Estimating the burden of foodborne diseases in Japan

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Objective To assess the burden posed by foodborne diseases in Japan using methods developed by the World Health Organization's Foodborne Disease Burden Epidemiology Reference Group (FERG).

Methods Expert consultation and statistics on food poisoning during 2011 were used to identify three common causes of foodborne disease in Japan: Campylobacter and Salmonella species and enterohaemorrhagic Escherichia coli (EHEC). We conducted systematic reviews of English and Japanese literature on the complications caused by these pathogens, by searching Embase, the Japan medical society abstract database and Medline. We estimated the annual incidence of acute gastroenteritis from reported surveillance data, based on estimated probabilities that an affected person would visit a physician and have gastroenteritis confirmed. We then calculated disability-adjusted life-years (DALYS) lost in 2011, using the incidence estimates along with disability weights derived from published studies.

Findings In 2011, foodborne disease caused by Campylobacter species, Salmonella species and EHEC led to an estimated loss of 6099, 3145 and 463 DALYs in Japan, respectively. These estimated burdens are based on the pyramid reconstruction method; are largely due to morbidity rather than mortality; and are much higher than those indicated by routine surveillance data.

Conclusion Routine surveillance data may indicate foodborne disease burdens that are much lower than the true values. Most of the burden posed by foodborne disease in Japan comes from secondary complications. The tools developed by FERG appear useful in estimating disease burdens and setting priorities in the field of food safety.

Abstracts in العربية, 中文, Français, Русский and Español at the end of each article.

Introduction

There have been few attempts to provide comprehensive, consistent and comparable estimates of the burden of acute foodborne diseases.1 In 2006, however, the World Health Organization (WHO) set up the Foodborne Disease Burden Epidemiology Reference Group (FERG) specifically to produce such estimates.2 FERG aims to provide the data and tools needed to set appropriate, evidence-informed priorities for food safety at country level. Since its launch, FERG has established several task forces that focus on parasitic and enteric diseases, chemicals and natural toxins, source attribution, computational modelling and country studies. The members of the country studies task force were asked to develop methods for estimating the burden posed by foodborne disease at national level. These methods were intended to facilitate the collection of national data on foodborne disease burdens and support the use of such data for policy-making and practice in food safety.3 FERG selected Albania, Japan, Thailand and Uganda as the locations for initial pilot studies estimating disability-adjusted life-years (DALYs) lost as a result of foodborne disease.4,5

In Japan, priorities for foodborne disease prevention are primarily based on the apparent public health significance of each disease, although impact on the food market, consumers' risk perceptions and public opinion are also taken into consideration.6 The Japanese Food Sanitation Act and Infectious Disease Control Act require collection of data on the incidence of food poisoning and infectious diseases, respectively. However, as there has never been a comprehensive, internally consistent and robust assessment of the burden posed by foodborne disease in Japan, robust and objective standards for ranking priorities are lacking. Surveillance data are not as useful as formal estimates when identifying and ranking diseases in terms of their contributions to the country's overall burden. Our objective is to assess the burden posed by common foodborne diseases in Japan, using the methods recommended by FERG and expressing the main findings in terms of DALYs.

Methods

Disease selection

After analysis of food poisoning statistics and consultation with experts, we identified Campylobacter species, Salmonella species and enterohaemorrhagic Escherichia coli (EHEC) as the first, second and third most common causes of foodborne disease in Japan in 2011.7 This ranking was entirely based on clinical cases in health facilities. To estimate the relative burden posed by each of these three causes of foodborne disease, we used a pyramid reconstruction method and supplemented routine surveillance and reporting data with information from telephone and patient surveys.

Data sources

We used data from four sources to estimate the annual incidence of acute gastroenteritis caused by Campylobacter, Salmonella and EHEC and to estimate associated mortality rates. The four data sources were: (i) food poisoning statistics that had been compiled using information collected by local governments on outbreaks of food poisoning; (ii) surveillance data on EHEC (routine collection of data on EHEC cases in Japan was not

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made a legal requirement until 1999; disease caused by Salmonella or Campylobacter species was not recorded).\textsuperscript{14} (iii) national patient surveys for 1996, 1999, 2002, 2005, 2008 and 2011. (These surveys record patients in hospitals and clinics on a single day in October, coded according to the International Classification of Diseases [ICD-10]);\textsuperscript{10} and (iv) vital registration records assimilated by the Japan Ministry of Health, Labour and Welfare.\textsuperscript{11}

Incidence estimation

Because of the limitations of the reported statistics, the annual numbers of cases of acute gastroenteritis attributable to foodborne disease caused by Campylobacter \( (Y_1) \), Salmonella \( (Y_2) \) and EHEC \( (Y_3) \) were estimated using the formulae:

\[
Y_1 = \frac{31 AW_1}{B CD} \quad (1)
\]

\[
Y_2 = \frac{31 AW_2}{B CD} \quad (2)
\]

\[
Y_3 = \frac{31 AW_3}{B CD} \quad (3)
\]

where 31 represents the number of days in October, \( A \) represents the corresponding reported incidence – \( A_1 \) and \( A_2 \) estimated from the patient survey data and disease durations\textsuperscript{12} and \( A_3 \) derived from the data collected from infectious disease surveillance. \( W \) represents the proportions of infection attributable to foodborne disease. \( B \) represents seasonality – calculated as the number of cases of acute gastroenteritis caused by Campylobacter or Salmonella on survey days divided by the corresponding daily mean numbers of cases of acute gastroenteritis caused by Campylobacter and Salmonella recorded in the survey years. \( C \) represents the proportion of incident cases confirmed by stool examination. \( D \) represents the proportion of incident cases who visited a physician. Data for the estimation of \( C \) and \( D \) were derived from population-based telephone surveys.\textsuperscript{13,14}

We used a Bayesian method to estimate the probability distributions of \( B \), \( C \) and \( D \). We assumed that \( C \) and \( D \) followed binomial probability distributions with a beta prior distribution for the binomial probability parameter. Because the beta prior is the conjugate distribution of the binomial likelihood, the posterior distribution is also beta-distributed.\textsuperscript{15} We assumed a uniform prior distribution – i.e. a special case of the beta distribution in which the probability parameter lies between 0 and 1.\textsuperscript{14} Once we had obtained three beta distributions, we assumed that the parameters underlying them were mutually independent and used Mathematica version 8 (Wolfram Research, Hanborough, United Kingdom of Great Britain and Northern Ireland) to calculate the distribution as the product of the three independent distributions.

