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Public health risk-benefit assessment of red meat in France: Current consumption and alternative scenarios

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ABSTRACT

Consumption of red meat has been associated with the risks of colorectal cancer (CRC), cardiovascular disease (CVD), foodborne-pathogen related diseases and with the potential benefit obtained by reduction of iron deficiency anemia (IDA). Based on probabilistic models, current risks and benefit for the French population were aggregated into a single metric, the disability adjusted life years (DALY).

In France, per 100,000 people, current red meat consumption was responsible for a mean of 19 DALYs due to CRC, 21 DALYs to CVD and 7 DALYs to foodborne diseases. Current consumption of iron throughout the diet led to a mean of 15 DALYs due to IDA.

To mitigate the risks, scenarios were built per sub-population of age and gender. Among adult and elderly population, the big meat eaters would benefit to adhere to the current recommendation (less than 500 g/w): the risks of CRC and CVD would decrease. Regarding IDA (scenario built with fixed ground beef amount), for young population, a consumption of 375g/w would be sufficient to eliminate the burden while for 25-44 years-old females, 455g/w would reduce IDA, but not entirely.

This study highlighted the importance of assessing health risk-benefit per sub-populations and the necessity of communicating the results accordingly.

1. Introduction

Food is essential for growth and survival, by providing indispensable nutrients and energy (Nauta et al., 2018). Unsafe food causes more than 200 different types of diseases. It is estimated that 600 million people in the world fall ill after eating contaminated food, from which 420,000 die each year (WHO, 2019). For this reason, dietary recommendations have been identified as a key factor for improving health status and reducing morbidity (GBD 2017 Risk Factor Collaborators, 2018; Wolk, 2017).

Balancing the risks and benefits of food has become an important public health topic (Nauta et al., 2020). To answer the demand for advice on safe and healthy diets and to establish new policies, tools for assessing the risks and benefits of food on health have been developed in recent years, thanks to the will of public health authorities (EFSA in particular). Risk-benefit assessment is an emerging discipline which has been carried out in several studies (Berjia et al., 2014; Cardoso et al., 2018; Farchi et al., 2017; Hoekstra et al., 2013; Thomsen et al., 2018, 2019; Wikoff et al., 2018) although mainly applied to fish consumption (ANSES, 2013; Becker et al., 2007; Domingo et al., 2007; EFSA, 2015; Hoekstra et al., 2013; Ponce et al., 2000). This type of assessment aims to quantify the risks and benefits in a comprehensive manner (chemical, microbiological and nutritional aspects) in order to assess all the effects of the consumption of food or its components on health and then to establish recommendations on this basis. Regarding food, microbiological and chemical components are almost exclusively considered as harmful to health, while for nutrition, food is a source of beneficial effects on health but can also have harmful effects (Nauta et al., 2020).

To be able to compare different risks and benefits from different disciplines, mathematical models have been built to balance the probability of an adverse health effect, in terms of incidence and severity, against the probability of beneficial effects attributable to an exposure to a specific dietary component (EFSA, 2010) using a common metric: the

Abbreviations: CRC, colorectal cancer; CVD, cardiovascular disease; IDA, iron deficiency anemia; DALY, disability adjusted life years; RR, relative risk; GBD, Global Burden of Diseases; YLD, years lived with disability; YLL, years of life lost; MC2D, Monte Carlo simulation in two dimensions; WHO, World Health Organization.

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Disability Adjusted Life Years (DALY). This metric considers mortality and morbidity, expressing the number of years of life lost (YLL) from premature death and the number of years lived with disability (YLD) (WHO and no,). DALY has been used by the Global Burden of Disease (GBD) study, supported by the World Health Organization (WHO), which has estimated the health effects of major diseases, injury and risk factors in the world since 1990.

In recent years, red meat consumption, including beef, pork, lamb and other small ruminants, has become a public health concern (Casalonga et al., 2017). In fact, due to its nutritional and chemical compounds, this food type has been classified by the World Cancer Research Found/Imperial College of London and the WHO as "probably carcinogenic to humans" for colorectal cancer (CRC) (Bouvard et al., 2015; WCRF/AICR, 2018a). This leads to dietary recommendations to limit red meat consumption to 500 g per week (ANSES, 2016). However, red meat remains widely consumed in France, with 41% of male and 24% of female French population consuming more than the guidelines in 2015 (Torres et al., 2019). In addition, this type of food was also associated with cardiovascular disease (CVD) mortality risk (Abete et al., 2014), stroke, coronary heart diseases and heart failure (Bechthold et al., 2017; Wolk, 2017). Microbiological risks are also a major concern when preparing and consuming red meat. Indeed, 10% of the total number of declared foodborne outbreaks were due to red meat consumption in 2017 (InVS, 2019). On the other hand, red meat also has beneficial effects by the nutritional contributions, in particular iron, which contributes to the decrease of iron deficiency (ID) and, subsequently, anemia (Czerwonka and Tokarz, 2017).

