Quantitative assessment of microbiological risks due to red meat consumption in France

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Short title: Foodborne burden from red meat intake in France

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Abstract

As reported by the European Centre for Disease Prevention and Control and the European Food Safety Authority, red meat is a major food source that is responsible for foodborne illnesses due to microbiological hazards. The first objective of this study was to aggregate the available data in the literature in order to identify and characterise the main microbiological hazards associated with red meat consumption in France. Next, the associated numbers of foodborne illnesses, deaths and the subsequent burden of diseases, expressed in Disability Adjusted Life Years (DALY), were estimated. Using the eight foodborne pathogens kept in the assessment, a probabilistic risk model was built and uncertainty from the data was considered. *Campylobacter* spp. was ranked as the worst pathogen in terms of the number of human cases associated with red meat consumption, with 210 [95% confidence interval (CI) = 500–520] cases per 100,000 population. The pathogen that induced the highest mortality was non-typhoidal *S. enterica*, with 0.04 [95% CI = 0.01–0.10] deaths per 100,000 population. These cases were mostly related to pork consumption. However, the major contributor to the number of years in good health lost from red meat consumption in France was hepatitis E, with 33 [95% CI = 1-64] DALY per 100,000 population; this effect was mainly due to pork liver consumption. In terms of foodborne bacteria, for beef and pork meat, *Campylobacter* spp., non-typhoidal *S. enterica*, *C. perfringens* and STEC represented a mean of 2.2 [95% CI = 1.0–4.0] DALY per 100,000 individuals per year. The estimations provided in this study might help authorities to focus on these hazards and ultimately reduce their impact on the health of the French population.

Keywords:

foodborne illnesses, risk ranking, public health, disability-adjusted life year, DALY

1. Introduction

In recent years, red meat consumption has become a public health concern in France and other western countries [1]. In addition, unprocessed red meat, including beef, pork, lamb and other small ruminants, is widely consumed in France. Indeed, in 2013, each adult consumed an average of 52.5 g/day of red meat, from which 31 g/day was beef and 11 g/day was pork [2]. However, red meat has been classified by the World Cancer Research Found/Imperial College of London and the World Health Organization (WHO) as "probably carcinogenic to humans" for colorectal cancer [3,4]. On this basis, there are dietary recommendations to limit red meat consumption to 500 g per week [5]. Red meat consumption was also associated with cardiovascular disease (CVD) mortality risk [6] and suspected to increase the risk of breast cancer, advanced prostate cancer, stroke, coronary heart diseases and heart failure [7,8].

Microbiological risks are also a major concern when preparing and consuming red meat. In 2017 in France, 10% of the total number of foodborne outbreaks declared to the Regional Health Agency and Departmental Directorate of Social Cohesion and Population Protection were due to red meat consumption. The main pathogens (confirmed or suspected) were *Staphylococcus aureus* (13%), *Clostridium perfringens* (11%) and *Bacillus cereus* (10%) [9]. In Europe, the European Food Safety Authority (EFSA) and the European Centre for Disease Prevention and Control (ECDC) are in charge of evaluating the annual trends and sources of zoonoses, zoonotic agents and foodborne outbreaks. In 2017, they estimated that pork meat was responsible for 4.2% of the total outbreaks and 6.9% of the total cases for strong-evidence outbreaks in Europe. Beef meat was responsible for 2% of total outbreaks and 3% of the total cases for strong-evidence outbreaks, with a reporting rate of 0.012 per 100,000 for both types of meat [10].

Nevertheless, the number of confirmed cases was underestimated because notification is not mandatory for every pathogen (e.g. campylobacteriosis in France [10]). Some studies have attempted to estimate the real number of cases. The WHO estimated the number of foodborne illness cases in 2010 by considering the effects of underestimation [11]. In France, Van Cauteren et al. [12] and Vaillant et al. [13] performed this estimation for 2008–2013 and 1990–1999, respectively. Nevertheless, the number of cases provides an incomplete estimation of the health impacts of foodborne diseases. Indeed, the severity and duration of sequela vary according to the pathogenic species and the immune status of the consumer. For example, salmonella infection may cause diarrhoea, with a duration of 8 days, while Guillain-Barré syndrome—after campylobacteriosis—is assumed to last a lifetime [11]. To overcome this limitation, the WHO has gone further than estimate the number of cases; it has used the disability-adjusted life year (DALY) metric [11] to estimate the disability caused by foodborne diseases. The use of the composite DALY metric enables to consider morbidity—encompassing the duration and the disability induced by the sequelae—and the number of years lost due to premature death [14,15]. The DALY metric was also used by ECDC through a software tool for the estimation of the infectious disease burden in Europe (BCoDE) [16]. Disease models were built for each microbiological hazard and country. Information about sequelae (health impact, death, proportion of people concerned, duration, etc.) were integrated, and the user had to complete the requested information per age group and gender

Despite these substantial efforts, the burden of diseases induced by microbiological pathogens on health that is exclusively attributable to red meat consumption in France remains incomplete. In particular, the number of foodborne cases attributable to red meat consumption, and its corresponding DALY values, has not yet been estimated. Moreover, the uncertainty associated with the different types of data has not been aggregated into one model to deliver final estimates of disease burdens with confidence intervals. Thus, the objective of this study was to combine the available data in the literature to determine the main microbiological hazards when consuming red meat and to estimate the associated number of foodborne illness cases and deaths and the subsequent burden of diseases in France. Moreover, this study aimed to estimate the burden of foodborne diseases attributable to red meat consumption to enable comparison and balancing with nutritional risks and benefits of red meat, expressed in DALYs, evaluated in recent publications [17,18].

2. Methods

2.1. Selection of the available data

The literature was searched using terms such as “foodborne disease(s)”, “foodborne outbreak(s)”, “foodborne illness(es)”, “foodborne attribution” and “microbiological risk assessment” to select the main foodborne pathogens in France and to estimate the incidence and the associated burden of diseases when eating red meat (beef, pork and other small ruminants). Official reports from the WHO, the EFSA, the French Agency for Food, the Environmental and Occupational Health & Safety (ANSES), the ECDC and Santé Publique France were searched. PubMed and Google Scholar searches identified complementary data specific to the French population and the proportion of foodborne disease burden attributable to each type of red meat.

