



BfR-EFSA

Uncertainty in Risk Analysis

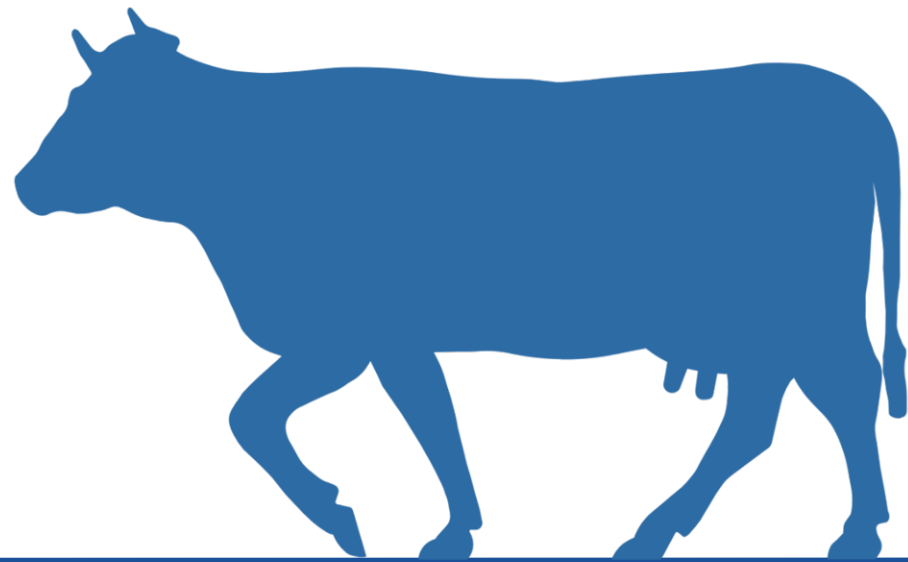
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Managing uncertainty and variability when assessing beneficial source of iron brought by red meat consumption in France

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Introduction



Iron and red meat

Red meat contains heme iron:

- High level in red meat
- High absorption: around 25% (10-40%)



Effects of heme iron on health:

- Increases colorectal cancer risk (*Cross et al 2010; Corpet et al, 2011; Bastide et al, 2011; Bastide et al, 2016....*) and cardiovascular disease mortality risk (*Sullivan, 1981; Ascherio et al, 1994; Qi et al, 2007; Wolk, 2017....*)



But

- Heme iron may reduce Iron Deficiency Anemia (IDA)
- Dietary iron deficiency is the **first** nutritional deficiency in the world → major risk factor of anemia (*Kassebaum et al 2016*)



Benefit quantification of red meat

Objective : Develop quantitative method to assess benefits when consuming red meat