Despite all these studies on the risks on the one hand and the potential benefits on the other hand, there is still no study that brings together all the health effects and then compares them quantitatively. The objective of this study was therefore to study altogether health risks and benefits related to the consumption of red meat and then to express the results in a single unit for comparison, the DALY. The originality was to carry out this comparison for sub-groups of different populations, ages and genders. Next, to overall balance health benefits and risks, several consumption scenarios were built for various sub-populations and analysed through *in-silico* approaches based on second order Monte Carlo simulations. The work focused on the French population, a relatively large consumer of red meat.

2. Methods

2.1. Model framework for risk and benefits balance attributable to red meat consumption

The model was developed for the French population aged from 3 years old. Age classes were defined according to the age classes of the incidence data (available for CRC, CVD and Anemia) and for the population of interest (Binder-Foucard et al., 2013; DREES, 2017; Santé Publique France, 2006–2007; Stoltzfus et al., 2004).

Risk assessment models for CRC, CVD and iron deficiency anemia (IDA) were built using probability distributions and simulated with Monte Carlo simulation in two dimensions (MC2D) to capture the uncertainty and the variability, in R software (3.6.2 version). For CVD and CRC risk quantification, methodology and data used were explained in a previous study (De Oliveira Mota et al., 2019a). ID quantification was also described in a previous study (De Oliveira Mota et al., 2019b). Microbiological burden of disease was extracted from a previous study (De Oliveira Mota et al., 2020), and the associated burden of disease was assumed not to be much affected by the levels of red meat consumed in the scenario. Indeed, as the increase of the number of bacteria is expressed in a logarithm scale, and the only parameter changed being the quantity of red meat consumed, the level of red meat should have to be increased enormously for a significant increase of the burden attributable to microbiological infection.

For each health outcome, the number of cases was estimated and the burden of diseases was expressed in DALY. This latter metric is commonly used in risk-benefit assessments (Hoekstra et al., 2012; Nauta et al., 2018; Tijhuis et al., 2012).

For CRC, CVD and foodborne pathogens estimations, the burden estimated in this study corresponded to red meat consumption exclusively. IDA benefit being the reduction of the risk, the estimations of the burden corresponded to the total burden of this health effect, including all dietary iron consumed (from red meat and other dietary sources).

2.2. Current consumption of red meat in France

Current consumption considers the level of red meat and iron consumption extracted from INCA 2 dietary survey (approved by the French National Commission for Computed Data and Individual Freedom, "Commission Nationale Informatique et Libertés"; CNIL, under the registration code 797859—v0, on 20 March 2002; publicly available at https://www.data.gouv.fr/fr/datasets/donnees-de-consommations-et-habitudes-alimentaires-de-letude-inca-2-3/). The survey was performed in metropolitan France and has identified French consumption habits between 2005 and 2007 for males and females from 3 to 79 years old (ANSES, 2014). Consumption of red meat, which included unprocessed muscle of beef, pork, veal, horse and lamb, in France is given in Table 1. A more recent dietary survey (INCA 3) was available (ANSES, 2017b), but, unfortunately, the raw data were not accessible when the estimations were done. Nevertheless, French food habits did not change drastically over time regarding meat consumption (De Oliveira Mota et al., 2019a). Red meat and iron consumption levels were implemented as explained in previous studies (De Oliveira Mota et al., 2019a, 2019b).

Males aged from 25 to 44 years old were the bigger consumers of red meat (Table 1). This population ate almost twice more red meat than females at this age class. For females, the highest consumers of red meat were aged from 45 to 64 years old. Even in each class of age and gender, there is a large heterogeneity of meat consumption profiles: the standard deviation is large, mean and median are different, revealing a non-symmetrical pattern.

2.3. Red meat consumption scenarios

Consumption scenarios were developed for the population of interest. For young population, two consumption scenarios were developed. For adult and elderly population, four consumption scenarios were developed as indicated in Table 2. When directing meat consumption, ground beef was used as type of meat.

2.3.1. Red meat consumption scenarios for young population

For children and adolescents aged from 3 to 14 years old, consumption scenarios were developed for IDA and *Escherichia coli* STEC (STEC). We considered that this age class was not concerned by CRC and CVD risk due to red meat consumption from previous studies conclusion (De Oliveira Mota et al., 2019a) and current knowledge (ANSES, 2019).

As the population aged from 3 to 14 years old suffered from IDA, it

Table 1
Levels of red meat consumed in France between 2005 and 2007, in grams per week, per age class and gender from INCA2 dietary survey (ANSES, 2014).