2.2. Determination of the main pathogens involved in foodborne outbreaks related to red meat consumption in France

To define the main foodborne pathogens of interest when eating red meat, three criteria were considered.

2.2.1. Incidence of foodborne illnesses in Europe and France for each pathogen, regardless of the source

To determine the hazards responsible for foodborne illness in Europe, a report from the WHO, which estimated the number of foodborne illness cases in 2010 in countries in the "EUR A" subregion, was used as a reference. It included Andorra, Austria, Belgium, Croatia, Cyprus, the Czech Republic, Denmark, Finland, France, Germany, Greece, Iceland, Ireland, Israel, Italy, Luxembourg, Malta, Monaco, Netherlands, Norway, Portugal, San Marino, Slovenia, Spain, Sweden, Switzerland and the United Kingdom [11].

For the French incidence, the work of Van Cauteren et al. [12] was considered. These authors estimated the number of French cases for the overall population. In order to make comparisons with future and other countries' estimations, the results were expressed per 100,000 population. The 2010 French population was considered to be 62,765,235 inhabitants (Table 1).

2.2.2. DALYs attributable to foodborne illnesses for each pathogen and for all sources

The WHO evaluated the disease burdens associated with foodborne illnesses in terms of DALYs [11]. To estimate this measure, data on the incidence, clinical outcomes, duration of the health state, age distribution and mortality rate were collected for each hazard by the WHO. The study estimated the number of years lived with disability (YLD) attributable to the hazard health impact and multiplied it by the disability weight factor, which reflects the severity of the health state [17]. Subsequently, the number of years of life lost (YLL)—due to a premature death—was added [11].

Our calculation considered the WHO's DALY estimations. For missing DALY values, the estimations from Havelaar et al. [19], recently used by Mangen et al. [20], were considered.

2.2.3. The proportion of foodborne illnesses attributable to red meat consumption for each pathogen

The burden that could be attributed to red meat consumption was mainly extracted from Hoffmann et al. [18], the most recent study on the attribution fraction per pathogen for beef, pork and other small ruminant meat. When data about the attribution fraction was missing from this latter study [18], attribution data from a French team was considered [19]. However, that source only estimated the attributable fraction to beef and pork. Finally, for the remaining missing data, the attributable fraction estimated by a Dutch team was utilised [20]. Attribution fractions per pathogen and type of meat is given in Table 1.

2.3. Incidence, death and disease burden of foodborne pathogens in Europe and France associated with red meat consumption

The number of cases, deaths and disease burden attributable to red meat consumption were estimated. The number of illness cases were calculated as represented in Equation 1:

$$Ncases.F_{rm} = \sum_{rm=1}^{3} \frac{Ncases.F_p \times 100{,}000}{Pop_{2010}} \times PA_{p,rm}, \tag{1}$$

where:

- rm is the type of red meat (1: beef; 2: pork; and 3: other small ruminant meat). For norovirus, rm = 1 also included lamb;
- p is the pathogen;
- $Ncases.F_{rm}$ is the number of cases of foodborne illness attributable to red meat consumption per 100,000 individuals in France;
- $Ncases.F_p$ is the number of cases of foodborne illness caused by a specific pathogen in France from Van Cauteren et al. [12];
- $PA_{p,rm}$ is the proportion of foodborne illness cases attributable to a pathogen and a type of red meat. *Campylobacter* spp., non-typhoidal *Salmonella enterica* and shiga-toxin producing *Escherichia coli* attribution fraction were extracted from Hoffmann et

al. [18]. The attribution fraction of hepatitis E and norovirus were extracted from Havelaar et al. [20] and *Staphylococcus aureus*, *Clostridium perfringens* and *Toxoplama gondii* were extracted from Fosse et al. [19];

- Pop_{2010} represents the 2010 population in France (62,765,235).

The number of deaths (Equation 2) was calculated by multiplying the number of foodborne illness cases per pathogen and red meat type by the proportion of deaths per pathogen-case. These latter values were obtained from the ratio between the number of deaths and the number of illness cases per pathogen from Van Cauteren et al [12].

$$Ndeath.F_{rm} = \sum_{rm=1}^{3} \frac{Ncases.F_p \times 100{,}000}{Pop_{2010}} \times PA_{p,rm} \times Rdeath.F_p \qquad (2)$$

Where:

- $Ndeath.F_{rm}$ is the number of deaths after of foodborne illness attributable to red meat consumption per 100,000 population in France;
- $Rdeath.F_p$ is the ratio of deaths after a foodborne illness per pathogen-case from Van Cauteren et al. [12].

DALYs issued from the WHO (2015) [11] were considered in the estimation, except for *C. perfringens*, *S. aureus*, hepatitis E and norovirus. For those cases, DALY values attributable to foodborne diseases were not available in the WHO estimations. Therefore, DALYs per 1,000 cases from a Dutch study were used as reference [21]. DALYs were estimated as follows (Equation 3):

(3)

$$DALY.F_{rm} = \left(\sum_{rm=1}^{3} DALY.EURA_{p=Camp.,Salm,E.coli,Toxo} \times PA_{p=Camp.,Salm,E.coli,Toxo} \right)$$

$$+ \left(\frac{Ncases.F_{p=C.perf,HepE,Noro,S.aureus} \times 100{,}000}{Pop_{2010}} \times DALY.case_{p=C.perf,HepE,Noro,S.aureus} \right),$$

Where:

- $DALY.F_{rm}$ is the number of DALYs caused by a specific pathogen and attributable to red meat consumption per 100,000 population in France;
- $DALY.EURA_p$ is the number of DALYs in the "EUR A" region due to the pathogen per 100,000 population from WHO [11];
- $DALY.case_p$ is the number of DALYs in the Netherlands due to the pathogen per 1,000 cases;
- Pop_{2010} is the 2010 population in France (62,765,235).

To compare the disease severity from any pathogen, considering the type of sequelae and their duration, the DALYs per case was estimated by dividing the number of DALYs by the number of cases.