Finally, the proportions \( (W_i) \) of \( Y_1 \), \( Y_2 \) and \( Y_3 \) attributable to foodborne disease were estimated using an expert elicitation process similar to that done in the Netherlands.\textsuperscript{16} We invited contributions to this estimation from experts from different scientific backgrounds – microbiology, epidemiology and food science. We invited 88 experts and thirty (34.1\%) agreed to participate. We asked the experts to provide their best estimate of the percentages of individuals with gastroenteritis caused by Campylobacter, Salmonella or EHEC that had become infected by each of five pathways: food, environment, animal–human, human–human and travel. We also asked the experts to estimate the 90\% confidence limits around their best estimates. Individual expert opinions were represented in terms of a Dirichlet distribution. Where more than one expert provided an opinion on the same pathway we combined the estimates using a Bayesian update method with equal weighting (details available from the corresponding author).

Complications

In our investigation of the burden caused by complications of gastroenteritis, we used outcome trees based on a European study.\textsuperscript{17} The complications resulting from Campylobacter included Guillain–Barré syndrome, inflammatory bowel disease and reactive arthritis; from Salmonella, inflammatory bowel disease and reactive arthritis and from EHEC, haemolytic–uraemic syndrome.\textsuperscript{17,18}

We used systematic reviews of prospective cohort studies to estimate the proportions of these complications that could be attributed to gastroenteritis caused by each infectious agent. We searched the Japan medical abstract society database and Embase for relevant articles published between 1 January 1983 and 29 February 2012 and Medline for relevant articles published between 1 January 1946 and 29 February 2012.\textsuperscript{19} The search terms were designed by an information specialist using the appropriate medical subheadings (available from the corresponding author). We included prospective cohort studies that described, in English or Japanese, the proportions of laboratory-confirmed sequelae that resulted from gastroenteritis caused by Campylobacter, Salmonella or EHEC. We only used published data and made no attempt to obtain any further data from the authors of relevant articles. We excluded case reports, review papers, letters, comments, conference proceedings, studies with insufficient information on criteria, studies that only provided aggregated data for multiple conditions and unpublished studies (Fig. 1).

The title, abstract and, if appropriate, the full text of each eligible article of potential interest were screened by two authors independently. Discrepancies were resolved by discussion and consensus. We collected information on the year of publication, study duration, country and area, data source or sources, follow-up period, sample size, serotype, age group, sex, case definition and the incidence of sequelae and their associated standard errors. We assessed the quality of each included study using the Newcastle-Ottawa scale.\textsuperscript{20}

Data analysis

Meta-analyses of the proportions of sequelae attributable to gastroenteritis caused by Campylobacter, Salmonella or EHEC were done to generate pooled values of prevalence with 95\% uncertainty intervals. Heterogeneity among studies was estimated using Cochran’s \( Q \) and the \( I^2 \) statistic. Either the Freeman–Tukey double arcsine transformation or log–normal random-effects were used to stabilize model variances.\textsuperscript{21–23} Potential sources of heterogeneity were investigated further by analysis of subgroups by age and methods of laboratory confirmation. We used random-effects models\textsuperscript{24} in Stata version 13 (StataCorp. LP, College Station, United States of America).

Estimation of mortality

Data on gastroenteritis-related deaths caused by Campylobacter, Salmonella or EHEC – (ICD-10 codes A045, A02 and A043 respectively) and sequelae such as Guillain–Barré syndrome, inflammatory bowel disease or haemolytic-uraemic
syndrome (ICD-10 codes G610, K50/K51 and D59.3 respectively) were obtained from the Japan vital registration system. These mortality estimates were adjusted based on the proportions estimated to be attributable to foodborne disease. We did not adjust for possible misclassification.

**Estimation of burden**

We used DALYs to assess the burden of foodborne disease caused by *Campylobacter, Salmonella* or EHEC in Japan in 2011. DALYs combine the years of potential life lost due to premature death with the years lived with disabilities. We estimated years of potential life lost by multiplying the number of deaths due to a particular form of foodborne disease by the number of potential life-years lost due to premature death from that disease. The latter was based on standard life expectancies from the Global Burden of Disease (GBD) 2010 study. The corresponding years lived with disabilities were calculated as the product of the number of incident cases of a particular form of foodborne disease, the mean duration of that disease and the disability weight for that disease. Age-specific disease incidences were estimated from the age distributions recorded in food poisoning and infectious diseases statistics for Japan. Whenever possible, we used disease durations and disability weights from studies conducted in Europe.

To be consistent with the assumptions made in the GBD 2010 study, we did not apply any discounting or non-uniform age-weighting. DALY components were calculated separately for each sex and age group and then summed to obtain estimates of the total burdens.

**Uncertainty analysis**

Uncertainty intervals were derived by Monte-Carlo simulation within the R statistical package (R Foundation for Statistical Computing, Vienna, Austria). Appropriate probability distributions were specified for parameters that, based on the published literature, were considered to be important sources of uncertainty. Estimates were repeatedly calculated from randomly drawn sets of input values, and 95% uncertainty intervals were derived from the 2.5th and 97.5th percentiles of the output values. The process was continued until the difference between the means of the incremental iterations satisfied the stopping criterion of less than 1 unit difference in the mean of the outcome estimates. The number of draws ranged from 22, for acute gastroenteritis caused by *Campylobacter*, to 52,951, for inflammatory bowel disease caused by *Salmonella*.