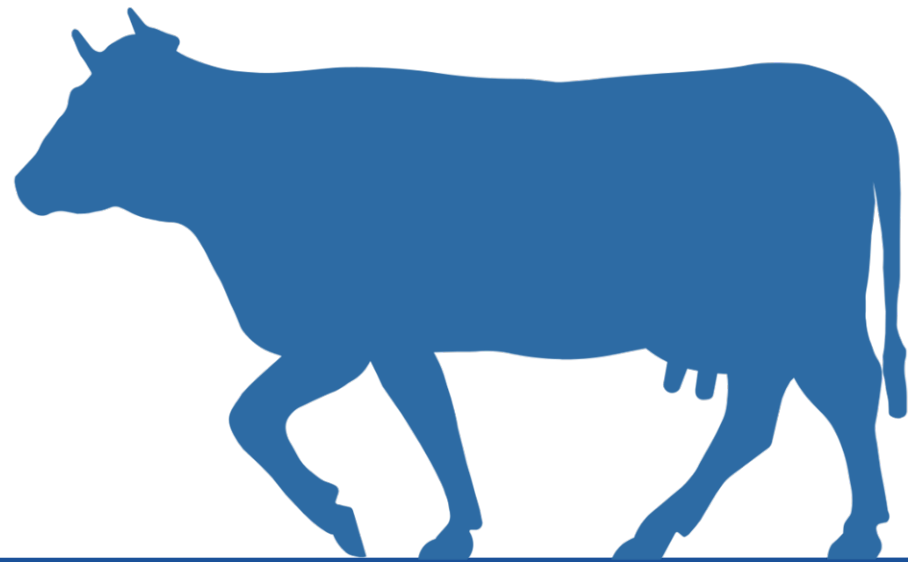
Scientific approaches

- Build probabilistic models able to assess **Benefit** ➔ **Expert elicitation**
- Identify, separate and take into account **Variability and Uncertainty**
- Express the output in **Disability Adjusted Life Years (DALYs)** to take into account the burden of diseases of the health effect

- Possibility to compare different **Intake Scenarios** and to be able to establish recommendations



Methods



Benefit quantification of red meat

How to evaluate the benefits of red meat on health?

1 Construct a model to quantify DALY due to iron intake

Consider 3 hypotheses:

Hypothesis 1: **Iron needs not covered by dietary iron = Iron deficiency**

Hypothesis 2: **Ratio between people deficient in iron and iron deficient anemia = constant**

Hypothesis 3: **The consumption of red meat decreases iron deficiency anemia (IDA)**

2 Apply consumption scenarios by adding ground beef to reduce DALYs

Framework: Quantifying the benefit of red meat consumption

1

H1

H2

Iron consumed by the French population

Absorbed iron by the French population

Proportion of iron deficiencies in France

Proportion of mild, moderate and severe IDA

Estimated number of mild, moderate and severe IDA

Estimated DALY due to IDA

Individual iron intake in mg/d
INCA 2 - Anses (2007)

Mean iron absorption per gender and age class
EFSA (2015)

Iron per gender and age class
EFSA (2015)

Levels of Hb
Stoltzfuz et al 2004
and *Galan et al 1998*

Threshold of HB to determine anemia per severity
Kassebaum (2016)

Disability weights
Salomon et al (2015)

Framework: Quantifying the benefit of red meat consumption

1 2

H3

Comparison with iron recommendation or iron needs ?
EFSA (2015)

Absorption rate of groundbeef iron
Tounian et al (2017)

Ground beef intake (g/d)

Absorbed iron (mg/d)

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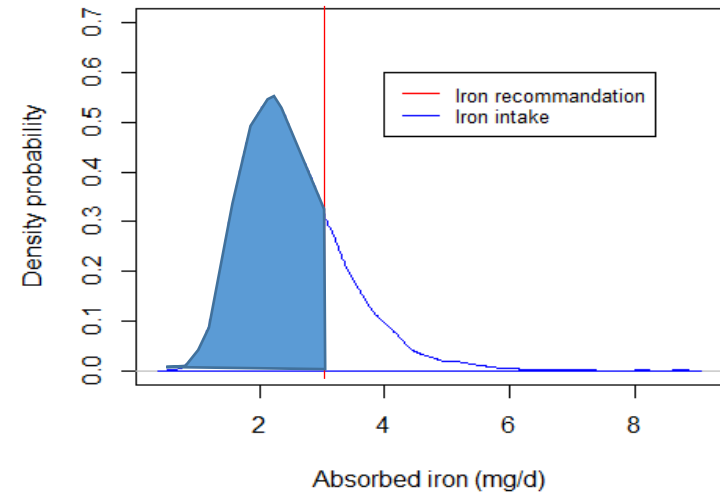
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Salomon et al (2015)

Recommendation vs Requirement

2 types of comparison:

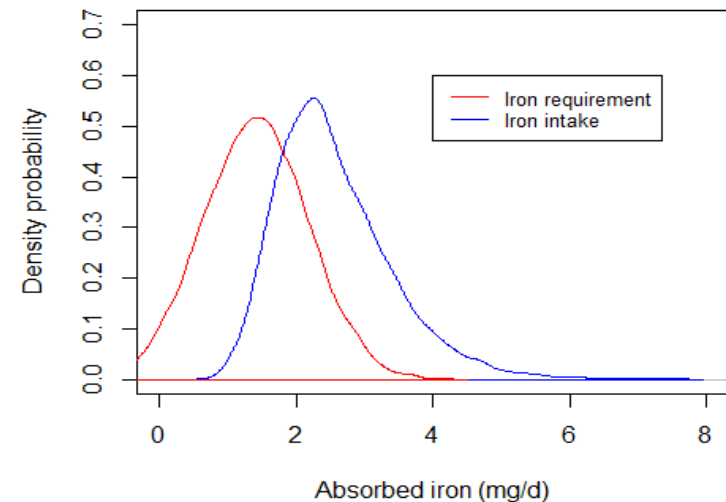
- According to EFSA **recommendations**:

→ Fixed amount of iron to cover 95% of the population



- Regarding the **needs** (as Norden 2012):

→ Probability distribution, to take into account the variability of the population regarding the need of iron intake



Assessing and managing uncertainty and variability

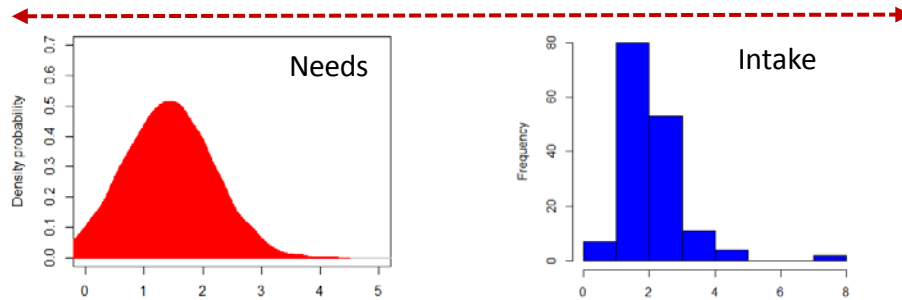
Probabilistic assessment model with **stochastic distributions**, sources of:

Variability: heterogeneity within populations

Uncertainty: lack of data and knowledge

Second order Monte Carlo simulation

Variability



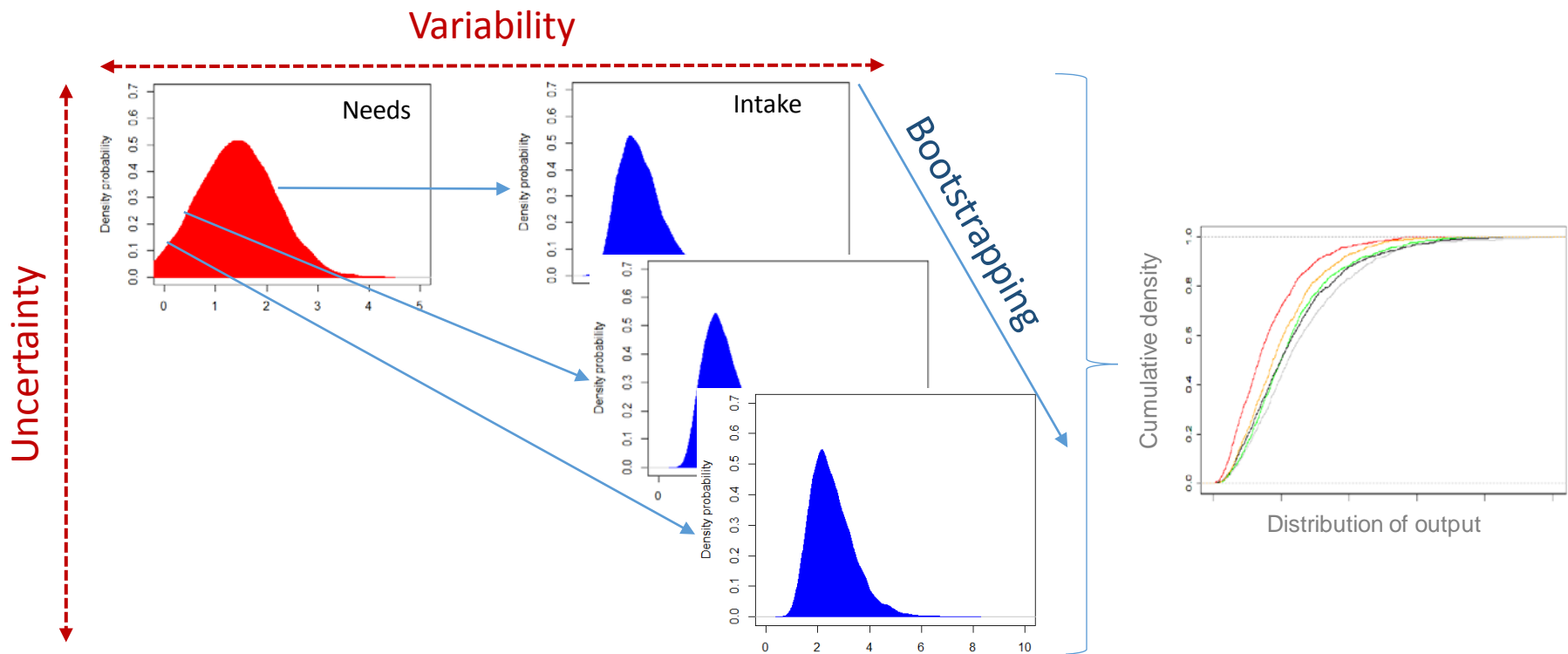
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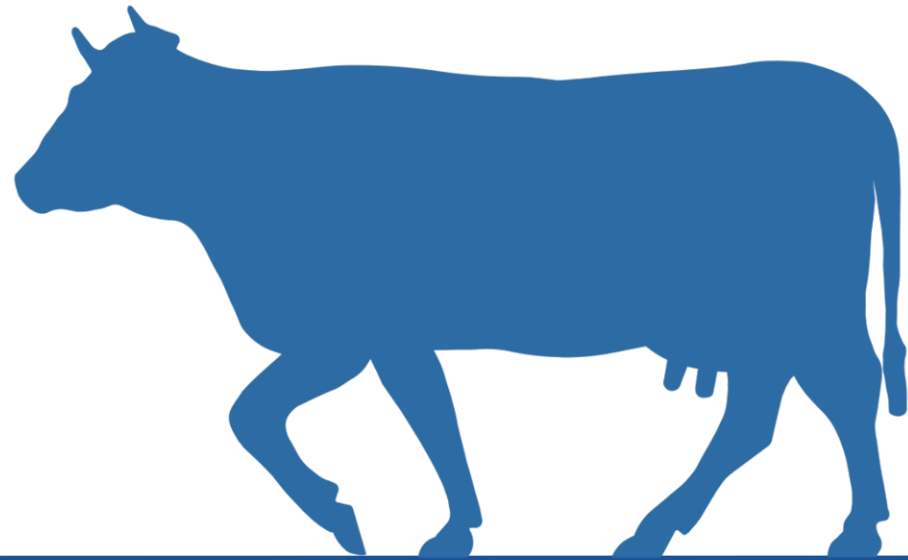
Uncertainty: lack of data and knowledge

Second order Monte Carlo simulation



Iterations: 10,000 for variability and 1,000 for uncertainty

Results



Assessing and managing uncertainty and variability

Sources of variability and uncertainty can be:

Quantifiable:

Variability:

Gender

Age classes

Iron intake by the French population → Probability distribution

Iron requirement for each individual → Probability distribution

Levels of haemoglobin in blood levels → Probability distribution

Uncertainty:

Fitted distribution of iron intake → Probability distribution

Variability or uncertainty:

Iron absorption proportion → Deterministic value: mean per age class

Anemias due to iron deficiencies proportion → Deterministic value: mean

Disability weight → Probability distribution taken into account as uncertainty

Unquantifiable:

Hypothesis made → Expert elicitation to built the model



Stephen Wilson © 2005

Actual situation in France

Number of cases and DALY per 100,000 French population per year

Age class	3-6	7-11	12-17		>18	
Gender	Both	Both	Male	Female	Male	Female
Number of IDA cases	8.68 [6.80-11.00]	23.45 [21.07-26.01]	7.74 [6.54-9.21]	58.62 [53.79-63.21]	26.16 [21.94-30.92]	619.91 [592.78-647.54]
DALYs due to IDA	0.07 [0.03-0.12]	0.46 [0.29-0.65]	0.06 [0.03-0.10]	0.58 [0.30-0.87]	0.14 [0.02-0.25]	11.24 [6.91-15.28]

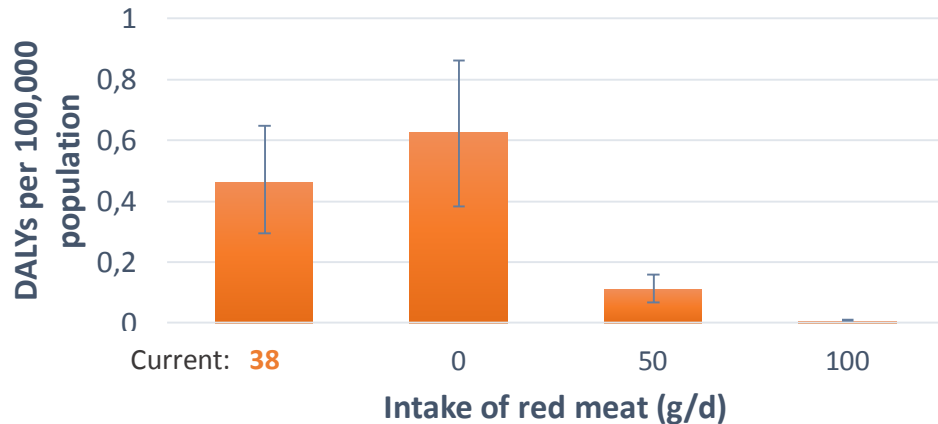
For total French population:

- **475,540 [95% CI =457,520-492,780]** cases of anemia due to iron deficiency
- **7,970 [95% CI =5,760-10,660]** DALY for the population → **0.02 [95% CI =0.01-0.02]**
DALY / case
- Female more affected than male on average

To reduce DALYs → Consumption scenarios of 0g – 50g -100g of red meat per day

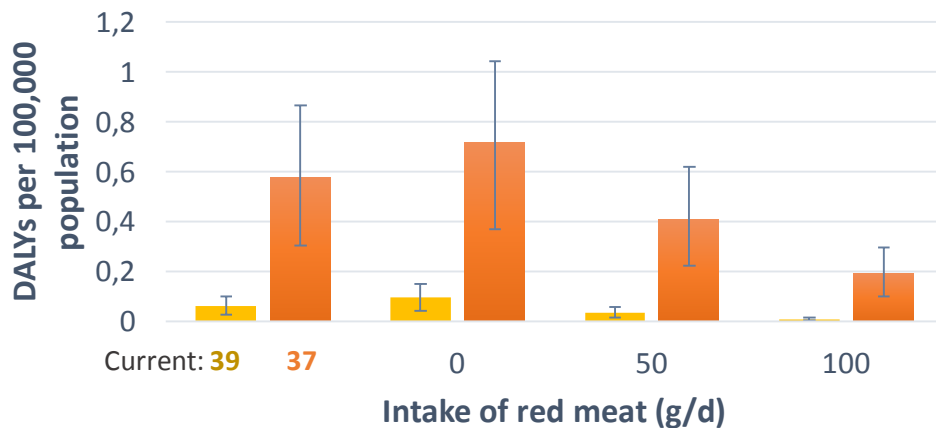
Consumption scenarios to reduce DALYs

Children aged from 7 to 11 years old



- Low DALYs due to Iron Deficiency Anemia (IDA)
- Consumption **over 50g/d** of red meat would be enough to significantly decrease IDA DALYs