2.4. Uncertainty propagated in the model

In literature and report, the data were expressed by their median values and corresponding 95% confidence intervals (CIs). Therefore, the probability distributions were re-built using these initial data, as explained hereafter:

- The number of foodborne disease cases was extracted from a previous study [12], specifically the median value of the estimations and the associated 95% CI. These data were integrated into our model with a lognormal distribution, which was the same distribution law used by Van Cauteren et al. [12]. The latter study did not specify whether this confidence interval reflected uncertainty or variability. Therefore, it was considered to represent uncertainty. The mean was approximated by the median value reported (on a ln scale), the standard deviation was estimated by using the interval confidence bounds. As an example, for *Campylobacter* spp., the estimated median incidence from Van Cauteren et al. study [12] was 392,177 with a confidence interval between 215,216 at the 5% limit and 862,747 at the 95% limit. The mean of the lognormal distribution was estimated to 12.88 and to match the confidence interval bounds, the standard deviation was approximated to 0. 375. This gave a lognormal distribution with a 5^{th} percentile of 12.27 and a 95^{th} percentile of 13.51. Once expressed in cell count, this interval was close to the one given in Van Cauteren et al. [12].

- The attribution fraction of foodborne illnesses per pathogen and type of meat followed a beta distribution; the available mean or the median was used to estimate the beta distribution parameters. When the value of the attributable proportion was expressed by the mean, the parameters were estimated using the equation mean=$\alpha/(\alpha+\beta)$. When the value of the attributable proportion was expressed by the median, the parameters were estimated using the equation median=$(\alpha-1/3)/(\alpha+\beta-2/3)$. Therefore, the values of α and β were estimated by approximation. As an example, for *Campylobacter* spp., the median of the attributable fraction from beef was 0.16 with a confidence interval between 0 at the 5% limit, and 0.37 at the 95% limit [18]. The best fit of α and β parameters were 3 and 14.3, respectively. This resulted to an estimation of beef *Campylobacter* spp. attribution by a beta distribution having a median of 0.16, a 5^{th} percentile of 0.05 and a 95^{th} percentile of 0.34, close to results given in Hoffmann et al. [18].

- Finally, the probability distributions of DALY, acquired from the literature, were assumed to follow normal distributions.

The implementation of the inputs in the model are represented in Table 1. Our models used 10,000 iterations to capture the uncertainty. This action was performed using R software (version 3.6.2). To verify the stability of the outputs, three simulations were performed. The variation between these three simulations was less than 5% for the mean of the DALY whatever the pathogen and type of meat.

3. Results

3.1. Main microbiological hazards associated with red meat consumption

From our literature search, 16 foodborne pathogens were identified to be involved in foodborne diseases associated with red meat consumption:

- 12 bacteria: *Bacillus cereus*, *Brucella* spp., *Campylobacter* spp., *Clostridium botulinum*, *C. perfringens*, Shiga-toxin producing *Escherichia coli* (STEC), *Listeria monocytogenes*, *Salmonella* spp. (mostly *Salmonella enterica*), *Shigella* spp., *S. aureus*, *Vibrio* spp. and *Yersinia* spp.;
- Two viruses: hepatitis E and norovirus;
- Two parasites: *Taenia saginata* and *Toxoplasma gondii*.

Some of these pathogens were discarded according to the criteria described below.

- *B. cereus*, *Shigella* spp., *Vibrio* spp. and *T. saginata* were excluded due to the lack of data about the proportion attributable to red meat. *Brucella* spp. was excluded due to the lack of information about the number of French cases. *C. botulinum* was excluded due to the lack of quantified DALYs.
- Foodborne illnesses due to *L. monocytogenes* and *Yersinia* spp. were not considered because these pathogens were mostly associated with ready-to-eat foods [22,23].

After the above exclusions, the selected pathogens associated with red meat consumption were *Campylobacter* spp., *C. perfringens*, *S. enterica*, *S. aureus,* STEC, *T. gondii*, hepatitis E virus and norovirus.

3.2. Estimation of the foodborne disease burden in France

In France, the number of foodborne diseases due to red meat consumption was estimated to have a mean of 670 [95% CI = 380–1100] illness cases per 100,000 inhabitants. *Campylobacter* spp. was responsible for 32% of foodborne incidents due to red meat consumption, with a mean of 210 [95% CI = 50–520] cases per 100,000 population (Figure 1). *C. perfringens* was the second pathogen responsible of the highest number of cases with a mean of 150 [95% CI = 40–420] cases per 100,000 population, followed by non-typhoidal *S. enterica* with a mean of 110 [95% CI = 30–280] per 100,000 population. The least frequent foodborne pathogen was *T. gondii*, which contributed to 12 [95% CI = 4–25] cases (estimated mean values) per 100,000 population. The pathogen that induced the highest mortality was non-typhoidal *S. enterica*, with a mean of 0.04 [95% CI = 0.01-0.10] death per 100,000 population (Table 2), followed by hepatitis E, *T. gondii* and *Campylobacter* spp., with means of 0.02 death per 100,000 population (Figure 2). The total number of deaths was estimated to a mean value of 0.12 [95% CI = 0.07–0.19] per 100,000 population.

Our study estimated a mean of 39 [95% CI = 8–71] DALYs per 100,000 population due to foodborne diseases in France. The major contributor to the loss of years in good health from red meat consumption in France was hepatitis E (mean: 33 [95% CI = 1–64] DALYs per 100,000 population), specifically due to pork consumption, even though it was ranked fourth in terms of the overall incidence of foodborne illnesses from red meat consumption (Table 2, Figure 1 and Figure 3). The main bacteria associated with burden of disease in terms of DALY from pork consumption were non-typhoidal *S. enterica*, which was three times higher than *C. perfringens* or *Campylobacter* spp. For beef, the main bacteria contributor of foodborne burden was *Campylobacter* spp., *C. perfringens,* STEC and non-typhoidal *S. enterica* (Table 2).