Age class	Male			Female		
	Mean	Median	Standard deviation	Mean	Median	Standard deviation
3–6	190	160	141	182	145	144
7–11	274	260	177	234	210	154
12–14	321	280	240	250	231	182
15–17	374	332	274	235	200	183
18–24	351	298	277	222	195	191
25–44	413	360	305	253	229	189
45–64	388	342	280	264	235	194
≥65	329	287	214	250	234	183

Table 2
Red meat consumption scenarios for young, adult and elderly population in France, considering colorectal cancer, cardiovascular disease, iron deficiency anemia and *Escherichia coli* STEC.

Population	Children and adolescents	Adult and Elderly	
Age class	3–14	≥25	25-44; 45–64 and ≥ 65
Consumption scenarios (grams per week)	375; 500	≤500 and ≤ 455	455 and 375
Type of red meat consumed	Ground beef	Current types of red meat	Ground beef
Harmful health effect	*Escherichia coli* STEC infection	Colorectal cancer Cardiovascular disease	Colorectal cancer Cardiovascular disease
Beneficial health effect	Decrease of iron deficiency anemia	Decrease of iron deficiency anemia	Decrease of iron deficiency anemia

was possible to suggest an increase in the consumption of red meat. Two scenarios were built by dictating a consumption of 375 and 500 per week for the entire population concerned (Table 2) corresponding to 75% and 100% of the maximal limit of the dietary recommendations for red meat consumption (500g/w) (ANSES, 2016; HCSP, 2017). For both genders, the age classes 15–17 were not considered in this study because no risks were available to balance with the benefits.

As consumption scenarios only consider the quantity of red meat consumed, the risk from STEC infection was considered as constant whatever the amount of ground beef included in the scenarios, as explained in section 2.1.

2.3.2. Red meat consumption scenarios for adult and elderly population

Consumption scenarios were built for adults and elderly, aged from 25 years old, considering CRC, CVD and IDA. For both genders, the age class 18–24 years old was not considered in this study because no risk was estimated for this category in a previous study (De Oliveira Mota et al., 2019a) to balance with the benefits.

The first scenario was to limit the consumption of red meat to the level of dietary recommendations for red meat consumption (less than 500 g per week) of French Agency for Food, Environmental and Occupational Health & Safety (ANSES) (ANSES, 2016; HCSP, 2017). The second scenario was to limit their consumption to 455 g per week which corresponded to the maximal amount of red meat consumed to prevent CVD attributable to the consumption of red meat for the most concerned populations (male and female aged from 45 years old), by referring to a previous study (De Oliveira Mota et al., 2019a). For these two latter consumption scenarios (Table 2), when the individuals ate less than the limits established by the scenario, then their consumption habits of red meat were considered unchanged. When individuals ate more than the limited consumption allowed in the scenario, then their amount of red meat was replaced by the maximum quantity allowed by the scenario. For example, for the scenario limiting the consumption of red meat to 500 g per week, when an individual currently ate 300 g per week then the amount of his/her consumption remained unchanged. On the opposite, when the individual currently ate 600 g per week of red meat, then his/her consumption was replaced by 500 g/w in the scenario.

Finally, two other scenarios were built by dictating the consumption to 455 g per week and 375 g per week. The scenarios with the dictated levels of red meat for overall subpopulation were built with cooked ground beef with 15% of fat, with an amount of 2.6 mg of iron per 100 g of meat and an average iron absorption of 25% (Tounian and Chouraqui, 2017). This type of meat was chosen because it was the type of beef meat most consumed by the French population (51 g per week) (ANSES, 2014) and the most accepted by the youngest populations.

2.4. Running scenario using Monte Carlo 2D simulation

To combine altogether health risks and benefits and next to generate scenarios, the probabilistic models were implemented in R software. In the MC2D models, 10,000 iterations were run to capture the uncertainty and 10,000 iterations for variability, using mcstoc function in R software (mc2d package). To verify the stability of the outputs, three simulations were carried out for each age class and gender. Variation less than 5% were achieved.

3. Results

3.1. Burden of diseases with current red meat consumption

Aggregation of previous studies estimating the risks or the benefit of red meat consumption (De Oliveira Mota et al., 2019a, 2019b, 2020) enabled to estimate the burden of diseases with current red meat consumption in France (Table 3). Per 100,000 people per year, current red meat consumption was associated with a mean of 7 [95% CI = 3–11] DALYs due to foodborne illness, 19 [95% CI = 8–33] DALYs due to CRC, and 21 [95% CI = 12–32] DALYs due to CVD. The French population suffered as well of a mean of 15 [95% CI = 10–20] DALYs per 100,000 people per year of IDA, this disease might be reduced by consumption of food rich in iron, such as red meat.

