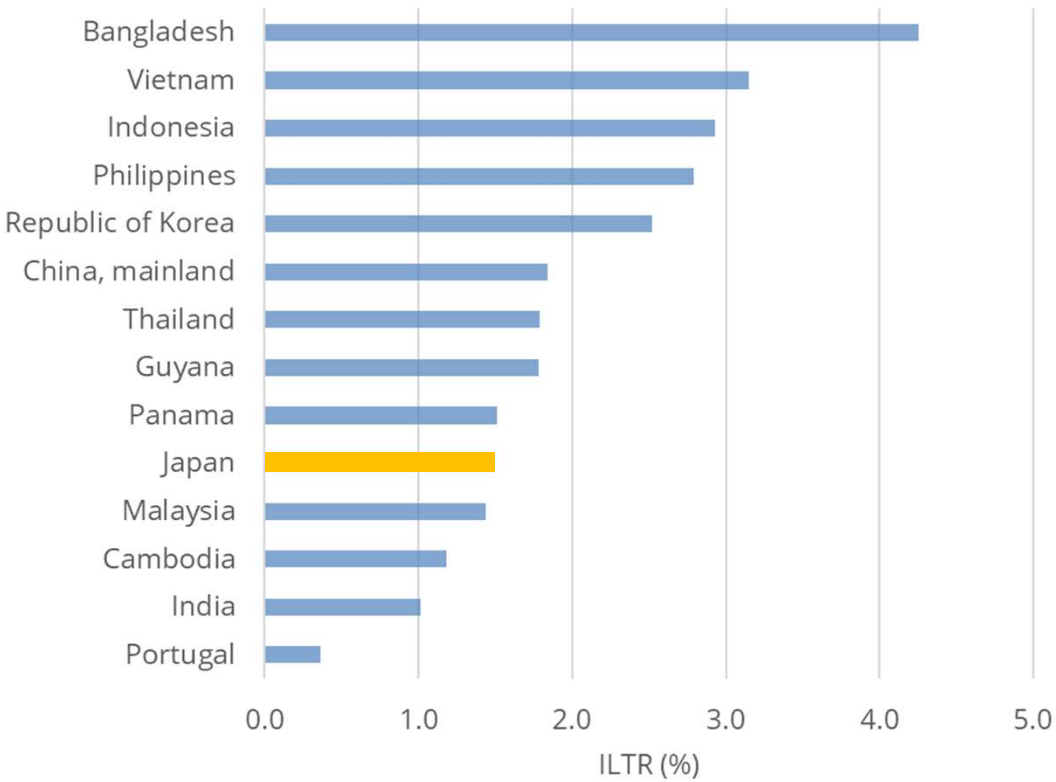
Index	Rho	Magnitude	Distribution
5	-0.003828414	0.004	IR(women)
4	-0.004865602	0.005	BW(women)
3	0.178218807	0.178	IR(men)
2	-0.187126705	0.187	BW(men)
1	0.959352312	0.959	CF



The **concentration of inorganic arsenic in rice (CF) is the most sensitive variable**, followed by the body weight (BW) and intake rate for rice (IR), having the first a weight about 5 times higher:

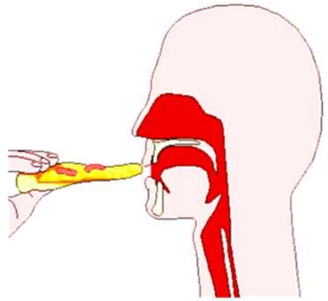
A small alteration in CF will have a marginal gain 5 times higher than for the two other variables.

P95 of ILTR for some high-exposure countries



Country	ILTR (%)
Bangladesh	4.3
Vietnam	3.1
Indonesia	2.9
Philippines	2.8
Republic of Korea	2.5
China, mainland	1.8
Thailand	1.8
Guyana	1.8
Panama	1.5
Japan	1.6
Malaysia	1.4
Cambodia	1.2
India	1.0
Portugal	0.4

