MULTICRITERIA METHODS FOR ASSESSING PHARMACEUTICAL HAZARD FOR THE ENVIRONMENT

S.COUTU, S.KHODADADI, L.ROSSI, N.CHEVRE
contact: sylvain.coutu@epfl.ch

Introduction:

The **hazard of pharmaceuticals** for the aquatic environment can be described by **different ecotoxicological parameters**. **Clustering analysis** of large database can help for gathering them into **groups of similard hazard**. But when it comes to select a **short list of pharmaceuticals** for an advanced experimental study, one has to select few of them among thousands that can potentially harm the environment. In this perspective, Multicriteria Analysis can be a very efficient tool.

PNEC
[37 $1.3.10^6$]

HUMAN-PNEC
[$4.0.10^4$ $5.1.10^7$]
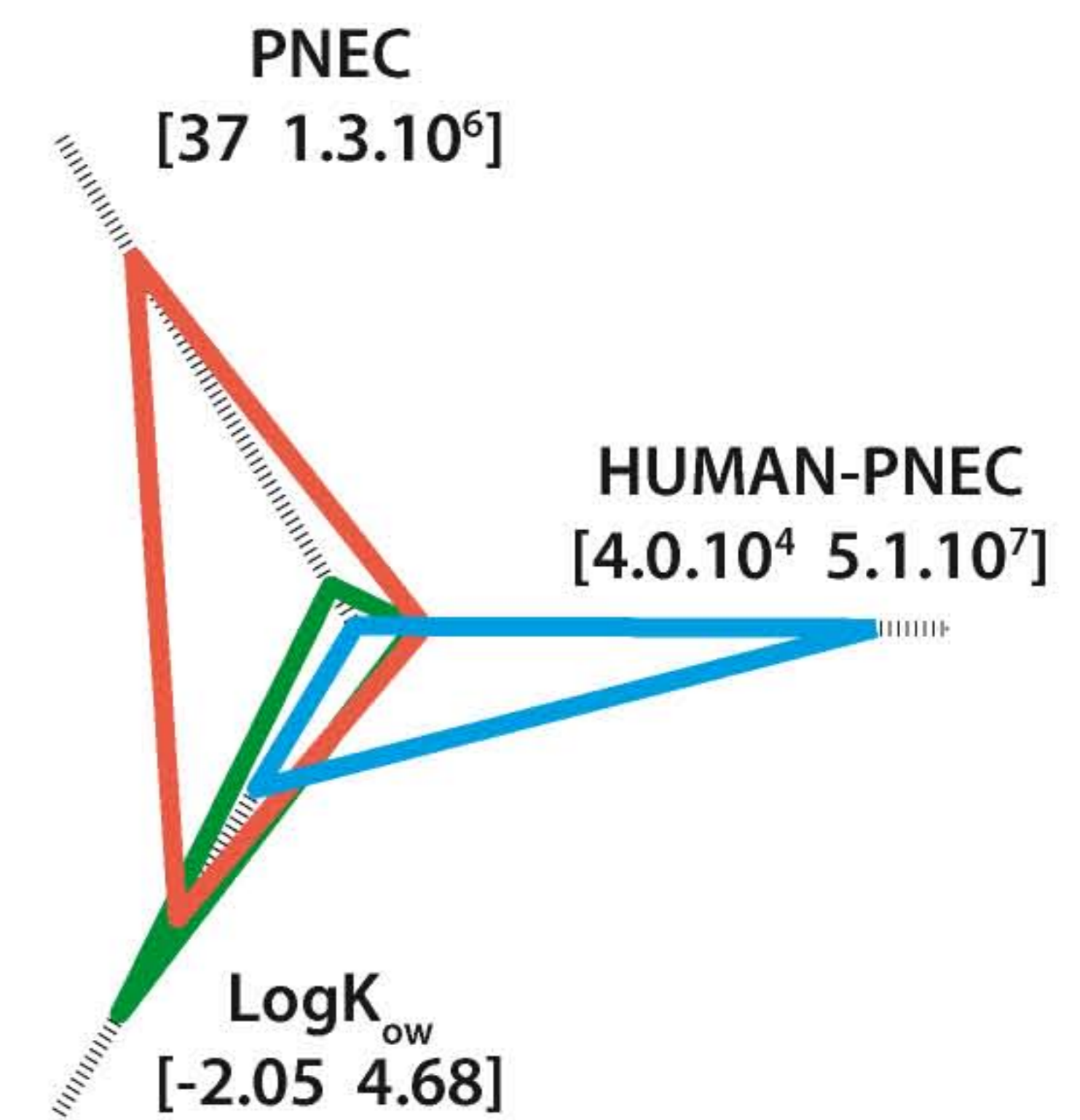
$LogK_{ow}$
[-2.05 4.68]