**Results**

**Incidences of acute gastroenteritis**

Table 1 shows the incidence of gastroenteritis caused by foodborne *Campylobacter, Salmonella* or EHEC reported in the routine surveillance data, and the corresponding – much higher – adjusted incidences that we estimated using the pyramid reconstruction method. Fig. 2 shows the estimated annual incidence of acute gastroenteritis caused by foodborne *Campylobacter, Salmonella* or EHEC between 1996 and 1999 and 2011. Over this period, there was no clear trend in the incidence of acute gastroenteritis caused by foodborne *Campylobacter* or EHEC but the incidence of gastroenteritis caused by foodborne *Salmonella* appeared to fall substantially after 2002.
Disease burdens

Table 2 summarizes the experts’ estimates of the proportions of the acute gastroenteritis incidence that can be attributed to foodborne transmission and other pathways. Table 2 also shows the corresponding Bayesian factors used to adjust for seasonality, physician visits and stool examination – i.e. the denominators of Equation 1, Equation 2 and Equation 3.

Table 3 shows the results of our systematic review and meta-analysis of the prevalence of various complications that may occur after infection with Campylobacter, Salmonella or EHEC (Fig. 3, Fig. 4, Fig. 5, Fig. 6, Fig. 7, Fig. 8 and Fig. 9; all available at: http://www.who.int/bulletin/volumes/93/08/-/14-148056).

The attributable proportions – i.e. the percentages of the cases of the sequelae that could be attributed to one of our pathogens of interest – varied from 0.03%, for Guillain-Barré syndrome and Campylobacter, to 9.14%, for haemorrhagic colitis.

Table 4 summarizes the numbers of deaths recorded in Japan in 2011 that were attributed to gastroenteritis caused by foodborne Campylobacter, Salmonella or EHEC or to the related complications. No deaths were attributed to gastroenteritis caused by Campylobacter, reactive arthritis or haemorrhagic colitis.

Table 4 also presents disability weights, disease durations, estimated incidences and disease burdens in terms of DALYs. Most of the overall disease burden posed by foodborne Campylobacter, Salmonella or EHEC was the result of a relatively small number of complications.

Discussion

Our study provides national estimates of incidence, deaths and disease burden in DALYs, caused by Campylobacter, Salmonella and EHEC in Japan in 2011.

Estimates of annual incidence were approximately 92.5, 31.7 and 80.7 cases per 100 000 population for gastroenteritis caused by foodborne Campylobacter, Salmonella and EHEC, respectively. These estimates were many-fold higher than the values indicated by the results of routine surveillance, which ranged from 0.6 to 2.4 cases per 100 000 population. In 2011 at least, Japan’s routine surveillance system for foodborne diseases appeared to grossly underreport the incidence of acute gastroenteritis caused by our pathogens of interest. One probable cause of such underreporting is that the surveillance system focuses on clusters, outbreaks and other large public health events and usually ignores individual sporadic cases.73

Our estimate of the annual incidence of gastroenteritis caused by foodborne Campylobacter appears relatively low for a high-income country. Previous estimates of such incidence in a high-income country have ranged from 440 per 100 000, in the United States in 2006, to 930 per 100 000, in the United Kingdom in 2008–2009.74 Apparent geographical variation in the incidence of such disease may partly reflect between-country and between-study differences in the surveillance
methods employed. In some countries, population-based cohort studies – e.g. the Sensor study in the Netherlands and two Infectious Intestinal Disease studies in the United Kingdom – are being used. In Australia, Canada and the United States, a surveillance pyramid method that included information on hospital visits and laboratory-confirmed cases is being employed. Harmonization of methods will be necessary if we are to make meaningful comparisons of incidence estimates between countries and over time. The results of this pilot study will hopefully help FERG to improve its recommendations and the production of comparable, consistent estimates of the incidences of foodborne diseases.

In our study, to address the potential bias resulting from the one-day hospital reporting period and the inclusion of laboratory-confirmed cases, we applied a pyramid reconstruction technique similar to that used in previous research. Although this technique allows some adjustment for seasonality, care-seeking and diagnostic factors, it has several limitations. First, we estimated the age-specific incidence of gastroenteritis based on food poisoning statistics from a passive surveillance system, that tends to miss sporadically occurring cases. To make the estimation of the number of cases occurring annually in each age group more accurate, active surveillance – via national surveys or a population-based surveillance network – would be needed.

Second, we restricted the sequelae we investigated to those previously identified in a European study. In Japan, there may be different or more complications than observed in Europe.

Third, we based some of our estimation process on a systematic review of sequelae from other countries, where the epidemiology of foodborne disease may differ from that in Japan – e.g. because of the geographical variation in dietary habits.

Fourth, the validity and comparability of the disability weights that we used may be limited. In the field of foodborne disease, information on disability weights for specific complications is scarce. Hopefully, relevant data will soon be provided by FERG.

Finally, our estimates of the proportion of gastroenteritis resulting from foodborne transmission were based on expert opinion instead of empirical data. The size of the so-called foodborne fraction appears to vary markedly depending on the country involved. Such a large variation may be due to differences in dietary habit, consumer tastes, food processing and food safety – but may also reflect differences in the methods used to investigate transmission pathways.

The approach recommended by FERG appears useful for understanding the magnitude of foodborne diseases, prioritizing food safety interventions and policies and harmonizing methods for the estimation of the foodborne disease burden.

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Competing interests: None declared.