While segmentation by age and gender was possible for nutritional and chemical risks, as well as for nutritional benefits, this was not feasible for microbiological risks. Only the infection due to *Escherichia coli* STEC (STEC) was assumed to be specific for children under 15 years old, which corresponded to the age limit for monitoring HUS (Hemolytic Uremic Syndrome) in France. For this specific sub-population, the burden of disease due to STEC was estimated to a mean of 0.4 [95% CI = 0.1–0.8] per 100,000 population per year (De Oliveira Mota et al., 2020) which was close to the IDA burden estimated to a mean of 0.6 [95% CI = 0.3–0.9] per 100,000 of this population per year (Table 3). The effect of red meat consumption in terms of CRC and CVD burden did not significantly affect individuals younger than 24-years old (Table 3).

Combining adults within the 25-64 years-old range and elderly people (≥65 years old), male plus female, the results showed that the current consumption of red meat corresponded to a burden of a mean of 19.4 [95% CI = 8.0–33.3] DALYs for CRC and 21.3 [95% CI = 11.9–31.5] DALYs for CVD per 100,000 population per year (Table 3). The most affected population by CRC and CVD burden of disease was the population aged over 45 years old. However, the population in the age class 25–44 years old was also concerned by these two health outcomes.

In terms of IDA, considering total iron consumption in diet, the 25-64 years-old adults, male plus female, contributed to a mean of 8.4 [95% CI = 5.4–11.5] DALYs for IDA per 100,000 population per year. The most affected population was women aged from 25 to 44 years old with a mean of 6.3 [95% CI = 3.9–8.8] DALYs. This latter burden of disease was 13–21 times higher than for CRC and CVD, respectively, for the same age class (Table 3).

Once the risks and benefits were established for the French population, consumption scenarios were built for various sub-populations and analysed through *in-silico* approaches based on Monte Carlo simulations.

3.2. Consumption scenarios for the young French population

For the French young population aged from 3 to 14 years old, two consumption scenarios were compared with current red meat consumption (mean = 247g/w; sd = 182 g/w). The first scenario corresponded to the maximum level of red meat consumption recommended for adults (less or equal to 500g/w) (ANSES, 2016; HCSP, 2017) and the second scenario corresponded to 75% of this maximal level (375g/w). The red meat used in the simulations was ground beef as it is the type of beef most accepted by the youngest population.

A consumption of 375 g per week or 500 g per week of ground beef

Table 3
Mean red meat consumption levels in grams per week and mean DALYs associated with red meat consumption in France per 100,000 population, with current levels of red meat consumed. For CRC and CVD, the DALY were exclusively due to red meat consumption, IDA DALY corresponded to the total burden of IDA.

Gender	Age class	Red meat consumed (mean in g/week)	DALYs per 100,000 population (95% confidence intervals in brackets)			
			IDA	CRC	CVD	Foodborne diseases
Male	3–6	190	0.3 [0.1–0.5]	0 [0–0.1]	0 [0-0]	6.6 [3.4–11.1]
	7–11	274	0 [0-0]			
	12–14	321	0 [0-0]			
	15–17	374	0 [0-0]			
	18–24	351	0 [0-0]			
	25–44	413	0.9 [0.1–1.8]	0.7 [0.1–1.5]	1 <[0.3–1.8]	
	45–64	388	0 [0-0]	5.7 [0.4–13.5]	5.5 [1.2–10.7]	
	≥65	329	0.6 [0.3–1]	5.2 [0.4–12.9]	7.1 [1.8–13.6]	
Female	3–6	182	0.3 [0.1–0.5]	0 [0–0.1]	0 [0–0.1]	
	7–11	324	0 [0-0]			
	12–14	250	0 [0-0]			
	15–17	235	4.0 [2.1–5.9]			
	18–24	222	1.6 [1.0–2.1]			
	25–44	253	6.3 [3.9–8.8]	0.5 [0–1.5]	0.3 [0–0.7]	
	45–64	264	1.2 [0.6–1.8]	3.2 [0.1–8.9]	1.3 [0.1–2.9]	
	≥65	250	0.1 [0.1–0.2]	4 [0.3–10.4]	5.8 [1.3–11.4]	
Male and Female[a]	Children (3–14 yo)		0.6 [0.3–0.9]	0 [0–0.1]	0 [0-0]	6.6 [3.4–11.1]
	Adolescents (15–17 yo)		4.0 [2.1–5.9]			
	Young adults (18–24 yo)		1.6 [1.0–2.1]			
	Adults (25–64 yo)		8.4 [5.4–11.5]	19.4 [8.0–33.3]	21.3 [11.9–31.5]	
	Elderly people (65 yo and over)		0.7 [0.4–1.1]			
Total[a]	Whole population		15 [10–20]	19 [8–33]	21 [12–32]	7 [3–11]

[a] a small difference between the sum of values and the reported values may occur due to the numerical simulation procedure.

was enough to decrease the burden attributable to IDA from red meat consumption (Fig. 1).It was assumed no change in DALYs associated with STEC infection considering that as the bacterial concentration is expressed in a logarithm scale, only huge intake increase would increase the burden.