The severity of each pathogen was estimated by dividing the number of DALY by the number of cases. As an example, the severity of *T. gondii* per case was estimated by dividing the number of DALY per 100,000 population (3.86 DALY) by the number of cases per 100,000 population (12 cases). The most severe pathogen per case was hepatitis E, with 0.46 DALY per case, followed by *T. gondii* (0.32 DALY per case), STEC (0.02 DALY per case) and non-typhoidal *S. enterica* (0.01 DALYs per case). *C. perfringens*, *Campylobacter* spp. and *S. aureus* had similar impacts in terms of severity, with 0.003 DALY per case. The least severe pathogen was norovirus, with 0.002 DALY per case.

4. Discussion

The first objective of the present study was to aggregate data available in the literature to identify and characterise the main microbiological hazards when consuming red meat in France. These sources included muscle and offal from beef, pork and other small ruminants, but not dairy products. Subsequently, a risk assessment model was built to estimate the associated number of foodborne illnesses and deaths. Finally, the goal was to estimate the consequent burden of diseases, considering the severity of the illness, and perform further comparisons with other health effects and compare consumption scenarios.

From the literature search, 17 foodborne pathogens were identified as involved in foodborne diseases attributable to red meat consumption. This number was less than the main zoonotic agents identified by Haddad et al. [24], who identified more than 31 agents from red meat, but those authors included additional transmission pathways of infection (e.g. occupational transmission, animal bites, etc.). A team from the Centre d'Information des Viandes (Meat Information Center) identified four bacterial diseases associated with meat product consumption (foodborne outbreaks, listeriosis, botulism and haemolytic uraemic syndrome [HUS]), three parasitic diseases (taeniasis, toxoplasmosis and trichinellosis) and one viral disease (hepatitis E) [25]. However, for *L. monocytogenes* and *C. botulinum* identified in that study, the main meat products were processed and consumed without pre-cooking [25]. In 2014, ANSES classified the main hazard-food pathogen couples. Meat was associated with STEC, *T. gondii*, non-typhoidal *Salmonella* spp., *Y. enterocolitica* and *T. saginata*. *Campylobacter* was mostly from poultry meat and hepatitis E with raw pork liver [23].

The incidence, attribution source and data availability were considered when selecting the pathogens to quantify the disease burden due to red meat consumption. Eight pathogens were selected for this study: *Campylobacter* spp., *C. perfringens*, non-typhoidal *S. enterica*, STEC, *S. aureus, T. gondii*, hepatitis E and norovirus. In the Netherlands, 12 pathogens were identified for red meat—including beef, lamb and pork—with the same criteria. In addition to the pathogens chosen in our study, *L. monocytogenes*, rotavirus, *C. parvum* and *Giardia lamblia* were considered in that study [26].

To estimate the attribution of foodborne diseases to red meat consumption, our estimations were mostly based on WHO data, which aggregated the judgments from 73 international experts [18]. Hereby, per 100,000 inhabitants, our study's estimated number of cases was 670 [95% CI = 380–1,100] illnesses, 0.12 [95% CI = 0.07–0.19] deaths and 39 [95% CI = 8–71] DALYs. These latter figures corresponded to 418,380 [95% CI = 238,480–691,800] illnesses, 73 [95% CI = 41–118] deaths and 24,750 [95% CI =4,900-–44,720] DALYs for the French population per year. Knowing the total number of foodborne illnesses estimated by the WHO in EUR A region [11,27] (2431 cases per 100,000 population) and the sum of the mean number of illnesses cases associated with *Campylobacter* spp., non-typhoidal *S. enterica*, STEC and *T. gondii*, attributable to red meat estimated here (353 per 100,000 French population), it could be concluded that *Campylobacter* spp., non-typhoidal *S. enterica*, STEC and *T. gondii* in red meat accounted for 15% of the total foodborne illnesses estimated. These pathogens infection associated with red meat also accounted for 16% of the total deaths and 15 % of the total DALYs due to foodborne pathogens

From our estimations, the major contributor of foodborne illness cases attributable to red meat consumption was *Campylobacter* spp. This pathogen has been the most commonly reported hazard that induced gastrointestinal issues in the European Union since 2005 [22]. Indeed, infection with this pathogen may cause diarrhoea, abdominal pain, bloody stools, fever, headaches, vomiting and acute enteritis. Moreover, campylobacteriosis was responsible for 30.1% of the total cases of Guillain-Barré syndrome according to a WHO study [28]. Even though the main reservoir of *Campylobacter jejuni* is birds—including poultry—beef and pork can also serve as a *Campylobacter* reservoir (essentially *Campylobacter coli*) [29]. In 2017, the EFSA/ECDC reported that 51% of the strong-evidence foodborne outbreaks caused by *Campylobacter* were due to milk consumption, versus 3% for meat and meat products (excluding strong-evidence waterborne outbreaks) [10]. However, this pathogen was reported to be present in fresh pork and beef meat (8.3% of positive units) [10]. In addition, in our study, it was estimated that 30% of foodborne illnesses from red meat were due to *Campylobacter* spp., from which 55% were attributable to beef meat. In terms of incidence, it was also determined that the second pathogen inducing the highest number of cases was *C. perfringens* (22%), followed by non-typhoidal *S. enterica* (17%) and hepatitis E (11%). *S. aureus* accounted for 6% of the cases related to red meat consumption.

The proportion of foodborne illnesses associated with the distinct pathogens in our study was different from Dutch studies. Indeed, in the same years in the Netherlands, the National Institute for Public Health and the Environment (RIVM) estimated that *C. perfringens* was the major contributor of foodborne illness from red meat consumption, with 56% of foodborne illness cases [26]. Moreover, the proportion of *Campylobacter* spp., *S. aureus* and *S. enterica* cases were approximately two-times higher in our study compared to the Dutch studies [20,30]. The strategy used to estimate incidence of foodborne illnesses in Van Cauteren et al. [12] was not the same as the Dutch studies. The former used an underestimation factor to calculate the number of illness from the reported cases [12], while the Dutch study based the incidence estimates for gastro-enteritis on population-based cohort studies [30]. Moreover, the disease surveillance system coverage is not the same in France as in the Netherlands, a factor that makes comparison difficult. For example, the campylobacteriosis and salmonellosis surveillance system coverage in 2016 was estimated to be 20% and 48%, respectively, in France, versus 52% and 64%, respectively, in the

Netherlands [10]. In addition, the list of mandatory notifiable infectious diseases is not the same for all countries. For instance, STEC infection is required to be reported in the Netherlands but not in France [10].