Table 3. Proportions of cases of sequelae attributable to Campylobacter spp., Salmonella sp. or enterohaemorrhagic Escherichia coli

| Pathogen, sequelae                  | Attributable proportion, % of cases of sequelae, (95% UI) | No. of studies | Country                                      |
|-------------------------------------|------------------------------------------------------------|----------------|----------------------------------------------|
| Campylobacter spp.                  |                                                            |                |                                              |
| Guillain-Barré syndrome             | 0.03 (0.02–0.06)                                           | 3              | Netherlands, Sweden                          |
| Inflammatory bowel disease          | 0.30 (0.27–0.34)                                           | 2              | Denmark, Sweden                             |
| Reactive arthritis                  | 5.01 (2.60–8.08)                                           | 14             | Denmark, Finland, Netherlands, Norway, United Kingdom, USA |
| Salmonella sp.                      |                                                            |                |                                              |
| Inflammatory bowel disease          | 0.43 (0.38–0.48)                                           | 2              | Denmark, Sweden                             |
| Reactive arthritis                  | 6.09 (2.81–10.47)                                          | 12             | Australia, Denmark, Finland, Netherlands, Switzerland, United Kingdom, USA |
| EHEC                                |                                                            |                |                                              |
| Haemorrhagic colitis                | 9.14 (4.17–15.51)                                          | 2              | Germany, United Kingdom                     |
| Haemolytic uraemic syndrome         | 6.13 (4.61–7.82)                                           | 23             | Austria, Belgium, Canada, Denmark, Finland, Germany, Hungary, Slovakia, United Kingdom, USA |

EHEC: enterohaemorrhagic Escherichia coli; UI: uncertainty interval.
Sources: Data drawn from the results of identified studies.

Table 2. Estimated proportions of gastroenteritis cases resulting from foodborne transmission and other pathways, Japan, 2011

| Causative agent       | No. of experts | Food                        | Environment | Animal–human | Human–human | Travel | Bayesian adjustment factor (95% UI) |
|-----------------------|---------------|-----------------------------|-------------|--------------|-------------|--------|-----------------------------------|
| Campylobacter spp.    | 15            | 82.0 (78.5–85.5)            | 8.3 (6.7–10.1) | 3.1 (2.1–4.3) | 0.2 (0.0–0.5) | 6.4 (5.0–8.0) | 0.17 (0.08–0.32) |
| Salmonella sp.        | 14            | 79.3 (74.7–84.0)            | 2.7 (1.7–3.8) | 10.1 (8.4–12.8) | 3.4 (2.4–4.7) | 4.5 (3.2–5.9) | 0.26 (0.12–0.47) |
| EHEC                  | 20            | 77.6 (73.4–81.8)            | 4.0 (2.8–5.3) | 8.5 (6.9–10.4) | 6.0 (4.6–7.6) | 3.9 (2.8–5.29) | 2.23 (0.97–4.00) |

EHEC: enterohaemorrhagic Escherichia coli; UI: uncertainty interval.

* These experts were asked to estimate the proportions of gastroenteritis cases resulting from each transmission pathway.
| Causative agent, condition | Incidence, cases (95% UI) | Fatal cases | Years of illness | Disability weight | Burden metrics YLD (95% UI) | Burden metrics YLL (95% UI) | Burden metrics DALY (95% UI) | YLD/DALY (%) |
|---------------------------|---------------------------|-------------|-----------------|------------------|---------------------------|-----------------------------|-----------------------------|---------------|
| **Campylobacter spp.**    |                           |             |                 |                  |                           |                             |                             |               |
| Gastroenteritis           | 118 502 (70 654–197 823) | –           | –               | –                | 122                       | 0                          | 122                         | 100.0         |
| Visiting a general practitioner | 4 833 (3 439–7 156)   | 0           | 0.03            | 0.39             | 50 (42–66)                | 0                          | 50 (42–66)                  | 100.0         |
| Not visiting a general practitioner | 114 219 (67 864–190 644) | 0           | 0.01            | 0.07             | 72 (42–122)               | 0                          | 72 (42–122)                 | 100.0         |
| Mild Guillain-Barré syndrome | 30 (14–66)          | 0           | 1.00            | 0.25             | 7 (5–12)                  | 0                          | 7 (5–12)                    | 100.0         |
| Severe Guillain-Barré syndrome | 5 (3–11)          | 1           | 29.26           | 0.16             | 29 (13–57)                | 12 (6–21)                  | 42 (24–69)                  | 69.0          |
| Reactive arthritis        | 6 087 (2 956–11 156)   | 0           | 0.61            | 0.14             | 520 (257–952)             | 0                          | 520 (257–952)              | 100.0         |
| Inflammatory bowel disease | 452 (93–1 051)       | 4           | 44.36           | 0.26             | 5 261 (1 095–12 393)      | 83 (31–150)                | 5 344 (1 173–12475)        | 98.4          |
| Total                     | –                        | –           | –               | –                | 6003 (1 651–13 687)       | 96 (42–160)                | 6 099 (1 745–13 778)        | 98.4          |
| **Salmonella sp.**        |                           |             |                 |                  |                           |                             |                             |               |
| Gastroenteritis           | 40 571 (24 607–66 382)  | –           | –               | –                | 70                        | 122                        | 192                         |               |
| Visiting a general practitioner | 3 866 (3 411–4 658)  | 3           | 0.03            | 0.39             | 47 (42–56)                | 122 (8–292)                | 169 (52–338)               | 27.8          |
| Not visiting a general practitioner | 36 667 (21 237–62 597) | 0           | 0.02            | 0.07             | 23 (13–37)                | 0                          | 23 (13–37)                 | 100.0         |
| Reactive arthritis        | 2 556 (1 190–4 774)    | 0           | 0.61            | 0.15             | 227 (119–390)             | 0                          | 227 (119–390)              | 100.0         |
| Inflammatory bowel disease | 202 (36–481)        | 2           | 50.52           | 0.26             | 265 (492–6 211)           | 38 (13–69)                 | 2 690 (522–6 236)          | 98.6          |
| Total                     | –                        | –           | –               | –                | 2 979 (753–6 795)         | 166 (49–350)               | 3 145 (806–6 950)          | 94.7          |
| **EHEC**                  |                           |             |                 |                  |                           |                             |                             |               |
| Gastroenteritis           | 103 338 (68 419–170 419)| –           | –               | –                | 75                        | 130                        | 205                         |               |
| Visiting a general practitioner | 2 064 (1 955–2 175) | 10          | 0.02            | 0.39             | 12 (11–13)                | 130 (53–232)               | 142 (65–244)               | 8.5           |
| Not visiting a general practitioner | 101 982 (60 428–169 268) | 0           | 0.01            | 0.07             | 63 (38–96)                | 0                          | 63 (38–96)                 | 100.0         |
| Haemorrhagic colitis      | 229 (115–361)         | 0           | 0.02            | 0.39             | 1 (1–2)                   | 0                          | 1 (1–2)                    | 100.0         |
| Haemolytic uraemic syndrome | 132 (108–155)      | 3           | NA              | NA               | 133 (109–159)             | 108 (42–196)               | 240 (169–326)              | 55.4          |
| Total                     | –                        | –           | –               | –                | 211 (171–266)             | 252 (129–395)              | 463 (325–609)              | 45.6          |

