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Quantitative risk assessment for *Escherichia coli* O157:H7 in frozen ground beef patties consumed by young children in French households

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ABSTRACT

A quantitative risk assessment for *Escherichia coli* O157:H7 in frozen ground beef patties consumed by children under 10 years of age in French households was conducted by a national study group describing an outbreak which occurred in France in 2005. Our exposure assessment model incorporates results from French surveys on consumption frequency of ground beef patties, serving size and consumption preference, microbial destruction experiments and microbial counts on patties sampled from the industrial batch which were responsible for the outbreak. Two different exposure models were proposed, respectively for children under the age of 5 and for children between 5 and 10 years. For each of these two age groups, a single-hit dose-response model was proposed to describe the probability of hemolytic and uremic syndrome (HUS) as a function of the ingested dose. For each group, the single parameter of this model was estimated by Bayesian inference, using the results of the exposure assessment and the epidemiological data collected during the outbreak. Results show that children under 5 years of age are roughly 5 times more susceptible to the pathogen than children over 5 years. Exposure and dose-response models were used in a scenario analysis in order to validate the use of the model and to propose appropriate guidelines in order to prevent new outbreaks. The impact of the cooking preference was evaluated, showing that only a well-done cooking notably reduces the HUS risk, without annulling it. For each age group, a relation between the mean individual HUS risk per serving and the contamination level in a ground beef batch was proposed, as a tool to help French risk managers.

1. Introduction

Shiga toxin-producing *Escherichia coli* (STEC) are linked to a large number of outbreaks and sporadic cases of human infections reported in many countries. *E. coli* O157:H7 seems to be responsible for roughly half of the reported cases and patients with O157:H7 infection are more likely to develop severe clinical manifestations such as hemolytic uremic syndrome (HUS) than patients with non-O157:H7 infection (CDC, 2007; Espié et al., 2007). HUS is the most common cause of acute renal failure in children and occurs preferentially among children under 10 years (Liu et al., 2007; Razzaq, 2006). In France, 73 to 105 HUS sporadic cases were reported each year over the last 10 years among children under the age of 15 (Espié et al., 2007). Among these cases, 78.7% of patients were children under 5 years of age and 16.1% children between 5 and 10 years of age. In a case-control study performed on the HUS cases reported in 2000 and 2001, the consumption of undercooked ground beef patties was identified as a significant risk factor (Espié et al., 2003). Moreover in 2005, an outbreak of *E. coli* O157:H7-associated illness occurred in France. This outbreak was linked to the consumption of frozen ground beef patties. Seventeen HUS cases were reported among which ten children under the age of 5, six children between 5 and 10 years and one adult. All the ill persons (HUS or diarrhea cases) had eaten at home frozen ground beef patties from the same industrial batch.

Quantitative microbial risk assessment modeling is now commonly used to evaluate food related health risks, and many studies on the risk associated to *E. coli* O157:H7 in ground beef have been published (Cassin et al., 1998; Lammerding et al., 1999; FSIS, 2001; Nauta et al., 2001; Duffy et al., 2006b). All of them are farm-to-fork studies, including an exposure model from the contamination of the feces of the cattle to the contamination of one serving. In a recent review (Duffy et al., 2006a), it appears that all of them give similar results in terms of risk factors ranking, but differ on their risk predictions. These differences may be partly due to different inputs of the models. Prevalence and concentration of *E. coli* O157:H7 may

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differ between countries, but other inputs such as cooking habits may also differ. The observed differences in risk predictions may also be due to differences in the choice of models, especially of the dose-response model.

Cassin et al. (1998) and Lammerding et al. (1999) use a beta binomial model based on the one developed by Haas (1983) from experimental human infections with *Shigella dysenteriae* (Crockett et al., 1996). The FSIS (2001) and Duffy et al. (2006b) use a model giving both a low and a high estimation of probability of illness, respectively based on an EPEC model and a *Shigella* one (Powell et al., 2000). That model assumes that the virulence of *E. coli* O157:H7 is between the one of the EPECS and the one of *Shigella*. In these four risk assessments, a single dose-response model is used for every consumer, whatever his age, even if the stronger sensitivity to the pathogen of young children is stated in every study. This choice is motivated by the lack of knowledge about the dose-response model for children. Nauta et al. (2001) use two different dose-response models for children and adults, established from data concerning an outbreak that occurred in an elementary school in Japan (Teunis et al., 2004). Both the adult and children models are close to the *Shigella* model and far from the EPEC one which seems to underestimate the human risk of infection. To our knowledge, the model of Teunis et al. (2004) is the only published one which differentiates children and adults, but since the Japanese outbreak occurred in an elementary school, the model applies to children over 5 year old and may still underestimate the risk for younger children. Indeed, the incidence of both *E. coli* O157:H7 infection and HUS is reported to be higher among children under the age of 5, with a median age of children HUS cases around 2 year old (FSIS, 2001; Tozzi et al., 2003; Espié et al., 2007). Other dose-response models were recently built by gathering data from various outbreaks (Strachan et al., 2005; Teunis et al., 2007), but none of them takes into account the age of the consumers.