3.3. Consumption scenario for the French adult and elderly populations

3.3.1. Consumption scenarios limited to 500 or 455 g per week

The current consumption of red meat among adults and elderly in France - aged from 25 years old - was estimated by the INCA2 study in average to be 380g/w for men and 256g/w for women. However, the standard deviation was large (275 g/w and 189g/w for men and women, respectively) showing that some people ate much more than the dietary recommendation, i.e. much more than 500 g per week (ANSES, 2016; HCSP, 2017).

Consequently, two alternative scenarios were set up. The first consumption scenario considered that the sub-population respected the dietary recommendations for red meat consumption, i.e. eating less than 500 g per week. The second scenario was more drastic, it considered that the sub-population ate less than 455 g per week of red meat, this latter value being the maximal amount of red meat to be consumed to prevent CVD in both male and female sub-populations older than 45 years (De Oliveira Mota et al., 2019a).

A decrease of DALYs was observed for CRC and CVD when the population respected the recommendation to limit the consumption of red meat to 500 g per week (Table 4). In fact, a mean of −4.7 DALYs per 100,000 people was gained for CVD plus CRC if recommendations were respected by the population of both genders, figure obtained by summing the gain of DALYs (Δ CC) between the current mean consumption and the scenario limiting the consumption to 500 g/w (−1.8 -2.0 -0.5 -0.4 = −4.7 DALYs). When adhering to a more drastic scenario (less than 455 g/w), the gain could reach a mean of −5.4 DALYs (−1.9 -2.3 -0.6 -0.6) per 100,000 people. On the other hand, both alternative scenarios did not affect the IDA burden of disease: a slight increase of +0.1 DALY was observed (Table 4).

3.3.2. Consumption scenarios with dictated quantities of ground beef

Two other alternative consumption scenarios were built. This time, it was considered a fixed value such as all the individuals of the sub-population were eating the same amount of red meat. Moreover, the red meat used in the scenario was ground beef with 15% of fat for the

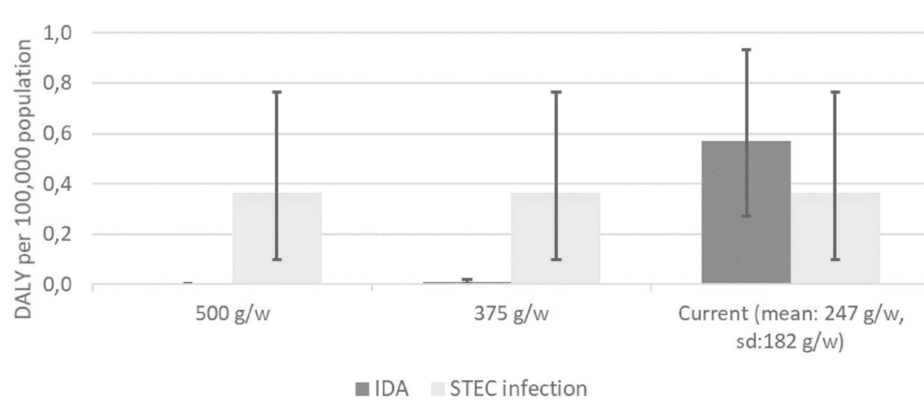

Fig. 1. Mean estimated DALYs from iron deficiency anemia (IDA) and *Escherichia coli* STEC infection with various levels of red meat consumption for young population (3–14 years old) in France per 100,000 population per year. Current situation based on red meat consumption distribution, alternative scenario based on ground beef consumption of a specific amount (375g/w or 500g/w).

Table 4
Mean estimated DALY and gain compared to current consumption when recommendations “less or equal to 500 g per week” or “less or equal to 455 g per week” are followed, for population aged of 25 years old or more. Expressed in mean and 95% confidence interval in brackets. Δ CC represents the gain compared to current consumption versus ≤500 g/w or ≤455 g/w.