Increased lifetime risk, ILTR



$$\textbf{Increased lifetime health risk} \cong 1.6\%$$

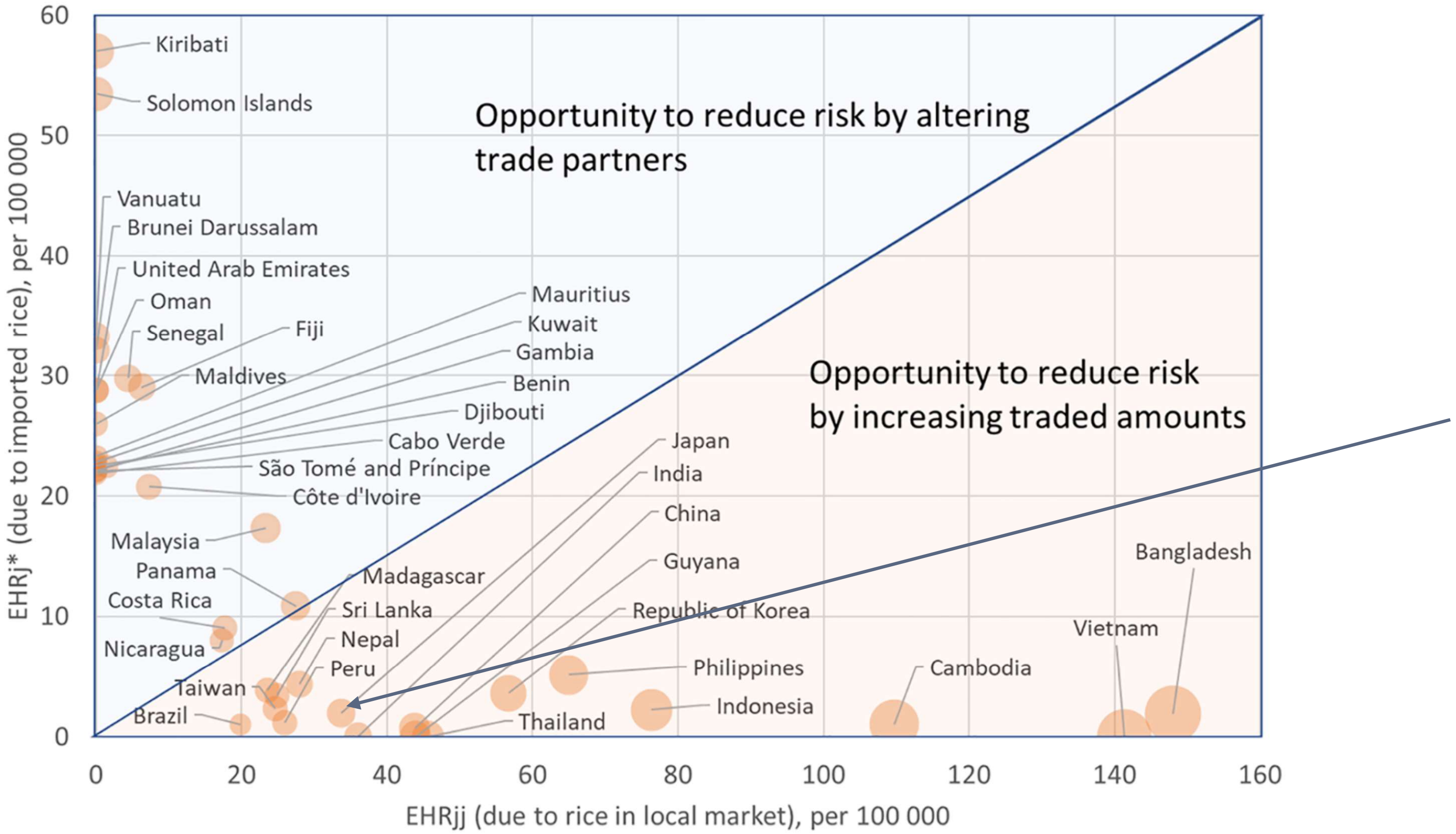
Meaning that Japanese men are exposed to an increased **1.6% risk** of developing cancer throughout their lifetime, only due to the ingestion of inorganic arsenic in white rice.

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%**

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

Practical work 2 – Health risk for Italian women due to exposure to cadmium in lipstick

We will use the exposure factors handbooks specific for consumer products

SCCS/1628/21

European Commission

Scientific Committee on Consumer Safety

SCCS

THE SCCS NOTES OF GUIDANCE FOR THE TESTING OF COSMETIC INGREDIENTS AND THEIR SAFETY EVALUATION

11TH REVISION

Scientific Committees
on Consumer Safety
on Health, Environmental and Emerging Risks

The SCCS adopted this guidance document
at its plenary meeting on 30-31 March 2021

RIVM report 320104001/2006

Cosmetics Fact Sheet
To assess the risks for the consumer
Updated version for ConsExpo 4

H.J. Bremmer, L.C.H. Prud'homme de Lodder,
J.G.M. van Engelen

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SCCNFP/0321/00 Final

THE SCIENTIFIC COMMITTEE ON COSMETIC PRODUCTS AND NON-FOOD PRODUCTS INTENDED FOR CONSUMERS

NOTES OF GUIDANCE FOR TESTING OF COSMETIC INGREDIENTS FOR THEIR SAFETY EVALUATION

Adopted by the SCCNFP during the plenary meeting of 24 October 2000

The estimate of exposure (ADI) is determined by:

$$\mathbf{ADI_{oral}} = \frac{\boldsymbol{F_{oral}} \cdot Q_{prod} \cdot Fc_{prod} \cdot \boldsymbol{n}}{\boldsymbol{BW}}$$

$\mathbf{F_{oral}}$ is the fraction of lipstick that is ingested. Assumed = 1.