Moreover, among all the published dose-response models previously cited, some describe the probability of infection, others the probability of illness and some indifferently use outbreak data for infection and illness. None of them directly gives the probability of HUS. As done by Cassin et al. (1998), the HUS risk may be estimated by multiplying the illness probability by a coefficient, but this coefficient fixed at 10% by Cassin et al. (1998) is not well known and may depend on the age (Razzaq, 2006). A mean value of 15% was reported for children under 10 years (Tarr et al., 2005), but this value may be overestimated as the whole number of illness cases is often unknown in epidemiological data. Results from a survey carried out in the Netherlands between 1990 and 2000 suggest a lower value, around 3% for children under 15 years of age (Havelaar et al., 2004). The range of values from 3 to 15% reported by Razzaq (2006) seems thus to be a reasonable summary of the knowledge of that probability and it seems not obvious to assign a unique value to it. As HUS is the most severe specific clinical manifestation of STEC infections, and the more documented one in epidemiological studies, it could be interesting to develop a dose-response model directly giving the probability of HUS.

Our objective was therefore to conduct a quantitative microbiological risk assessment for *E. coli* O157:H7 in frozen ground beef patties consumed by young children (under 10 years of age) in French households. Different models were considered for children under 5 years of age ([0–5]) and children over 5 years of age ([5–10]), both in the exposure assessment and in the hazard characterization. A three-stage approach was considered: (1) an exposure assessment from distribution to consumption by Monte Carlo simulations, (2) a hazard characterization by Bayesian inference using both the results of the exposure assessment and the epidemiological data on the HUS cases reported during the French outbreak and (3) a scenario analysis to validate the use of the model and to suggest appropriate guidelines in order to prevent new outbreaks.

2. Materials and methods

2.1. Exposure assessment

An exposure model was built to describe the French outbreak, covering the food pathway from packaging to consumption (Table 1). The exposure aimed at estimating the number of contaminated products ingested by children under 5 years ($N_{[0-5[}$) and over 5 years ($N_{[5-10[}$) and the respective distributions of the ingested dose of *E. coli* O157:H7 ($D_{[0-5[}$ and $D_{[5-10[}$).

During the outbreak, the ill persons (HUS or diarrhea cases) had eaten at home frozen ground beef patties from the same industrial batch. The patties from this batch were retailed by only one retailer who was able to precisely estimate the number of patties really sold for home consumption and not returned (N_{tot}). The part of these patties consumed by children in each age group ($p_{[0-5[}$ and $p_{[5-10[}$) was estimated by combining data from two French consumer surveys (Fantino, 2005; Lafay et al., 2006) and demographic data (Insee, 2007). The first survey was carried out from January to March 2005 on 706 children from 0 to 3 year old. The second survey was carried out from December 2005 to May 2007 on 4079 persons over the age of 3 among which 482 children under 10 year old. Data collected in these surveys enabled us to estimate a mean consumption of ground beef at home of respectively 26.88, 33.88 and 37.33, 31.31 and 23.30 servings per year in the respective age groups: [0–3[, [3–5[, [5–10[, [10–16[and 16 or more. The values of $p_{[0-5[}$ and $p_{[5-10[}$ were estimated using both these estimations and the French demographic data (Insee, 2007).

The initial concentration of *E. coli* O157:H7 in the identified batch (C) was estimated from microbial detection and counts were performed on 22 frozen patties sampled from the batch. All the samples were positive after enrichment of 25 g of each sample. After plating 0.1 g of each of the 22 patties, we counted resp. 0, 1, and 2