Among microbiological hazards relevant to beef consumption, STEC is the most studied[31]. In 2010, 122 cases of HUS, which is characterised by acute kidney and renal failure in young children [32], were reported in France [23] following STEC ingestion from ground beef [23,33]. Ground beef is considered the most common source of STEC foodborne illnesses, along with raw milk [23]. In a previous report, ANSES estimated a probability of HUS between 0.02 and 0.05 of illness after STEC infections [34]. In our estimations, 19 cases per 100,000 population were due to STEC infections attributable to red meat consumption, from which the incidence due to beef consumption was estimated at 14 [3–34] per 100,000 population. This finding suggests between 0.3 (14 x 0.02) and 0.7 (14 X 0.05) HUS cases per 100,000 population are attributed to beef. In other words, between 190 and 440 HUS cases in France in 2010 resulted from beef consumption. The slightly lower number of HUS cases reported in 2010 (122) compared with our beef estimations (190–440) might be due to under-reporting because there is no surveillance of the whole population. Rather, only individuals less than 15 years old are monitored [23]. Indeed, in Havelaar et al., 72% of all HUS cases were in individuals under 15 years of age [35]. If we assumed the same proportion distribution as in the Dutch study, then the HUS estimation reported in 2010 in France (122) would be around 170 cases, which is close to the lower bound of our estimations.

The major contributor of deaths due to red meat consumption was non-typhoidal *S. enterica* associated with pork, followed by hepatitis E, *T. gondii* and *Campylobacter* spp. In terms of DALYs, hepatitis E was responsible for the highest loss of years in good health resulting from consumption of red meat. In France, this loss was exclusively due to pork meat, specifically pork liver. After hepatitis E, *T. gondii* and non-typhoidal *S. enterica* were responsible for the greatest loss of years in good health. This reversal of ranking can be explained by an overestimation of the hepatitis E severity. Indeed, the majority of the DALYs estimated for hepatitis E by the Dutch team were from deaths [30]. However, the proportion of deaths due to this virus in the Netherlands (1.4% [30]), which was the reference study, was higher than that observed in France (0.03% [12]). Havelaar et al. [30] assumed that mortality from hepatitis E resulted in 33.4 years of life lost. Therefore, if we considered mortality in France (0.02 deaths [95% CI: 0–0.04] per 100,000 population) and the number of years lost from hepatitis E estimated by the Dutch study, the most probable DALY from hepatitis E in France would be 0.7 per 100,000 population.

Without considering hepatitis E, the mean number of DALYs due to consumption of red meat muscle was 6.6 [95% CI: 3.4–11.1] per 100,000 population, from which 2.8 [95% CI: 1.2–5.2] per 100,000 population were associated with beef meat. Pork meat accounted for 1.5 [95% CI: 0.4–3.8] DALYs per 100,000 population per year. These values were of the same order of magnitude as the estimations from the Netherlands based upon the following calculations: 934 DALY for beef & lamb and 1280 DALY for pork in 2012 for the all Netherlands population [26] (16.73 million of inhabitants considered according Eurostat), corresponding to 5.6 DALYs per 100,000 population and 7.7 DALYs per 100,000 population, respectively

T. gondii infection was ranked second in terms of DALYs. The burden of this parasite might affect the general population (but mostly in a benign form). The most severe forms in France, including deaths, concern immunosuppressed populations (acquired form) [36,37] [38]; congenital forms have a lower effect on burden. In fact, in the French population, pregnant women are very aware of the toxoplasmosis risk, and blood samples are taken from the beginning of pregnancy for the detection of immunisation following possible contamination. Indeed, it is one of the four infectious diseases—with rubella, syphilis and hepatitis B and maternal anti D-fetal allo—for which screening is mandatory. This protocol has been a part of prenatal screening programmes in France since the late 1970s [39]. Almost all of the congenital forms of *T. gondii* infection are identified in France, in contrast to other European countries where the screening is not performed or is not mandatory [40]. When fetal infection occurs, the treatment against toxoplasmosis infection in utero was demonstrated to allow children to have a similar quality of life to those not infected [41]. The proportion of congenital toxoplasmosis sequela in France might be lower than estimated by WHO [11,28]. Therefore, the burden estimated in our study is likely to be overestimated.

In this study, red meat consumption was responsible for a mean of 0.37 [95% CI: 0.10–0.77] DALY per 100,000 population from STEC infection. This value corresponded to a mean of 232 [95% CI: 62–489] DALYs annually for the population in France*,* which is one-half the DALYs estimated by the ANSES (465 years in good health lost) [33]. This discrepancy might be due to the higher proportion of deaths considered by the BCoDE toolkit, which was used for the ANSES estimations, compared to the proportion of deaths considered for the 2015 WHO estimations. However, we could not use the BCoDE toolkit for comparison with our estimations due to the lack of foodborne illness incidence data per age class and gender, which is required for BCoDE estimations. The estimations from Havelaar et al. [35] were also higher than ours, even though the considered disability weight was lower than the one used by the WHO (0.123 versus 0.210, respectively). This finding might be explained by the duration of the sequelae, which was considered to be longer in the Dutch's study, i.e. 1 year against 28 days in the Hoffmann study [28,35].

Using existing studies in the literature allowed us to estimate the number of cases and deaths and the foodborne disease burden in France attributable to red meat consumption, without generating new data with additional monitoring costs. The estimations might be improved by considering the effect of age on outcomes of foodborne diseases, such as sequela and mortality. Indeed, if deaths or permanent sequela occur during childhood, the number of years lost will be higher than if death occurs at an advanced age. However, this estimation was not possible in this study because all the information was given for a global population.

The study by Hoffmann et al. [18] was chosen to determine the attribution fraction of a pathogen to a red meat type because it is the most recent and reliable study conducted by the WHO with expert elicitation. Although it did not specifically refer to France, data from the "EUR A" region included France. Nevertheless, we are aware that the estimations provided by this study are somewhat different from other published estimates [18]. This discrepancy introduced unquantifiable uncertainty into our results. Moreover, to increase the reliability of this work, the existing French attribution study might be updated. Additionally, considering other red meat types, including a larger number of pathogens selected and separate attribution of unprocessed and processed red meat types, might improve the reliability.