Gender	IDA		CRC		CVD	
	Scenario 1: ≤500 g/w					
	≤500 g/w	Δ CC*	≤500 g/w	Δ CC	≤500 g/w	Δ CC
Male	1.6 [0.5–2.9]	0.1 [-1.4 - 1.7]	10.1 [1.5–21.0]	−1.8 [-15.7–12.6]	11.8 [4.3–20.6]	−2.0 [-13.5–9.9]
Female	7.8 [4.7–11.1]	0.1 [-4.5 - 4.1]	7.4 [1.5–15.8]	−0.5 [-8.5 - 7.7]	7.0 [2.2–12.7]	−0.4 [-8.2 - 7.3]
	Scenario 2: ≤ 455 g/w					
	≤455 g/w	Δ CC	≤455 g/w	Δ CC	≤455 g/w	Δ CC
Male	1.7 [0.5–2.9]	0.1 [-1.5 - 1.7]	9.4 [1.3–20.6]	−1.9 [-16.1–12.1]	11.2 [3.8–20.1]	−2.3 [-14.0–9.0]
Female	7.7 [4.8–10.9]	0.1 [-4.1 - 4.5]	6.9 [1.0–15.6]	−0.6 [-11.2–10.1]	6.6 [2.1–12.7]	−0.6 [-8.2 - 7.2]

same reasons as previously mentioned.

The quantity was either 455g/w corresponding to the maximal amount of red meat to be consumed to prevent CVD in both male and female sub-populations older than 45 years (De Oliveira Mota et al., 2019a) or 375 g/w corresponding to 75% of the of the maximal limit of the dietary recommendations for red meat consumption.

When dictating the same level of consumption, for the overall population, the loss of DALYs from IDA if all the population consumed 455 g/week was not sufficient to compensate the increase of DALYs due to CRC and CVD for female. Similar results were obtained with 375 g/week (Table 5).

However, a deeper analysis per age class and gender revealed extra information. For instance, if females aged from 25 to 44 ate 455 g of ground beef per week, a decrease of the burden of disease compared to the current situation would be expected. Indeed, while their current consumption of red meat (mean of 253g/w, sd = 189g/w) led to a mean of 6.3 [3.9–8.8] DALY due to IDA, a ground beef consumption of 455g/w would lead to mitigate IDA burden: mean of 4.5 [2.8–6.1] DALY (Fig. 2). On the opposite, if all the females older than 65 years had a consumption of 455g/w (scenario based on ground beef), they would increase their CRC and CVD risks: mean DALYs due to CRC shifting from 3.5 [0.3–10.4] to 5.7 [0.3–12.6], due to CVD from 5.8 [1.3–11.4] to 8.9 [2.8–14.8] mean DALYs per 100,000 people per year (Table 5).

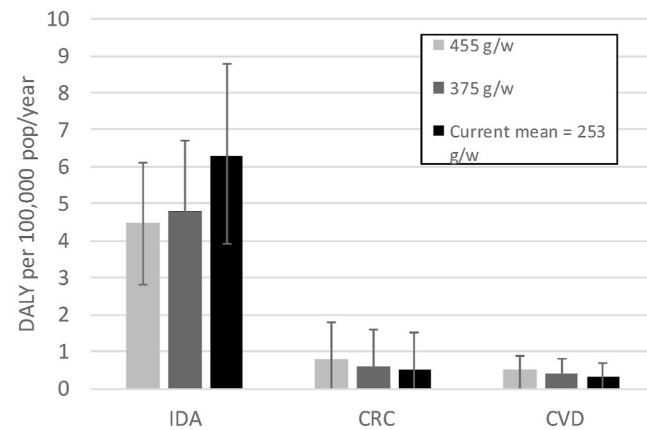

Fig. 2. Mean estimated DALYs due to iron deficiency anemia (IDA), colorectal cancer (CRC) and cardiovascular disease (CVD) for 25–44 years old female population in France per 100,000 population per year. Current situation based on red meat consumption distribution, alternative scenario based on ground beef consumption of a specific amount (375g/w or 455g/w).

4. Discussion

Current risks and benefits of red meat consumption for specific subpopulations of gender and age in France were aggregated and compared. Per 100,000 people per year, current red meat consumption was responsible for a mean of 19 DALYs due to CRC, 21 DALYs to CVD and 7 DALYs to foodborne pathogens. Current consumption of iron throughout the diet led to a mean of 15 DALYs due to IDA. Overall, the risk associated with red meat consumption (47 DALYs per 100,000 people per year) in France is higher than the potential benefit (reduction of IDA burden by red meat consumption). However, it is important to keep in mind that this estimated risk remains low compared to the burden of other diseases in France, e.g. CVD attributable to alcohol (162 DALYs per 100,000 people per year)(IHME, 2019).

Consumption scenarios revealed the difficulty of conveying one single message for the whole population. For instance, regarding IDA, for 25–44 females, a consumption of 455 g/w seems beneficial while for females older than 65 years, 455 g/week seems negative due to CRC and CVD. Moreover, how the scenarios are built may influence the outcomes. Here, two types of scenarios were carried out. The simplest one was to

Table 5
Mean estimated DALY due current red meat consumption in France per 100,000 adult population (mean and 95% confidence interval in brackets), and for 455 and 375 g per week of ground beef consumption. For CRC and CVD, the DALY were exclusively due to red meat consumption, IDA DALY corresponded to the total burden of IDA.