Table 1
Overview of the exposure model and its assumptions

Variable	Description	Distribution	Source or hypothesis
N_{tot}	Total number of contaminated ground beef patties sold	Fixed, 2155	Retailer data
p_{age}	Proportion of total servings consumed by age group	Fixed, 0.0740 for [0–5[, 0.0905 for [5–10[	Consumer surveys and demographic data
N_{age}	Number of servings by age group	Fixed, $N_{tot} \times p_{age}$	Total number of servings = total number of sold patties
C	Initial mean contamination level (CFU g^{-1})	Fixed, 5.9	Experimental data
S_{age}	Serving size (g)	Empirical distribution	Consumer surveys
R_0	Number of decimal reductions due to raw consumption	Fixed, 0	Evidence
R_1	Number of decimal reductions due to "rare" cooking	Uniform (0, 0.9)	Experimental data
R_2	Number of decimal reductions due to "medium" cooking	Uniform (0.2, 1.4)	Experimental data
R_3	Number of decimal reductions due to "well-done" cooking	Uniform (1.2, 2.8)	Experimental data
CP_{age}	Consumption preference (0=raw, 1=rare, 2=medium, 3=well-done)	Discrete (n, p) with n={0, 1, 2, 3}, p={0, 0.097, 0.41, 0.493} for [0–5[, p={0.008, 0.166, 0.540, 0.286} for [5–10[	Consumer survey
D_{age}	Ingested dose (CFU for a serving)	Poisson (λ) with $\lambda_{age} = C \times 10^{-R_{CP_{age}}} \times S_{age}$ for each age group	Homogeneous distribution of the cells

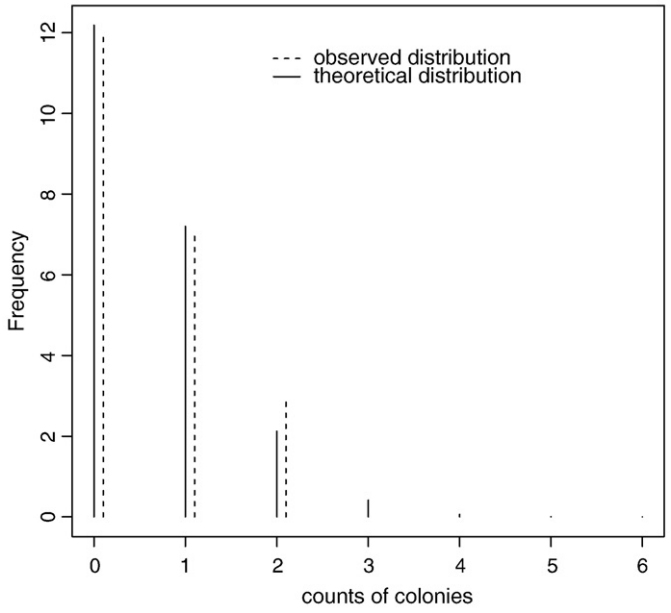

Fig. 1. Observed and theoretical distribution of *E. coli* O157:H7 colonies counted from the 22 frozen ground beef 0.1 g samples from the French outbreak.

colonies (resp. from 12, 7 and 3 patties). These results were consistent with the assumption of a Poisson distribution of the number of cells in a given portion of ground beef, with a mean concentration of $C = 5.9$ UFC g^{-1}, estimated by the moment method. No significant difference was observed between observed values and theoretical values plotted on Fig. 1, using a chi-squared goodness-of-fit test. Hence, the use of the simple Poisson distribution seems to be a reliable procedure for describing the observed data. Indeed, as concluded in a recent study (Toft et al., 2006), data did not allow us to observe any overdispersion of contamination. Moreover the C estimation was precise enough: a Bayesian estimation, based on both detection results and microbial counts on the 22 samples, with a vague prior on C ($\log_{10} C$ between −3 and 3), gave a narrow 95% credibility interval of [3–9 CFU g^{-1}].

Although a variety of scientific literature has been published on the modeling of *E. coli* O157:H7 thermal destruction in ground beef, none of it could be used to describe thermal destruction occurring from the use of a frying pan to cook meat in. This is the most popular way of cooking in French households. A consumer survey was thus conducted by the AFSSA study group, based on 4 photos of ground beef patties, illustrating different consumption preferences (0: raw, 1: rare, 2: medium, 3: well-done). The three photos of cooked patties were obtained after cooking in a frying pan with one turnover. Children of 6 to 15 years of age or parents of young children of 0 to 6 years of age were interviewed in elementary schools and child care centers with regards the consumption preferences corresponding to home consumption of ground beef patties. The survey was carried out from June to September 2005 in 16 different departments of continental France, detailed results are presented in the study report (available upon request, in French). The distribution of the consumption preference (CP), reported in Table 1, was thus estimated from respectively 144 answers from the age group [0–5[and 241 answers from the age group [5–10[.