Our study estimates the number of foodborne illnesses and DALYs dedicated to red meat in France, with French incidence data. In terms of foodborne bacteria, for beef and pork meat, *Campylobacter* spp., non-typhoidal *Salmonella enterica*, *C. perfringens* and STEC represented a mean of 2.2 [95% CI = 1.0–4.0] DALYs per 100,000 individuals per year. Overall, the estimations provided in this study might help authorities to focus on these hazards and ultimately reduce their impact on the health of the French population.

With the use of the DALY metric, we were able to compare our estimates to include the effects of other foods components on health. The burden estimated in this study was lower than the burden caused by diet high in sugar-sweetened beverages (46 DALYs [95% CI = 15–83] per 100,000 population) and the use of alcohol (1,818 [95% CI = 1,359–2,368] DALYs per 100,000 population) [42]. In future studies, the microbiological burden will be balanced by nutritional risks and benefits brought by red meat consumption in a broader risk-benefit assessment as done by other studies [43-45]. It was recently estimated that a mean of 19 [95%

CI = 8–33] DALYs per 100,000 people per year were due to colorectal cancer, and a mean of 21 [95% CI = 12–32] DALYs per 100,000 people per year due to cardiovascular disease, were associated with the consumption of red meat [46]. Red meat consumption does have some benefits with regard to the nutrients it provides, especially iron, which may help decrease the major nutritional deficiency in the world [47]. This condition accounts for a mean of 16 [95% CI = 11–20] DALYs per 100,000 individuals per year [48].

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Figure captions:

Fig. 1. Mean number of foodborne cases per 100,000 French population per year and per pathogen attributable to red meat estimated in this study. The full lines represent the 95% uncertainty around the mean value.

Fig. 2. Mean number of deaths per 100,000 French population per year and per pathogen attributable to red meat estimated in this study. The full lines represent the 95% uncertainty around the mean value.

Fig. 3. Mean number of disease-adjusted life years (DALYs) per 100,000 French population per year and per pathogen attributable to red meat estimated in this study. The full lines represent the 95% uncertainty around the mean value.

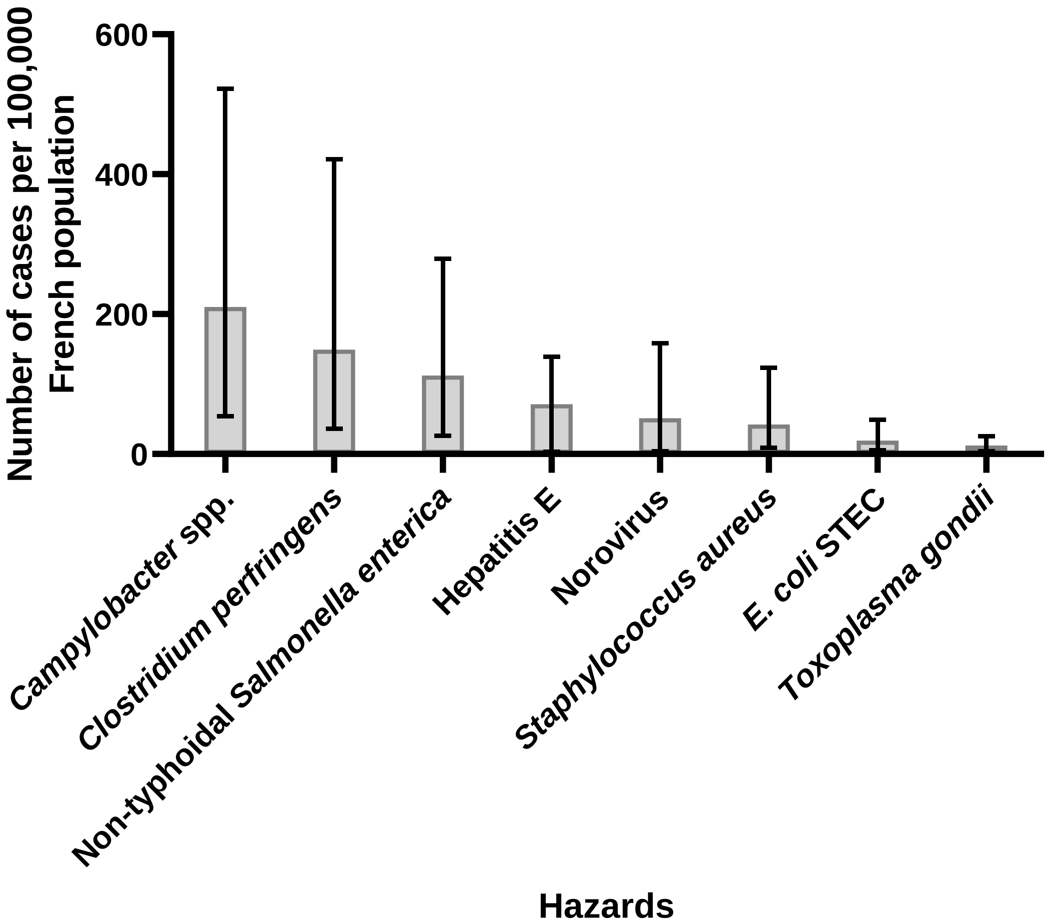
Table 1: Implementation of the model inputs per hazard in the quantification model and data sources.