DALY: disability-adjusted life-years; EHEC: enterohaemorrhagic Escherichia coli; NA: not available; UI: uncertainty interval; YLD: years lived with disability; YLL: years of life lost.

* Every case was estimated to correspond to 1.05 years lived with disability.

Values provided by Van Lier and Havelaar and Kemmeren et al.
Foodborne disease burden in Japan

Estimation of the charge of the maladies d’origine alimentaire au Japon

Objectif Evaluer la charge des maladies d’origine alimentaire au Japon, à l’aide de méthodes développées par le Groupe de travail de référence de l’OMS sur l’épidémiologie des maladies d’origine alimentaire (FERG).

Méthodes Des avis d’experts et des statistiques sur les intoxications alimentaires pour l’année 2011 ont été utilisés pour identifier les trois principales causes des maladies d’origine alimentaire au Japon : à savoir les espèces Campylobacter, Salmonella et Escherichia coli entérogenoméragique (ECEH). Nous avons procédé à des revues systématiques de la littérature anglaise et japonaise sur les complications causées par ces agents pathogènes, en faisant des recherches dans Embase (base de données bibliographiques de la société médicale du Japon) et Medline. Nous avons évalué l’incidence annuelle de la gastro-enterite aiguë à partir des données de surveillance disponibles, sur la base des probabilités estimées qu’une personne affectée ira consulter un médecin et sera diagnostiquée comme souffrant de gastro-enterite. Nous avons ensuite calculé les AVCI (années de vie corrigées du facteur incapacité) perdues en 2011, en utilisant les évaluations d’incidence ainsi que les coefficients de pondération de l’incapacité tirés des études publiées.

Résultats En 2011, au Japon, les maladies d’origine alimentaire causées par les espèces Campylobacter, Salmonella et ECEH ont respectivement entraîné une perte estimée à 6 099, 3 145 et 463 DALY. Nous avons procédé de la même façon pour le risque de mort, estimé à 609, 314 et 46 DALY. Les pourcentages sont donc largement inférieurs à la réalité.

Conclusion Il est possible que les données de surveillance de routine reflètent des chiffres largement inférieurs à la réalité. La charge des maladies d’origine alimentaire au Japon est principalement liée à leurs complications secondaires. Les outils développés par le FERG semblent être utiles pour évaluer les charges des maladies et définir les priorités en matière de sécurité sanitaire des aliments.
Резюме
Оценка бремени болезней пищевого происхождения в Японии

Цель Оценка бремени болезней пищевого происхождения в Японии с применением методов, разработанных Справочной группой Всемирной организации здравоохранения по эпидемиологии бремени болезней пищевого происхождения (FERG).

Методы С помощью экспертных консультаций и статистических данных по пищевым отравлениям за 2011 год были определены три основные причины болезней пищевого происхождения в Японии: бактерии Campylobacter и Salmonella, а также энтерогеморрагический штамм кишечной палочки Escherichia coli (EHEC). Был проведен систематический обзор английской и японской литературы по осложнениям, вызванным данными патогенными микроорганизмами, которая была найдена в базах данных Embase, Medline и реферативной базе данных публикаций медицинского сообщества Японии. Оценился уровень ежегодной заболеваемости острым гастроэнтеритом и получены данными эпиднадзора. Для его оценки использовалась расчетная вероятность того, что заболевшие придут к врачу и врач поставит диагноз «гastroэнтерит». Затем рассчитывался процент лет жизни, утраченных в связи с бременем (DALY) в 2011 году.

Результаты В 2011 году болезни пищевого происхождения, вызванные бактериями Campylobacter, Salmonella и EHEC, привели к потере 6099, 3145 и 463 лет жизни, утраченных в связи с болезнью, соответственно. Выявленное бремя болезней, рассчитанное путем реконструкции пирамиды заболеваемости, в большей степени связано с заболеваемостью, а не с смертностью. Оно оказалось наносное, выше показателей, полученных в результате обычного эпиднадзора.

Вывод Данные обычного эпиднадзора могут свидетельствовать о бремени болезней пищевого происхождения, которое намного ниже его истинных значений. Большая часть бремени болезней пищевого происхождения в Японии приходится на вторичные осложнения. Методы, разработанные FERG, оказались эффективными для оценки бремени болезней и определения приоритетов в сфере безопасности пищевых продуктов.

Resumen
Estimación de la carga de enfermedades de transmisión alimentaria en Japón

Objetivo Evaluar la carga que plantean las enfermedades de transmisión alimentaria en Japón mediante la utilización de métodos desarrollados por el Grupo de Referencia sobre Epidemiología de la Carga de Enfermedades de Transmisión Alimentaria (FERG) de la Organización Mundial de la Salud.