Microbial decimal reductions R_i were associated with each of the four consumption preferences. R_0, the decimal reduction for raw consumption, was assumed to be nil. R_1, R_2 and R_3, the decimal reductions for rare, medium and well-done cooking preferences, were deduced from the results of microbial destruction experiments. Industrial fresh raw ground beef (15% fat, 4.05 $\log_{10}$ CFU $g^{-1}$of mesophilic aerobic flora, pH 5.79) was obtained from a local retail market. It was inoculated with a preculture of *E. coli* O157:H7 strain C267 in stationary phase (9.26 $\log_{10}$ CFU mL^{-1}) and gently mixed using a sterile Kitchen Aid mixer bowl, to achieve a theoretical initial contamination level of 7.26 $\log_{10}$ CFU g^{-1} in the meat. From the inoculated mixture, 100 g-patties were made by using a sterile metallic patty mold. The meat was pressed, flattened and reshaped in the patty mold. Patties were then frozen at −24 °C. The patties were then cooked unfrozen in a frying pan on an electric cooking plate (1500 W). The plate was preheated at a temperature of ca. 280 °C, and the pan with 7 mL of oil at an internal temperature of ca. 180 °C. Eighteen patties were individually cooked in the pan for 4 to 10.5 min, with one turnover at mid-time. Nine cooking times were tested in a random order. Immediately after each cooking, the patty was cut in 2 halves and 7 people compared the patty to the photos according to three criteria: color of the inner meat, dry aspect of the inner meat, and thickness of the brown external meat. Immediately after the visual judgment, each patty was stored 30 min at −18 °C to achieve rapid cooling and then transferred at +3 °C till microbial analysis. Both halves of a patty were diluted (1:1) in buffered 0.1% peptone solution and homogenized using a Stomacher lab-blender. After a 45-minute revivification step, serial dilutions of the slurry were made in buffered 0.1% peptone solution and plated onto sorbitol MacConkey agar. The initial contamination level was checked for 7 uncooked thawed patties. The mean result, 7.25 $\log_{10}$ CFU g^{-1}, with a standard deviation 0.08 $\log_{10}$ CFU g^{-1}, was consistent with the theoretical contamination level. Detailed results for the 18 cooked patties deduced from this initial contamination level are presented in the study report (available upon request, in French). From these results, uniform distributions were assumed for R_1, R_2 and R_3, see Table 1.

The distribution of the ground beef serving size (S) was characterized from 488 values corresponding to 488 ground beef intakes by children under 10 year old, reported in the two French consumer surveys previously described (Fantino, 2005; Lafay et al., 2006).

Finally the dose D (ingested dose of *E. coli* O157:H7) for each serving was assumed to follow a Poisson distribution of mean $\lambda = C \times 10^{-R_{CP}} \times S$ (CFU per serving). From this model, the distribution of the dose D was computed by Monte Carlo simulations (100,000 iterations) using the R-software (R Development Core Team, 2007).

2.2. Dose response

As a greater susceptibility to the pathogen of children under 5 year old was suspected from epidemiological data (FSIS, 2001; Tozzi et al., 2003, Espié et al., 2007), we chose to develop two new dose-response models from the data of the French outbreak, one for each age group ([0–5[and [5–10[). As only HUS cases were exhaustively reported in the French outbreak data (10 cases in [0–5[and 6 cases in [5–10[), we chose to directly model the probability of HUS (p_{HUS}) as a function of the ingested dose D by a single-hit model: $p_{HUS} = 1 - (1 - r)^D$, where r is the probability of HUS from a single cell. Even if single-hit models were first proposed to describe infection models, they are often used to describe illness models and there is no strict argument against their use to do it (Teunis et al., 1999; FAO/WHO, 2003). The FAO used this dose-response model in the risk assessment of *Listeria monocytogenes* in ready-to-eat foods (FAO/WHO, 2004), by defining different values of r for susceptible and healthy consumers. We proposed to use the same type of approach by defining different values of r for two age groups, [0–5[and [5–10[.

In order to estimate the r values from the French outbreak data, a Bayesian framework was used (Carlin and Louis, 2000). Such an approach was already used by Teunis et al. (2004) from the Japanese outbreak data. In that study, it was considered that the serving size was similar for each child, and in addition the food was uncooked. For the modeling of the French outbreak, we chose to take into account the variability on the serving size (S) and the consumption preference