Gender	Age class	Red meat consumed (mean in g/w)	IDA			CRC			CVD		
			Current consumption	455 g/w	375 g/w	Current consumption	455 g/w	375 g/w	Current consumption	455 g/w	375 g/w
Male	25–44	413 (sd = 305)	0.9 [0.1–1.8]	0.4 [0–0.8]	0.5 [0–1.0]	0.7 [0.1–1.5]	0.6 [0–1.5]	0.5 [0–1.4]	1 [0.3–1.8]	1 [0–1.9]	0.8 [0–1.7]
	45–64	388 (sd = 280)	0	0	0	5.7 [0.4–13.5]	6 [0–13.9]	5 [0–13]	5.5 [1.2–10.7]	5.9 [0–11.4]	5 [0–10.5]
	≥65	329 (sd = 214)	0.6 [0.3–1.0]	0.2 [0.1–0.4]	0.3 [0.1–0.6]	5.2 [0.4–12.9]	6.2 [0.1–14.4]	5.3 [0–13]	7.1 [1.8–13.6]	8.8 [1.9–15.7]	7.3 [1.1–14]
Female	25–44	253 (sd = 189)	6.3 [3.9–8.8]	4.5 [2.8–6.1]	4.8 [3.1–6.7]	0.5 [0.0–1.5]	0.8 [0–1.8]	0.6 [0–1.6]	0.3 [0.0–0.7]	0.5 [0–0.9]	0.4 [0–0.8]
	45–64	264 (sd = 194)	1.2 [0.6–1.8]	0.8 [0.4–1.2]	0.9 [0.5–1.4]	3.2 [0.1–8.9]	4.5 [0–10.6]	3.8 [0–9.6]	1.3 [0.1–2.9]	1.9 [0–3.7]	1.6 [0–3.4]
	≥65	250 (sd = 183)	0.1 [0.1–0.2]	0 [0–0.1]	0.1 [0–0.1]	3.5 [0.3–10.4]	5.7 [0.3–12.6]	4.8 [0–11.6]	5.8 [1.3–11.4]	8.9 [2.8–14.8]	7.3 [1.6–13.3]

consider that all individuals belonging to a given sub-population ate the same amount of meat. This method enabled to show for instance that 455g/w is already too much for females older than 65 years. This type of scenario is easy to communicate ("what-if everyone ate a given amount") however unlikely to be implemented: in all age and gender classes, some individuals are small meat eaters while the others are high eaters (in the current red meat consumption dataset summarized in Table 1, the ratio standard deviation on mean was greater than 65%, whatever the age and gender class). The second type of scenario built in this study was to use the probability distribution obtained for each age and gender class but to truncate it at a given limit. Two limits were chosen: 500g/w and 455 g/w. Both scenarios indicated that having a recommendation formulated as "what-if everyone ate less than" would have a beneficial effect for adults and elderly. In other words, 455 g/w set as an upper limit seems relevant, even for the female-older-than-65-years group. In that sense, our study illustrates the importance of setting risk-benefit assessment framework per sub-populations, the importance of clarity in scenario settings and finally the necessity of communicating the results adequately.

DALY was the metric used in this study. It has the advantage of making the comparison between different possible health effects. In fact, in addition to the number of cases and deaths, this metric considers morbidity and mortality (Murray, 1994), which was required here to make a proper comparison between severe disease such as cancer with mild-symptom disease such as anemia, between chronic disease (CRC, CVD) and acute disease (foodborne diseases are generally acute). DALY metric is the most used one in risk and benefit assessments (Hoekstra et al., 2012; Membré et al., 2020; Nauta et al., 2018), it has the advantage of making risk-benefit assessment of food comprehensive, it enables to encompass nutrition, chemical and microbiological aspects.

Although making a quantitative comparison provides an added-value before making any recommendation when a food causes risks and brings benefits at the same time, it is important to keep in mind that these risks and benefits refer to different biological domains with different methodology used to obtain and analyze data. In particular, the weights of evidence of each health effect were not at the same level, indeed, while CRC evidence was high according to the conclusions of WCRF, the weight of evidence of CVD and IDA health effect related to meat consumption was lower because no global institution had clearly stated on the potential effect of red meat consumption on these latter health effects. This difference in weight of evidence status adds a non-quantifiable uncertainty to the assessment presented here. Besides, in our previous study based on epidemiological data, consumption and disease incidence data were analysed at the same time interval (De Oliveira Mota et al., 2019a) while it may have a delay between food consumption and development of cancer or CVD. Thus, for females, if our results seem to indicate that consumption of 455 g/week is beneficial against IDA for the 25–44 year period leading to a dietary recommendation of higher consumption in the 25–44 years period, we cannot exclude that this higher consumption during the 25–44 year period may contribute to the increased risk of CRC and CVD in women over 65 (shown in our data analysis). Indeed, some studies have assumed a period of eight years of latency between the exposure and the outcome for CRC (Grundy et al., 2016) and 10 years for CVD (Milner et al., 2015). The consumption of red meat during the younger period of the population may affect the incidence of chronic diseases in a further age class as shown by Ruder et al. (2011) who found a significant association between red meat consumption and CRC incidence after 10 years of latency (Ruder et al., 2011).