Métodos Se utilizaron consultas de expertos y estadísticas en intoxicación alimentaria durante 2011 para identificar tres causas comunes en las enfermedades de transmisión alimentaria en Japón: las bacterias Campylobacter, Salmonella y E. coli enterohemorrágica (EHEC). Se llevaron a cabo revisiones sistemáticas de bibliografía inglesa y japonesa sobre las complicaciones causadas por estos patógenos buscando en Embase, la base de datos de la sociedad médica japonesa, y Medline. Se estimó la incidencia anual de gastroenteritis aguda de los datos de vigilancia informados, en base a probabilidades estimadas de las bacterias comunes en las enfermedades de transmisión alimentaria en Japón: intoxicación alimentaria durante 2011 para identificar tres causas principales por las bacterias encontradas. Luego, se calcularon los pesos de la discapacidad (AVAD) perdidos en 2011, utilizando los cálculos de incidencia junto con los pesos de la discapacidad derivados de estudios publicados.

Resultados En 2011, las enfermedades de transmisión alimentaria causadas por las bacterias Campylobacter, Salmonella y EHEC condujeron a una pérdida de 6.099, 3.145 y 363 AVAD, respectivamente. Estas cargas estimadas están basadas en el método de reconstrucción de la pirámide de vigilancia, se deben en gran parte a la morbilidad más que a la mortalidad y son mucho más altas que aquellas indicadas por los datos obtenidos a partir de la vigilancia rutinaria.

Conclusión Los datos de la vigilancia rutinaria pueden indicar que las cargas de enfermedades de transmisión alimentaria son mucho más bajas que los valores reales. La mayoría de la carga que plantean las enfermedades de transmisión alimentaria en Japón proviene de complicaciones secundarias. Las herramientas desarrolladas por el FERG parecen útiles a la hora de estimar las cargas de enfermedades y de configurar prioridades en el área de la seguridad alimentaria.

References
1. Newell DG, Koopmans M, Verhoef L, Duizer E, Aidara-Kane A, Sporning H, et al. Food-borne diseases - the challenges of 20 years ago still persist while new ones continue to emerge. Int J Food Microbiol. 2010 May 30;139 Suppl 1:S3–15. doi: http://dx.doi.org/10.1016/j.ijfoodmicro.2010.01.021 PMID: 20139070
2. Havelaar AH, Cawthorne A, Angulo F, Bellinger D, Corrigan T, Cravioto A, et al. WHO initiative to estimate the global burden of foodborne diseases. First formal meeting of the Foodborne Disease Burden Epidemiology Reference Group (FERG). Geneva: World Health Organization; 2012. Available from: www.who.int/foodsafety/publications/foodborne_disease/FERG_Nov07.pdf [cited 2014 Sep 15].
3. WHO initiative to estimate the global burden of foodborne diseases. First formal meeting of the Foodborne Disease Burden Epidemiology Reference Group (FERG). Geneva: World Health Organization; 2012. Available from: www.who.int/foodsafety/publications/foodborne_disease/FERG_Nov07.pdf [cited 2014 Sep 15].
4. Polinder S, Haagsma JA, Stein C, Havelaar AH. Systematic review of general burden of disease studies using disability-adjusted life years. Popul Health Metr. 2012;10(1):21. doi: http://dx.doi.org/10.1186/1478-7954-10-21 PMID: 22113929
5. Haagsma JA, Polinder S, Stein CE, Havelaar AH. Systematic review of foodborne burden of disease studies: quality assessment of data and methodology. Int J Food Microbiol. 2013 Aug 16;166(1):34–47. doi: http://dx.doi.org/10.1016/j.ijfoodmicro.2013.05.029 PMID: 23827806
6. Ono T, Shibuya K. Policy situation analysis of the Japanese food safety system. Tokyo: Ministry of Health, Labour and Welfare; 2012.
7. Food poisoning statistics (data for foodborne disease outbreaks) [Internet]. Tokyo: Ministry of Health, Labour and Welfare, 2015. Available from: http://www.mhlw.go.jp/toukei/list/112-1.html [cited 2014 Apr 10]. Japanese.
8. Infectious diseases weekly survey [Internet]. Tokyo: National Institute of Infectious Diseases, 1998. Available from: http://www.nih.go.jp/nidien/ [cited 2014 Apr 10].
9. Infectious agents surveillance report [Internet]. Tokyo: National Institute of Infectious Diseases, 1998. Available from: http://www.nih.go.jp/nidien/iias-e.html [cited 2014 Apr 10].
10. The patient survey [Internet]. Tokyo: Ministry of Health, Labour and Welfare, 2015. Available from: http://www.mhlw.go.jp/toukei/list/10-20.html [cited 2014 Apr 10]. Japanese.
29. Pönkä A, Pitkänen T, Sarna S, Kosunen TU. Infection due to Campylobacter

28. Pitkänen T, Pönkä A, Pettersson T, Kosunen TU. Campylobacter enteritis in

27. Johnsen K, Ostensen M, Melbye AC, Melby K. HLA-B27-negative

25. Kosunen TU, Pönkä A, Kauranen O, Martio J, Pitkänen T, Hortling L, et al.

22. McCarthy N, Giesecke J. Incidence of Guillain-Barré syndrome following

20. Wells GA, Shea B, O’Connell D, Peterson J, Welch V, Losos M, et al. The

16. Havelaar AH, Galindo AV, Kurowicka D, Cooke RM. Attribution of foodborne

15. Gelman A, Carlin JB, Stern HS, Dunson DB, Vehtari A, Rubin DB. Bayesian

13. Kubota K, Iwasaki E, Inagaki S, Nokubo T, Sakurai Y, Komatsu M, et al. The

12. Freeman J, Hutchison GB. Prevalence, incidence and duration. Am J

11. Vital statistics (data for Japanese demographic situation) [Internet]. Tokyo:

10. Campylobacter jejuni enteritis: a population-based study. Rheumatology (Oxford). 2002 Mar;41(3):312–8. doi:

9. Campylobacter jejuni enteritis: a population-based study. J Rheumatol. 2008 Mar;35(3):480–7. PMID:

8. Patient-reported complications associated with Campylobacter jejuni

7. Schildt V, Asp, Svenungsson E, Wadström T, Persson M, Björkén-Olsen J. Persistent

6. Rees JR, Pannier MA, McNeis A, Szwaj S, Angulo FP, Vugia DJ. Persistent
diarrhoea, arthritis, and other complications of enteric infections: a pilot