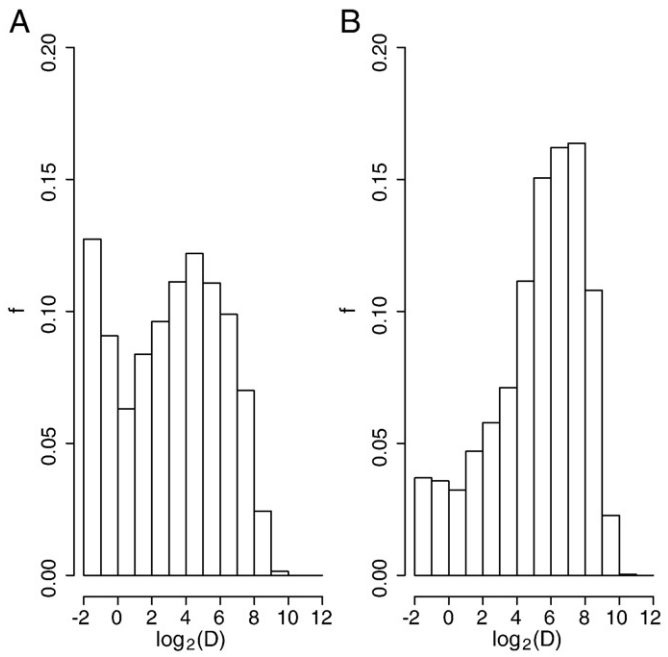

Fig. 2. Histograms of the simulated values of the ingested dose $\log_2$ (D), with values for null doses arbitrarily fixed to −1. A for the group [0–5[and B for the group [5–10[years of age. Reading key for panel A: 12.8% of null doses and 0.2% of doses between 2^9=512 CFU and 2^{12}=4096 CFU. Reading key for panel B: 3.6% of null doses and 2.3% of doses between 2^9=512 CFU and 2^{12}=4096 CFU.

(CP) by using the outputs of the exposure model as an input of the Bayesian framework. The dose *D* was thus supposed to follow the empirical distribution resulting from the exposure model for each age group. The number of servings in each age group was also defined from the exposure assessment results (Table 1).

The same prior distribution for *r* was defined for both age groups. In order to define it, a range of possible values was defined from literature considering the following information. In a beta-Poisson model, the mean value of the probability of infection from a single cell corresponds to the mean of the beta distribution ($\alpha/(\alpha+\beta)$). With *p* (illness|infection)=0.55 (value reported by Teunis et al. (2004)) and *p* (HUS|illness) between 0.03 and 0.15 (Razzaq, 2006), this gives a range for *r* from 9×10^{-4} to 5×10^{-3}. This range was enlarged for the prior distribution not to be too informative and the prior distribution was expressed as a uniform distribution on $\log_{10}(r)$ (uniform (−5, −1)).

For each age group, a sample posterior distribution of *r* was constructed by means of Markov chain Monte Carlo (MCMC) procedure using BRugs (Thomas et al., 2006). For each model, after an adaptation of 10^3 iterations, the convergence of the MCMC algorithm was checked by visually analysing ten independent MCMC chains using different initial values and Gelman and Rubin convergence statistics, as modified by Brooks and Gelman (1998). Inferences were made on the pool of 10^3 iterations following the adaptation phase for the ten chains, i.e. 10×10^3 iterations.

In order to compare the simulations obtained using the two new dose-response models to the ones obtained using models from the literature, three other dose-response models were also considered: Teunis model for children (Teunis et al., 2004), Crockett model from *Shigella* data (Crockett et al., 1996) and Strachan model (Strachan et al., 2005). In order to calculate the probability of HUS from these three models, *p* (HUS|illness) was assumed to be between 0.03 and 0.15 (Razzaq, 2006) and for Teunis model which describes the probability of infection, *p* (illness|infection) was fixed to 0.55 (value reported by Teunis et al., 2004). Models based on EPEC human data (Powell et al., 2000) or STEC rabbit data (Haas et al., 2000) were not considered as they were already known to underestimate the human risk (Teunis et al., 2004).

2.3. Scenario analysis

For each age group, a complete risk assessment model was built by combining the exposure and the dose-response models, fixing *r* to its Bayesian estimation for each age group. This model was used to estimate the mean individual HUS risk per serving (R_{HUS}) as a function of the mean contamination level in a ground beef batch (*C* in CFU g^{-1}). For this purpose, *C* was kept as a variable in the exposure assessment model. A realistic range from 5×10^{-5} to 6 CFU g^{-1} was defined for *C*. The higher value corresponds to the contamination level estimated from the outbreak data and the lower one was estimated from the results of a survey of French industrial minced beef, assuming that all the batches were contaminated at a very low level (Vernozy-Rozand et al., 2002). In this study, 115 batches were investigated, 30 samples of 25 g of minced beef being tested. Three of the 115 batches tested were positive, one with only two positive samples among the 30, and two with only one positive sample. The contamination level of detected batches was thus very low and data were not sufficient to guarantee that the other non-detected batches were not also contaminated. It seems thus not relevant to separately estimate prevalence and contamination level and this is why we chose to assume all the batches contaminated at the same level, corresponding to a regular level of contamination outside any outbreak.

The number of HUS sporadic cases due to frozen ground beef consumed in French households in each age group was estimated from the value of R_{HUS} corresponding to the lower value of the estimation of the regular mean level of contamination of batches ($C=5\times10^{-5}$ CFU g^{-1}). This calculation requires the estimation of the number of frozen ground beef eaten at home per year for each age group. This number was estimated at 48×10^6 for [0–5[and 58×10^6 for [5–10[children, from the French consumer surveys and demographic data previously described, assuming that 44% of the eaten ground beef patties were frozen ones (information from French market data of the SECODIP: société d'étude de la consommation et des investisseurs publicitaires).