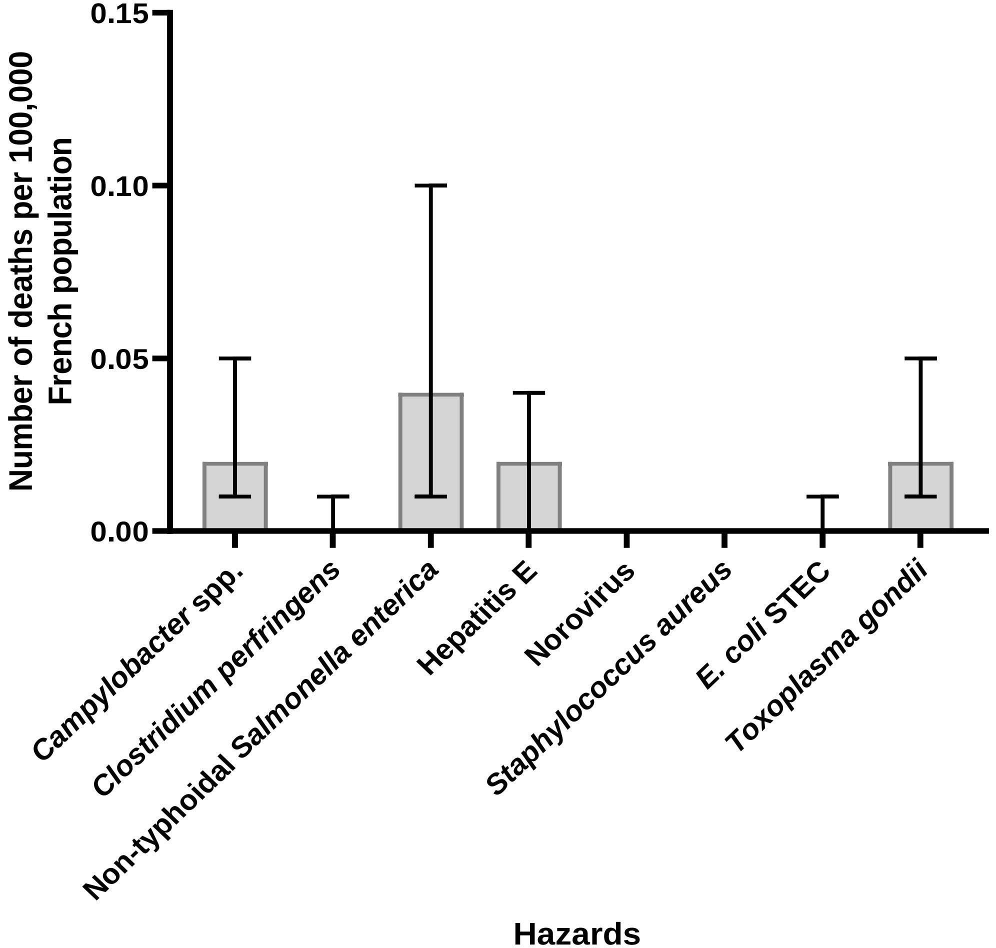
Characteristic	Initials	Equations	Distribution or deterministic value implemented	Hazard	Values implemented per type of hazard and meat[1]			Reference from which raw data was obtained
Number of illness cases	$Ncases.F_p$	(1)	$LogNormal(\mu, \sigma)$	*Campylobacter* spp.		μ = 12.88	σ = 3.75×10^{-1}	[12]
				Non-typhoidal *Salmonella enterica*		μ = 12.12	σ = 3.55×10^{-1}	
				Staphylococcus aureus		μ = 11.20	σ = 6.5×10^{-1}	
				Shiga-toxin producing *Escherichia coli* (STEC)		μ = 9.79	σ = 4.60×10^{-1}	
				Clostridium perfringens		μ =11.69	σ = 6.00×10^{-1}	[12]
				Hepatitis E		μ =10.99	σ = 2.45×10^{-1}	
				Norovirus		μ =13.16	σ = 1.50×10^{-1}	
				Toxoplasma gondii		μ =9.37	σ = 2.00×10^{-1}	
Proportion of foodborne diseases attributable to red meat	PA	(1), (2) and (3)	$Beta(\alpha, \beta)$	*Campylobacter* spp.	Beef	α = 3	β = 14.3	[18]
					Pork	α = 1	β = 10.78	
					Other	α = 1	β = 16.33	
				Non-typhoidal *Salmonella enterica*	Beef	α = 0.7	β = 9.13	
					Pork	α = 2.5	β = 7.19	
					Other	α = 0.8	β = 23.2	
				Staphylococcus aureus	Beef	α = 200	β = 954	[49]
					Pork	α = 15	β = 107,95	
				Shiga-toxin producing *Escherichia coli* (STEC)	Beef	α = 5	β = 6.8	[18]
					Pork	α = 0.5	β = 5.72	
					Other	α = 1.1	β = 9.15	
				Clostridium perfringens	Beef	α = 8.5	β = 13.52	[49]
					Pork	α = 240	β = 655.52	
				Hepatitis E	Pork	α = 0.74	β = 0.26	[20]
				Norovirus	Beef and Lamb	α = 1	β = 32.3	
					Pork	α = 0.6	β = 19.4	
				Toxoplasma gondii	Beef	α = 2.5	β = 6.96	[18]
					Pork	α = 1	β = 5.72	
					Other	α = 1.6	β = 5.4	
Proportions of deaths after foodborne illness	$Rdeath.F_p$	(3)	Deterministic value	*Campylobacter* spp.		1.04×10^{-4}		[12]
				Non-typhoidal *Salmonella enterica*		3.66×10^{-4}		
				Staphylococcus aureus		0.16×10^{-4}		
				Shiga-toxin producing *Escherichia coli* (STEC)		2.23×10^{-4}		
				Clostridium perfringens		0.17×10^{-4}		[12]
				Hepatitis E		3.03×10^{-4}		
				Norovirus		0.15×10^{-4}		
				Toxoplasma gondii		18.67×10^{-4}		
Number of DALYs per 100,000 population	$DALY.EURA$	(3)	$Normal(\mu, \sigma)$	*Campylobacter* spp.		μ = 10	σ = 2.04	[28]
				Non-typhoidal *Salmonella enterica*		μ = 12	σ = 2.81	
				Shiga-toxin producing *Escherichia coli* (STEC)		μ = 0.6	σ = 2.04×10^{-1}	
				Toxoplasma gondii		μ = 6	σ = 1.53	
Number of DALYs per case	$DALY.case$	(3)	Deterministic value	*Staphylococcus aureus*		2.6×10^{-3}		[30]
				Clostridium perfringens		3.2×10^{-3}		
				Hepatitis E		4.6×10^{-1}		
				Norovirus		2.5×10^{-3}		