5. Estimated the burden of acute gastroenteritis and foodborne illness caused

4. Schildt V, Asp, Svenungsson E, Wadström T, Persson M, Björkén-Olsen J. Persistent
diarrhoea, arthritis, and other complications of enteric infections: a pilot

3. Adenovirus associated with Campylobacter jejuni enteritis. Scand J Rheumatol.

2. McCarthy N, Giesecke J. Incidence of Guillain-Barré syndrome following infection with Campylobacter jejuni. Epidemiol Infect. 2010 Jul;138(7):1004–11. doi:

1. Kubota K, Iwasaki E, Inagaki S, Nokubo T, Sakurai Y, Komatsu M, et al. The

Research

Foodborne disease burden in Japan

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11. Vital statistics (data for Japanese demographic situation) [Internet]. Tokyo:

10. Ministry of Health, Labour and Welfare; 2012.

9. Miyagi Prefecture, Japan, 2005 to 2006. J Rheumatol. 2008 Dec;35(12):2211–7. PMID:

8. Campylobacter jejuni enteritis: a population-based study. J Rheumatol. 2008 Mar;35(3):480–7. PMID:

7. Schildt V, Asp, Svenungsson E, Wadström T, Persson M, Björkén-Olsen J. Persistent
diarrhoea, arthritis, and other complications of enteric infections: a pilot

6. Rees JR, Pannier MA, McNeis A, Szwaj S, Angulo FP, Vugia DJ. Persistent
diarrhoea, arthritis, and other complications of enteric infections: a pilot

5. Estimated the burden of acute gastroenteritis and foodborne illness caused

4. Schildt V, Asp, Svenungsson E, Wadström T, Persson M, Björkén-Olsen J. Persistent
diarrhoea, arthritis, and other complications of enteric infections: a pilot

3. Kubota K, Iwasaki E, Inagaki S, Nokubo T, Sakurai Y, Komatsu M, et al. The

2. McCarthy N, Giesecke J. Incidence of Guillain-Barré syndrome following infection with Campylobacter jejuni. Epidemiol Infect. 2010 Jul;138(7):1004–11. doi:

1. Kubota K, Iwasaki E, Inagaki S, Nokubo T, Sakurai Y, Komatsu M, et al. The

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Bull World Health Org 2015;93:540–549. doi: http://dx.doi.org/10.2471/BLT.14.148056

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**Fig. 3.** *Campylobacter* spp. associated cases of Guillain-Barré syndrome, 1999–2008

| Study             | n   | Guillain-Barré syndrome (n) | Effect size (95% CI) | Weight, % |
|-------------------|-----|-----------------------------|----------------------|-----------|
| McCarthy et al. (1999) | 352 | 0                           | 0.00 (0.00–1.04)     | 1.16      |
| McCarthy et al. (2001) | 29563 | 9                         | 0.03 (0.01–0.06)     | 97.33     |
| Doorduyn et al. (2008) | 457 | 0                           | 0.00 (0.00–0.80)     | 1.51      |
| Pooled prevalence  | 30372 | 9                       | 0.03 (0.02–0.06)     | 100.00    |

CI: confidence interval.  
Notes: Heterogeneity, $I^2$: 0.0%. Logistic normal random-effects model was used to test effect size $z = -24.37, P = 0.000$.

**Fig. 4.** *Campylobacter* spp. associated cases of reactive arthritis, 1981–2010

| Study             | n   | No. of reactive arthritis cases | Effect size (95% CI) | Weight, % |
|-------------------|-----|---------------------------------|----------------------|-----------|
| Gumpel et al. (1981) | 42  | 8                              | 19.05 (9.98–33.30)   | 5.43      |
| Kosunen et al. (1981) | 342 | 8                              | 2.34 (1.19–4.55)     | 7.66      |
| Pitkanen et al. (1981) | 55  | 3                              | 5.45 (1.87–14.85)    | 5.89      |
| Johnston et al. (1983) | 57  | 1                              | 2.70 (0.45–13.82)    | 5.20      |
| Pitkanen et al. (1983) | 188 | 9                              | 4.79 (2.54–8.85)     | 7.31      |
| Ponka et al. (1984) | 283 | 6                              | 2.12 (0.98–4.55)     | 7.57      |
| San Joaquin et al. (1984) | 135 | 1                              | 0.74 (0.13–4.08)     | 7.04      |
| Honu et al. (2002) | 699 | 45                             | 7.19 (5.57–9.74)     | 7.86      |
| Lucht H et al. (2002) | 173 | 27                             | 15.61 (10.95–21.75)  | 7.25      |
| Rees et al. (2004) | 324 | 9                              | 2.78 (1.47–5.19)     | 7.64      |
| Doorduyn et al. (2008) | 434 | 20                             | 4.61 (3.00–7.01)     | 7.76      |
| Schellekens et al. (2008) | 1083 | 151                          | 13.06 (11.12–15.29)  | 7.97      |
| Towner et al. (2008) | 2184 | 33                            | 1.38 (0.99–1.94)     | 8.07      |
| Schonberg-Hoist et al. (2010) | 199 | 8                             | 4.02 (2.05–7.73)     | 7.36      |
| Pooled prevalence  | 6208 | 309                         | 5.01 (2.60–8.08)     | 100.00    |

CI: confidence interval.  
Notes: Heterogeneity, $I^2$: 94.7%. Freeman-Tukey double arcsine transformation was used to test effect size $z = 6.13, P = 0.000$.  