Teenager aged from 12 to 17 years old



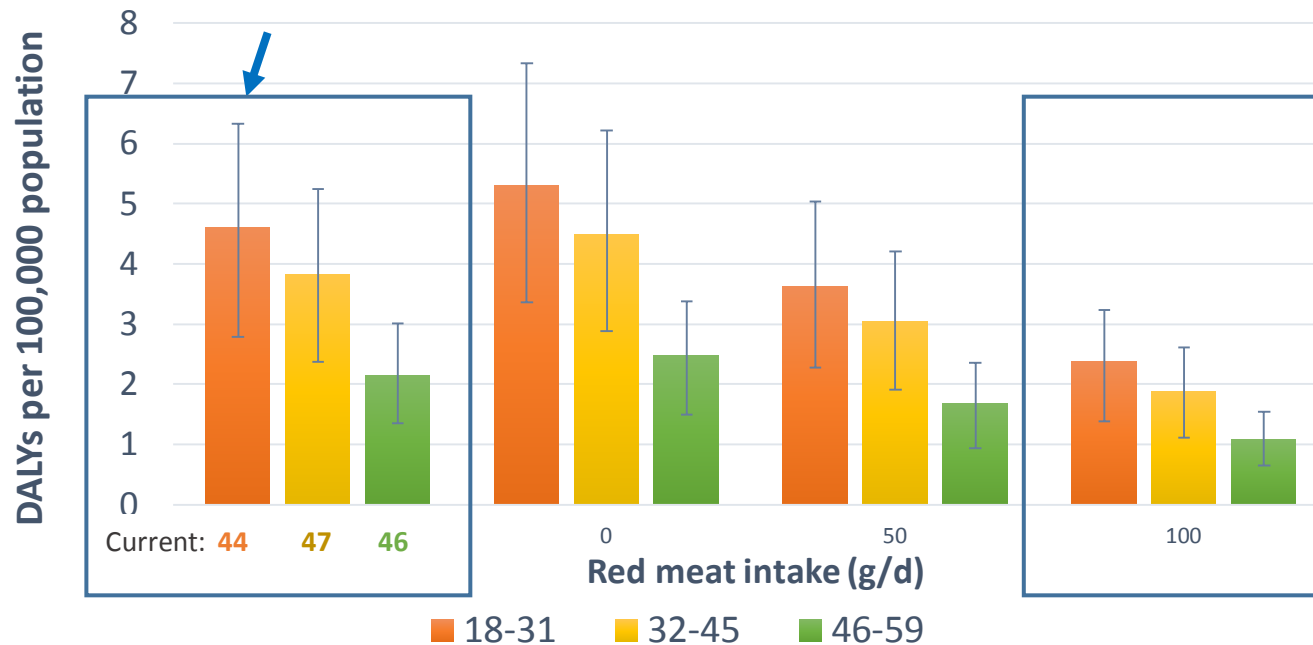
Consumption of 100g/d of red meat :

Boy: IDA close to 0 DALYs

Girl: Decrease of 65% of DALYs
Should consume more than 100g/d to eliminate IDA

Consumption scenarios to reduce DALYs

Premenopausal woman



→ **Age class 18-31 years old:** the most concerned with IDA

→ **100g/d of red meat:** reduction of 50% of actual DALYs from IDA for Premenopausal women

Conclusion

First model estimating IDA from iron intake:

- Optimization of the benefit thanks to the scenarii of red meat consumed
→ Up to - 8,000 DALY through red meat consumption
- Built with confidence intervals that reveal uncertainty
- But:
The difficulty of separating uncertainty from variability
→ Iron absorption proportion, disability weight...

More studies needed to confirm the hypothesis

- Results can contribute to decision-making for the formulation of recommendations
- Comparison of possible benefits and risks through inclusion of other health effects of red meat consumption



**THANK
YOU!**