It should be highlighted that the health effects retained in this risk-benefit assessment are limited to those health effects for which the epidemiological level of evidence between red meat consumption and health effect was high, the mechanistic evidences were strong and the quantity of data or knowledge sufficient to convert the effects into DALYs. It is likely that some health effects have been omitted; for instance, the effects of environmental contaminants (Domingo and Nadal, 2016) have not been taken into account and the suspected impact on other localizations of cancer (pancreas and lung) has been excluded because the evidences were too limited (WCRF/AICR, 2018b). Likewise, although the reduction of sarcopenia by protein intake have been initially considered in this study, it could not be included in the risk-benefit assessment by lack of data showing a quantitative link between meat intake and health benefit.

The intake scenario in this study enabled to identify the amount of red meat that may be eaten to increase the benefit without increasing the risk per age class and gender. For the population who might have a beneficial effect, for instance 25-44 years-old females, increasing red meat consumption may lead to the decrease in the consumption of another food in the diet. This change of dietary habits must be considered, as it may result in a beneficial or a harmful effect on human health. In addition, some individuals will not accept to consume more red meat due to organoleptic reasons, beliefs, or ethics (e.g. vegetarian or vegan diet). As far as IDA is concerned, it is iron, and more specifically heme iron, that is an issue (Pierre et al., 2003a; Sullivan, 1981; Wolk, 2017). There are foods other than red meat which provide iron: white beans (7.97 mg iron per 100 g), lentils (6.51 mg iron per 100 g), etc (ANSES, 2017a). However, these foods must be consumed in greater quantities because the absorption of iron from these products is lower than the heme iron of red meat (De Oliveira Mota et al., 2019b). These possibilities of replacing one food or one type of food with another are beginning to be studied quantitatively. In Denmark, a risk-benefit assessment estimated total burden when replacing red meat with fish. It was then estimated that replacing 14 g of red meat by 25 g of fish would lead to an average decrease of 13 DALYs per 100,000 adults (Thomsen et al., 2018) from CRC risk decrease. Nevertheless, fish has a lower proportion of iron in the food compared to red meat and then it is less efficient to decrease the burden due to IDA.

Likewise, some of the scenarios carried out in our study revealed the need of reducing red meat consumption for some sub-populations. Another option to reduce the risk is to include vegetables when eating red meat. In fact, when these two types of food are eaten in the same meal, the risk of colorectal cancer is reduced: studies on CRC carcinogenic mechanism have shown that consumption of dietary calcium salts from dairy products and chlorophyll from vegetables reduces the harmful effect of heme iron (Balder et al., 2006; Bastide et al., 2016; Pierre et al., 2003b).

Beside risk and benefit associated with heme-iron, beneficial effect of proteins is important to take into consideration. In France, the National Nutrition and Health Program recommends to have a diet with 50% animal protein and 50% vegetable protein (INRAE, 2019). This recommendation plus the conclusions of our study seem to push forward a flexitarian-type diet, based mostly on plant-origin food while allowing for occasional meat dishes. Anyhow, for environmental considerations, meat consumption is likely to decrease in Western countries in the near future (Farchi et al., 2017; Willett et al., 2019).

In conclusion, this study was the first to aggregate and compare both risks and benefits from red meat consumption, considering distinct health outcomes: CRC, CVD, foodborne pathogen diseases and IDA. Although the risk-benefit assessment presented here covered already four major health outcomes, it has been performed with knowledge and data on time being. It will need to be consolidated with results from new studies either on adverse or beneficial effects in order to fine-tune future recommendations. In this study it was highlighted the need to distinguish different sub-populations of age and gender to both assess the risks and communicate the outcome. This fragmentation into sub-populations will become increasingly necessary in risk-benefit analyses as the diversity of consumer types increases in the near future.

CRediT authorship contribution statement

Juliana De Oliveira Mota: Methodology, Writing - original draft, Formal analysis, Software. **Sandrine Guillou:** Supervision, Writing -

review & editing, Conceptualization. **Fabrice Pierre:** Supervision, Writing - review & editing, Conceptualization. **Jeanne-Marie Membré:** Funding acquisition, Supervision, Writing - review & editing, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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