The amount of lipstick applied per application, $\mathbf{Q_{prod;}}$

The number of applications, **n;**

The fraction of Cd in the lipstick, $\mathbf{Fc_{prod}}$ (from world data – in the provided Excel file);

Body weight, BW, for Italian women (Hall et al., 2011), **BW**

Consider the following information and the data file.

Use
The amount of lipstick used per application is 0.01 g[2, 37]. It is assumed that the entire product is taken in orally.

Default lipstick/ lip salve

	Default value	Q	References, comments
General			
Frequency	1460 x/year	3	2-6 x/day [2]; default: 4 x/day
Body weight female	61 kg	4	[8]
Oral			
Exposure, direct intake			
Amount ingested	0.01 g	3	See above
Uptake, fraction model			
uptake fraction	1	2	potential dose

EU, (1996). Technical guidance documents in support of the commission directive 93/67/EEC on risk assesments for new notified substances and the commission regulation (EC) 1488/94 on risk assessment for existing substances. European Commission, Brussels.

H.J. Bremmer, L.C.H. Prud'homme de Lodder, J.G.M. van Engelen (2006). Cosmetics Fact Sheet. To assess the risks for the consumer. Updated version for ConsExpo 4. RIVM report 320104001 /2006. RIVM, The Netherlands.

Frequency: Triangular distribution {2; 4; 6}

Body weight: lognormal:
use statistics from Hall et al 2007

Amount ingested, Normal, sd= 0.01

Body weight data:

Table 2
Bodyweight distributions for each country and those of the panellists in the ALBA study (mean (kg), ±standard deviations).

Country	Male	Female
ALBA/Scotland	lognormal (82.30, 15.96)	lognormal (71.52, 17.11)
France	lognormal (77.73, 13.48)	lognormal (66.78, 12.71)
Germany	lognormal (84.51, 13.48)	lognormal (71.63, 12,71)
Spain / Italy	lognormal (73.23, 13.48)	lognormal (62.56, 12.71)
GB	lognormal (80.00, 13.48)	lognormal (67.30, 12.71)
Denmark	lognormal (83.61, 13.48)	lognormal (68.46, 12.71)

Hall et al. (2011): doi:10.1016/j.fct.2010.11.016

Compute the 90th or 95th percentile of the exposure dose (ADI) and compare with the **Reference Dose (RfD)** (USEPA): **$5x10^{-4}$ mg/kg.d**) or $5x10^{-1}$ µg/kg.d

And with

EU (EFSA) **tolerable daily intake (TDI)** (though not specifically for cosmetics, it provides a measure of a safe dose): **$3.6x10^{-4}$ mg/kg.d** or $3.6x10^{-1}$ µg/kg.d

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EFSA sets lower tolerable intake level for cadmium in food

Published: 20 March 2009 | 4 minutes read

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Cadmium

CASRN 7440-43-9 | DTXSID1023940

- IRIS Summary (PDF) (13 pp, 118 K)

Key IRIS Values | Chemical Documents | Other EPA Information

Noncancer Assessment

Reference Dose for Oral Exposure (RfD) (PDF) (13 pp, 118 K)

Last Updated: 10/01/1989

System	RfD (mg/kg-day)	Basis	PoD	Composite UF
Urinary	5×10^{-4} (water)	Significant proteinuria	NOAEL : 5×10^{-3} mg/kg-day	10
Urinary	1×10^{-3} (food)	Significant proteinuria	NOAEL : 1×10^{-2} mg/kg-day	10

https://www.efsa.europa.eu/en/news/efsa-sets-lower-tolerable-intake-level-cadmium-food

https://iris.epa.gov/ChemicalLanding/&substance_nmbr=141

Using this information, compute the **margin of safety (MoS)** and the **Hazard Quotient (HQ)** using the 95th percentile of exposure (ADI).

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

Hazard Quotien (HQ) = ADI / Reference Dose

(Results in the Excel file: MODEL Cd in lipstick.xlsx)

Please answer through the form:

https://forms.office.com/Pages/ResponsePage
.aspx?id=MQkPE_aguUSuhbnxbImtgnkngR0s
CxpJhcC88DOeBh1UOE0zVlZEWUtQMEoz
Tks1N0JSV0gyTjRPOC4u

With this example we finish the workshop.

Please feel free to put some questions.

Thank you very much for attending and your active collaboration.

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