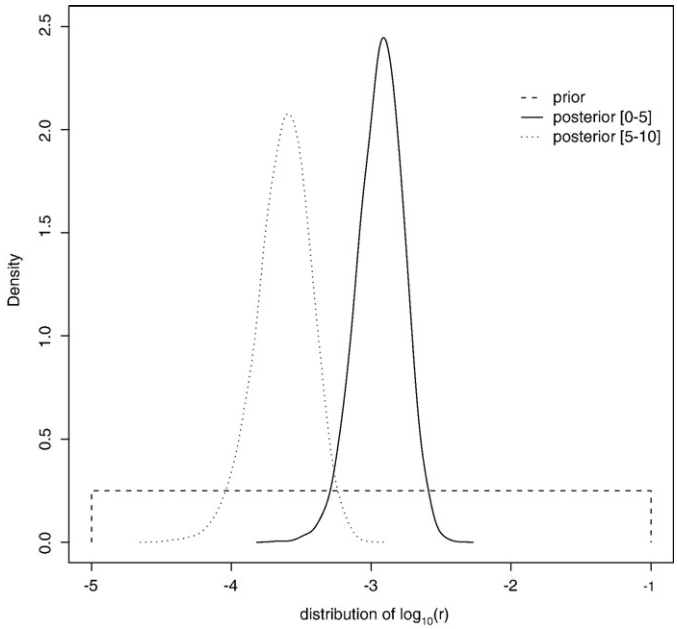

Fig. 3. Prior and posterior distributions of the dose-response parameter *r* for each age group.

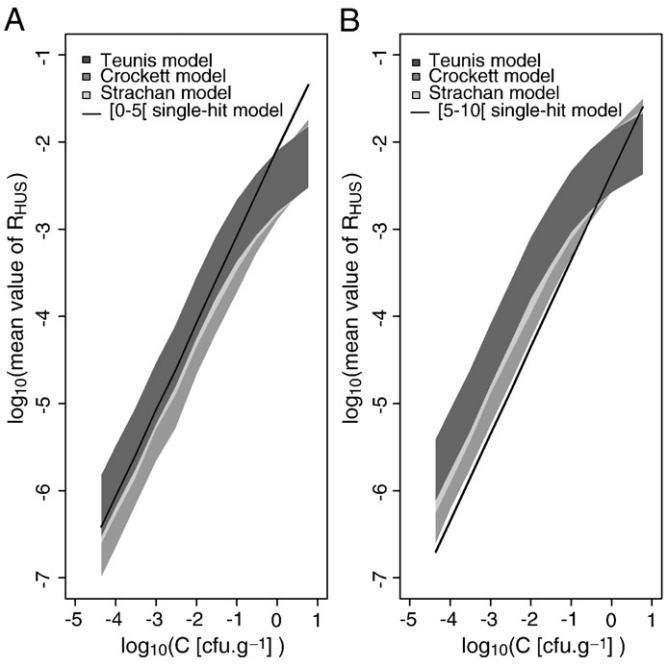

Fig. 4. Mean individual HUS risk per serving estimated for each age class, and each dose-response model, as a function of the *E. coli* O157:H7 concentration in the frozen ground beef before cooking (C). Plain line: with the single-hit model with one parameter estimated from the French outbreak by Bayesian inference. Grey bands: with each of the three models from the literature, lower level corresponding to p (HUS|illness) = 0.03, and higher level to p (HUS|illness) = 0.15. A for the group [0–5[and B for the group [5–10[years of age.

Moreover, in order to quantify the impact of the consumption preference on the mean individual HUS risk per serving, the exposure model was also modified just by fixing the value of the consumption preference to one of the four possible values ("raw", "rare", "medium" and "well-done").

3. Results

3.1. Exposure assessment

The distribution of the dose was reported in Fig. 2 for each age group ($D_{[0-5[}$ and $D_{[5-10[}$). In order to make the histogram more readable, values of $\log_2(D)$ were reported and values for null dose were arbitrarily fixed to −1 (corresponding to a fictive dose of 0.1 CFU). Most of the servings were expected to still contain the pathogen with respectively 87% and 96% of non-null values for $D_{[0-5[}$ and $D_{[5-10[}$. The range of simulated values is the same for both age group, from 0 to 4×10^3 cells per serving, with respective median of 50 and 80 cells for $D_{[0-5[}$ and $D_{[5-10[}$.