[1] Following R parametrisation: μ = mean; σ = standard deviation; α = shape 1 of the beta distribution, β = shape 1 of the beta distribution

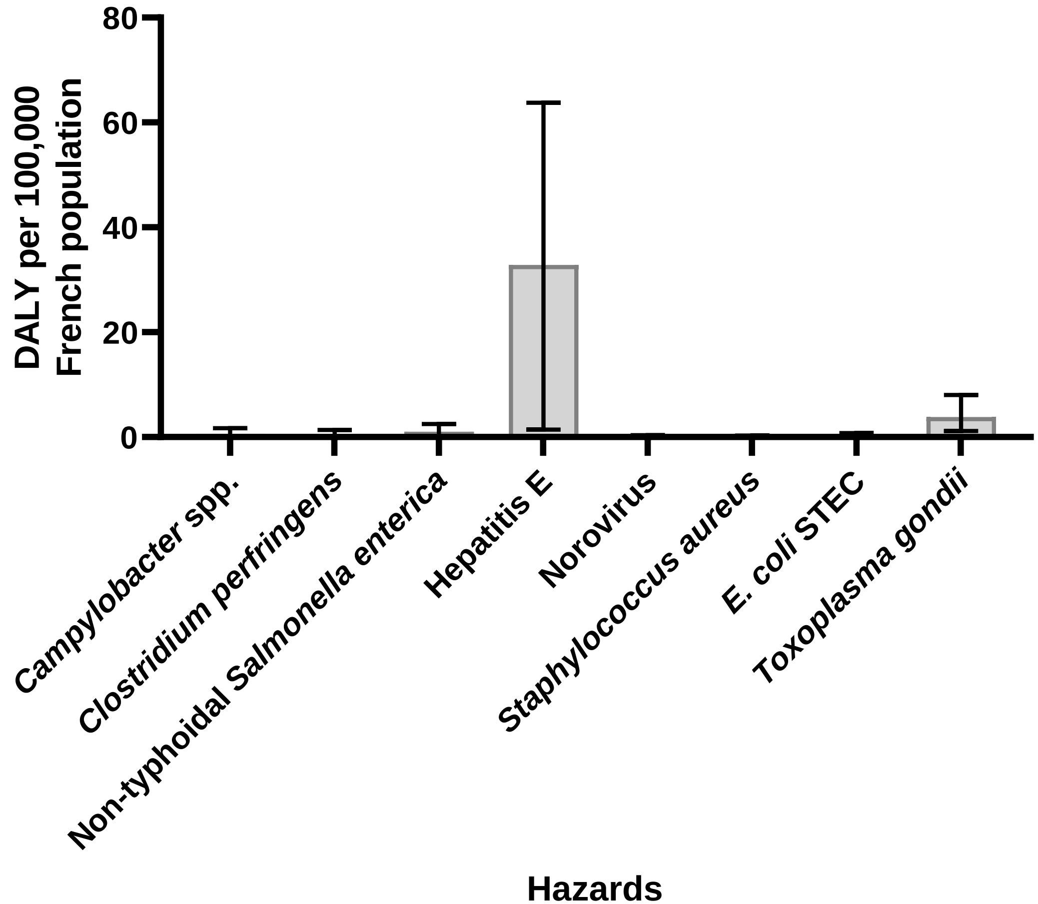
Table 2: Mean deaths and diability-adjusted life years (DALYs) per 100,000 population attributable to red meat estimated in this study. The means are presented with the 2.5 and 97.5 percentiles in parentheses.

Hazard	Beef		Pork		Other small ruminants	
	Deaths	DALY	Deaths	DALY	Deaths	DALY
***Campylobacter* spp.**	0.012 (0.002–0.033)	0.37 (0.04–1.03)	0.006 (0–0.023)	0.18 (0–0.74)	0.004 (0–0.015)	0.12 (0–0.49)
Non-typhoidal *Salmonella enterica*	0.008 (0–0.035)	0.20 (0–0.88)	0.029 (0.005–0.078)	0.73 (0.10–1.89)	0.004 (0–0.016)	0.0.9 (0–0.41)
Staphylococcus aureus	0 (0–0.001)	0.07 (0.01–0.19)	0 (0–0.001)	0.05 (0.01–0.14)	-	-
Shiga-toxin producing *Escherichia coli* (STEC)	0.003 (0.001–0.008)	0.25 (0.06–0.53)	0 (0–0.001)	0.05 (0–0.24)	0.001 (0–0.003)	0.07 (0–0.23)
Clostridium perfringens	0.001 (0–0.004)	0.28 (0.06–0.83)	0.001 (0–0.003)	0.20 (0.05–0.54)	-	-
Hepatitis E	-	-	0.023 (0.001–0.042)	32.82 (1.46–63.79)	-	-
Norovirus	0 (0–0.001)	0.06 (0–0.23)	0 (0–0.002)	0.06 (0–0.29)	-	-
Toxoplasma gondii	0.009 (0.001–0.022)	1.59 (0.29–3.82)	0.005 (0–0.018)	0.90 (0.03–3.51)	0.008 (0.001–0.022)	1.37 (0.13–3.79)
Total	0.035 (0.015–0.068)	2.80 (1.24–5.19)	0.064 (0.026–0.119)	34.96 (3.58–66.69)	0.017 (0.005–0.037)	1.65 (0.33–4.12)


Number of cases per 100,000
French population
600
400
200
0
Campylobacter spp.
Clostridium perfringens
Non-typhoidal Salmonella enterica
Hepatitis E
Norovirus
Staphylococcus aureus
E. coli STEC
Toxoplasma gondii
Hazards



Number of deaths per 100,000 French population
0.15
0.10
0.05
0.00
Campylobacter spp.
Clostridium perfringens
Non-typhoidal Salmonella enterica
Hepatitis E
Norovirus
Staphylococcus aureus
E. coli STEC
Toxoplasma gondii
Hazards


DALY per 100,000
French population
80
60
40
20
0
Campylobacter spp.
Clostridium perfringens
Non-typhoidal Salmonella enterica
Hepatitis E
Norovirus
Staphylococcus aureus
E. coli STEC
Toxoplasma gondii
Hazards