Fig 1: based on their values of PNEC, H-PNEC and $LogK_{ow}$, 36 pharmaceuticals are separated into 3 groups of similar toxicological characteristics.

2 methods: SMAA and ELECTRE III

Relative hazard is compared for **36 pharmaceuticals** based on **5 parameters**: HUMAN-PNEC, ENV-PNEC, LogKow, Kümmerer toxicity, Solubility.
Pharmaceuticals where chosen among the 88 **most consumed substances** in the area of study for which we have **all data necessary** to compute the methods.

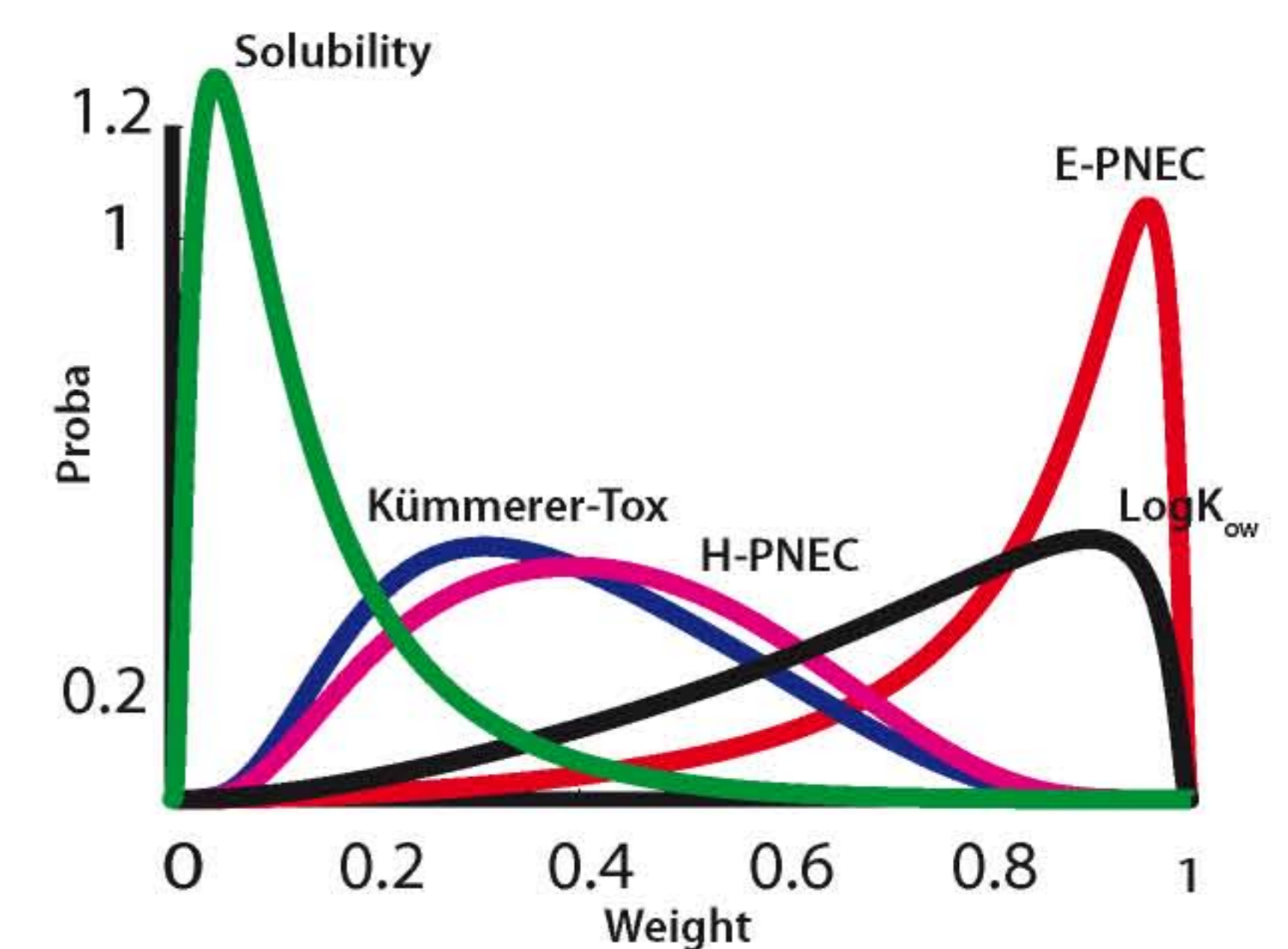Introduction of **subjectivity** via the use of weight distributions extrapolated from expert commitee consultation