3.2. Dose response

A rapid convergence of MCMC chains was obtained. Fig. 3 shows that the posterior distributions of the dose-response parameter r are far narrower than prior ones, which means that data improves our knowledge of the parameter. For each age group, r was estimated from the median of its posterior distribution and its 95% credible interval (95% CI) from the 2.5th quantile to the 97.5th one of this distribution. Respective values of 1.2×10^{-3} (95% CI: $[5.3\times10^{-4}$–$2.3\times10^{-3}]$) for the group [0–5[and 2.4×10^{-4} (95% CI: $[9.0\times10^{-5}$–$5.3\times10^{-4}]$) for the group [5–10[were obtained. From these estimations, the probability to develop a HUS from a fixed ingested dose of *E. coli* O157:H7 is expected to be 5 times greater for [0–5[children than for [5–10[ones.

3.3. Scenario analysis

The mean individual HUS risk per serving (R_{HUS}) was plotted as a function of the mean contamination level in a ground beef batch (C in UFC g^{-1}) for each age group (Fig. 4). Four dose-response models were used for the calculation of R_{HUS}, the new single-hit model specifically defined for the age group, and the three other models selected from the published ones: Teunis, Crockett and Strachan models. The exposure model was specific for each age group, taking into account for variable consumption preferences and serving sizes as described in the material and methods. Values predicted with the new single-hit models (respectively 18 and 12 cases per year for [0–5[and [5–10[) were consistent with French epidemiological data for [0–5[and somewhat a little high for [5–10[. Indeed on average respectively 64 and 13 HUS cases were reported in France in the age group [0–5[and [5–10[respectively, from which only 60% could be linked to ground beef consumption, without certainty (so respectively 38 and 8 cases), and the packaging of ground beef was not known, so the amount of frozen patties as opposed to the amount of unfrozen patties could not be estimated.

For the age group [0–5[, the three dose-response models selected from literature give predictions of R_{HUS} close to the new single-hit model for low contamination levels. But for the high contamination level estimated in the French outbreak, all of these models underestimate the mean individual risk, compared to the single-hit model which was estimated from the data of this outbreak. For the age group [5–10[, the three dose-response models from the literature give predictions slightly higher than the new single-hit model for low contamination levels, and slightly lower for high contamination levels.

In order to quantify the impact of the consumption preference on the mean individual HUS risk per serving, the mean individual HUS risk per serving for children under the age of 5 was calculated separately for each consumption preference (Fig. 5). For the higher contamination level corresponding to the French outbreak, mean HUS risk was estimated to respectively 0.283, 0.133, 0.072 and 0.006 for "raw", "rare", "medium" and "well-done" patties. These results show that only the "well-done" cooking notably reduces the HUS risk.

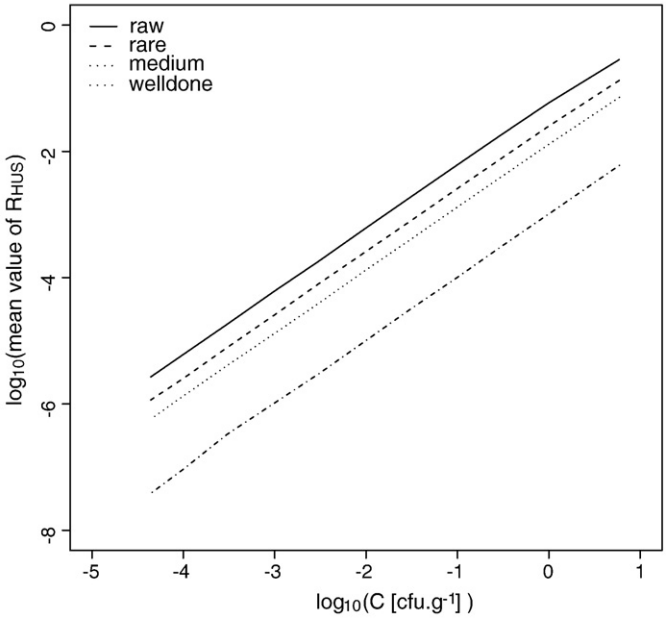

Fig. 5. Mean individual HUS risk per serving estimated as a function of the *E. coli* O157:H7 concentration in the frozen ground beef before cooking (C), for the age group [0–5[with the single-hit model with one parameter estimated from the French outbreak by Bayesian inference. Each line corresponds to a different consumption preference.

4. Discussion

The proposed risk assessment model accounts for the greater susceptibility to *E. coli* O157:H7 of the younger children and could be used as a scientific base for French risk managers in order to prevent future outbreaks. The probability of developing a HUS from the ingestion of one cell of *E. coli* O157:H7 was estimated at 1.2×10^{-3} (95% CI: $[5.3\times10^{-4}$–$2.3\times10^{-3}]$) for [0–5[year old children, which is 5 times higher than for [5–10[ones, for which the estimated value was 2.4×10^{-4} (95% CI: $[9.0\times10^{-5}$–$5.3\times10^{-4}]$). The effect of this higher susceptibility of very young children is diminished by the fact that in France younger children usually eat smaller portions and more cooked patties. Indeed, 49% of children under 5 years of age usually eat "well-done" patties as opposed to 29% of children between the age of 5 and 10. The mean individual HUS risk per typical serving (R_{HUS}) for children under 10 years may be roughly approximated by $\log_{10} R_{HUS} = -2+\log_{10} C$ for both age groups. The knowledge of this relation is capital for risk managers in order to define food safety objectives (FSO).

This relation takes into account consumer data, especially French cooking habits. It may be pointed out that even among younger children, few consumers eat "well-done" patties as opposed to other countries. In Ireland and in the USA, more than 80% of the consumers eat "well-done" patties, despite their age (Duffy et al., 2006a). As our risk assessment clearly shows that only the "well-done" cooking notably reduces the HUS risk, a French consumer information program on cooking ground beef patties, especially those consumed by young children, could help to reduce the number of sporadic cases and to prevent future outbreaks.

In this study, only the most common way of cooking ground beef patties in French households was considered: the direct cooking of the frozen patty in a frying pan with one turnover. In order to take into account other ways of cooking, further experiments should be performed. Higher microbial reductions could be expected with a multi-turnover method or a double-sided grill, which have been shown to be more efficient on non-frozen ground beef patties (D'Sa et al., 2000; Rhee et al., 2003). These methods should be tested on frozen ground beef patties, as they could also help to reduce the number of sporadic cases and to prevent future outbreaks. More generally, this study raised the need for microbial destruction models directly usable for such a risk assessment, by taking into account ordinary ways of food preparation before consumption in households. For this purpose, approaches mixing heat and mass transfer models and microbial inactivation models should be encouraged (Ou and Mittal, 2006).

In the exposure assessment model, the potential effect of freezing was not taken into account as the input data for the initial contamination level of ground beef patties was obtained from already frozen ground beef. The use of this model from input data corresponding to initial contamination level of ground beef before freezing should consider a potential effect of freezing. In the FSIS model (2001), a microbial reduction between 0 and 3 $\log_{10}$ was modeled. This range of values may yet be very optimistic. In contradiction to other previous studies, a recent experimental study reports that the microbial reduction greatly depends on the freezing profile and that only slight reductions (0 to 0.2 $\log_{10}$) could be expected with profiles with short freezing times (Dykes, 2006). This study thus clearly demonstrated that the current industry practice is unlikely to result in a reduction of *E. coli* O157:H7. It seems then cautious to neglect the potential effect of freezing on microbial reduction, as far as this effect is not better known. Future research should be carried out in order to know if a controlled long freezing profile could help to control the pathogen.

This study includes an exposure assessment from distribution to consumption and does not consider the earlier stages of the production of ground beef. This choice was motivated by the lack of data on the contamination by *E. coli* O157:H7 in these earlier stages for French production of ground beef. The acquisition of such data would enable us to enlarge this quantitative risk assessment and to explore other ways of reducing the HUS risk than improve consumer cooking, by reducing the initial contamination of ground beef.

Among the results of this study, new *E. coli* O157:H7 human single-hit dose-response models for two age groups ([0–5[and [5–10[) were proposed. The retained single-hit model, with only one parameter, is simpler than the beta-Poisson model used by many authors, which describes the variability on the parameter r by a beta distribution, characterized by two parameters. Such variability may be due to host variability and/or to strain variability (FAO/WHO, 2003). Yet, as reported by Teunis and Havelaar (2000), a correct estimation of the two parameters of the beta distribution of r is difficult due to a strong structural correlation between them. Moreover, in our study, the host variability is reduced by the fact that the r value is defined on a narrow age group, and the potential strain variability cannot be estimated from the data linked to only one outbreak. It must be pointed out that the proposed dose-response models may be specific to the *E. coli* O157:H7 strain implied in the French outbreak, that might have been specifically virulent. Nevertheless, the modeling of this outbreak was interesting as it was well documented and concerned very young children. The development of more general dose-response models requires the use of data from various outbreaks within more complex hierarchical models such as those carried out by Teunis et al. (2007).

This work showed the interest of conducting a quantitative risk assessment in order to model a dose-response relation from data collected after an outbreak. It should be improved by taking into account not only variability sources as done, but also uncertainty sources (especially random sampling errors associated to survey results). Finally, further analyses of French epidemiological data are planned in order to propose a global dose-response model for children under 10 year old, explicitly including the age in the model as a covariate.

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