Fig 2: weight distribution for each parameter considered.

Results:

SMAA
(Stochastic Multicriteria Acceptability Analysis)
20% uncertainty is assigned to each parameter
Uncertainty on weights is described by distribution (*Fig 2*)
Hazard is evaluated by computing the eulerian weighted distance for each pharmaceuticals which is described by a weighted set of parameters
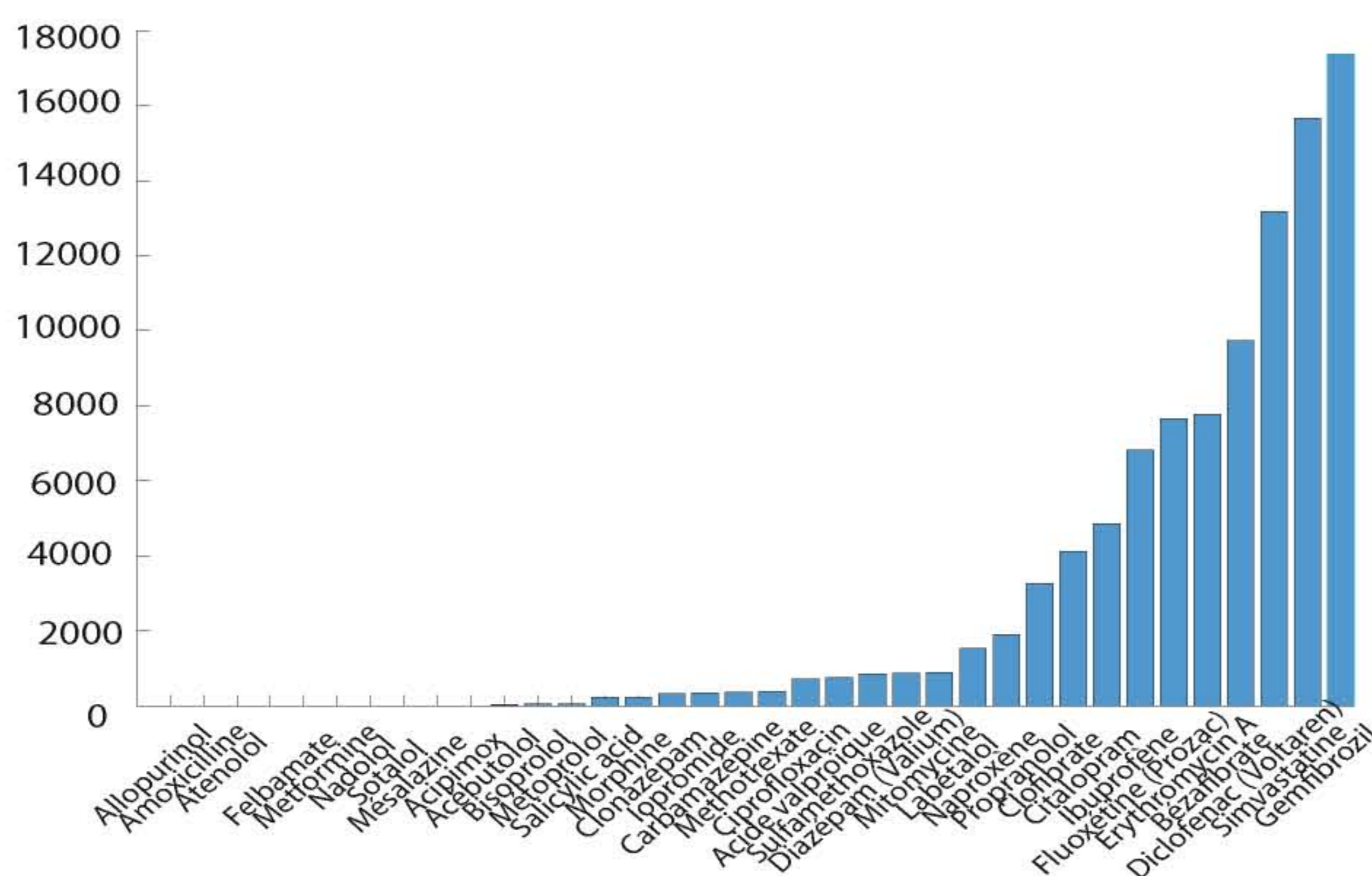We count the number of times each pharmaceuticals is ranked first in each simulation using a Monte-Carlo method.

Fig 3: pharmaceuticals ranked on their occurence in having the highest weighted norm after 100 000 simulations.

ELECTRE III
The ELECTRE III allows imprecise, indeterminate and uncertain criteria inherent to complex human decision processes by relying on the use of pseudo-criteria and indifference and preference thresholds.
The method relies upon the construction and the exploitation of the outranking relations.

Rank	Pharmaceutical
1	Ethinylestradiol
2	Diclofenac (Voltaren)
3	Amoxicilline, Ciprofloxacin, Propranolol
6	Mitomycine, Citalopram, Ibuprofène
9	Erythromycin A, Fluoxétine (Prozac)
11	Morphine, Labétalol
13	Methotrexate, Sulfamethoxazole, Bisoprolol, Clofibrate, Métoprolol
18	Atenolol, Diazépam (Valium), Bézafibrate, Salicylic acid
22	Allopurinol, Sotalol, Carbamazépine, Simvastatine
26	Metformine, Clonazépam,
28	Iopromide, Gemfibrozil, Acébutolol, Acide valproïque
32	Naproxène, Mésalazine, Acipimox
35	Felbamate
36	Nadolol

Table 1: pharmaceuticals ranked using the ELECTRE III method. In red are the pharmaceuticals that are ranked in the top ten in both methods. Ethinylestradiol present as comparison substance.

Discussion:

6 pharmaceuticals present in **top ten** of both rankings, with some of them **poorly studied** in litterature.
Some pharmaceuticals **extensively studied** in litterature appear **not to be ranked prior substances with these methods**. It is partly due to the fact that this approach does **not consider directly medical consumption** or excretion rate. As a first step it is interesting to evaluate pharmaceutical hazard without considering their consumption and in a second step, pharmaceutical consumption will be included to evaluate the **risk** of each substance in a specific area of interest.