**Fig. 5. Campylobacter spp. associated cases of inflammatory bowel disease, 2008–2011**

| Study                  | n   | No. of inflammatory bowel disease cases | Effect size (95% CI) | Weight, % |
|------------------------|-----|----------------------------------------|----------------------|-----------|
| Ternhag et al. (2008)  | 57 425 | 69 | 0.12 (0.09–0.15) | 53.75 |
| Jess et al. (2011)     | 49 420 | 306 | 0.62 (0.55–0.69) | 46.25 |
| Pooled prevalence     | 106 845 | 375 | 0.10 (0.27–0.34) | 100.00 |

CI: confidence interval.
Notes: Heterogeneity, $I^2$: 0%. Freeman-Tukey double arcsine transformation was used to test effect size $z = 34.65, P = 0.013$.

**Fig. 6. Salmonella sp. associated cases of reactive arthritis, 1986–2008**

| Study                  | n   | No. of reactive arthritis cases | Effect size (95% CI) | Weight, % |
|------------------------|-----|---------------------------------|----------------------|-----------|
| Trull et al. (1986)    | 448 | 6                              | 1.34 (0.62–2.89)     | 8.64 |
| Mattila et al. (1994)  | 246 | 16                             | 6.50 (4.04–10.30)    | 8.44 |
| Samuel et al. (1995)   | 495 | 6                              | 1.21 (0.56–2.62)     | 8.67 |
| Mattila et al. (1998)  | 191 | 22                             | 11.12 (7.73–16.82)   | 8.31 |
| Bonam et al. (2000)    | 198 | 8                              | 4.04 (2.96–7.77)     | 8.33 |
| Uffer et al. (2000)    | 156 | 1                              | 0.64 (0.11–3.54)     | 8.19 |
| Hannu et al. (2002)    | 63  | 5                              | 7.94 (4.64–12.72)    | 7.32 |
| Rees et al. (2004)     | 100 | 2                              | 2.00 (0.55–7.00)     | 7.83 |
| Lee et al. (2005)      | 261 | 38                             | 14.56 (10.79–19.33)  | 8.46 |
| Schellerup et al. (2008)| 619 | 104                           | 16.80 (14.06–19.95)  | 8.72 |
| Towner et al. (2008)   | 1356| 204                           | 15.04 (13.24–17.85)  | 8.82 |
| Doordyyn et al. (2008) | 181 | 8                              | 4.42 (2.26–8.48)     | 8.28 |
| Pooled prevalence     | 4314| 420                           | 6.09 (2.81–10.47)    | 100.00 |

CI: confidence interval.
Notes: Heterogeneity, $I^2$: 96.0%. Freeman-Tukey double arcsine transformation was used to test effect size $z = 5.43, P = 0.000$.

**Fig. 7. Salmonella sp. associated cases of inflammatory bowel disease, 2008–2011**

| Study                  | n   | No. of inflammatory bowel disease cases | Effect size (95% CI) | Weight, % |
|------------------------|-----|----------------------------------------|----------------------|-----------|
| Ternhag et al. (2008)  | 34 664 | 43                              | 0.12 (0.09–0.17)     | 45.44 |
| Jess et al. (2011)     | 41 628 | 342                             | 0.82 (0.74–0.91)     | 54.56 |
| Pooled prevalence     | 76 292 | 385                             | 0.43 (0.38–0.48)     | 100.00 |

CI: confidence interval.
Notes: Heterogeneity, $I^2$: 0%. Freeman-Tukey double arcsine transformation was used to test effect size $z = 34.9, P = 0.029$. 

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### Fig. 8. **Enterohaemorrhagic Escherichia coli**-associated cases of haemorrhagic colitis, 1997–1998

| Study            | n   | No. of haemorrhagic colitis cases | Effect size (95% CI)      | Weight, % |
|------------------|-----|----------------------------------|---------------------------|-----------|
| McDonell et al. (1997) | 23  | 4                                | 17.39 (6.98–37.14)        | 20.80     |
| Beutin et al. (1998)     | 89  | 7                                | 7.87 (3.86–15.36)         | 79.20     |
| Pooled prevalence       | 112 | 11                               | 9.14 (4.17–15.51)         | 100.00    |

CI: confidence interval.

Notes: Heterogeneity, $I^2$: 43.8%. Freeman-Tukey double arcsine transformation was used to test effect size $z = 3.60; P = 0.000$.

### Fig. 9. **Enterohaemorrhagic Escherichia coli**-associated cases of haemolytic-uraemic syndrome, 1984–2012

| Study            | n   | Haemolytic-uraemic syndrome (n) | Effect size (95% CI)      | Weight, % |
|------------------|-----|---------------------------------|---------------------------|-----------|
| Pai et al. (1984)        | 20  | 3                                | 15.00 (5.24–46.04)        | 1.60      |
| Carter et al. (1987)     | 73  | 12                               | 16.44 (9.66–26.57)        | 4.16      |
| Salmon et al. (1989)     | 26  | 1                                | 3.85 (0.68–18.89)         | 1.98      |
| Pierard et al. (1990)    | 14  | 2                                | 14.29 (4.01–31.94)        | 1.18      |
| Simor et al. (1990)      | 31  | 1                                | 3.23 (0.57–16.19)         | 2.27      |
| Oer et al. (1994)        | 152 | 21                               | 13.82 (9.22–20.15)        | 6.13      |
| Sharp et al. (1994)      | 16  | 3                                | 18.75 (6.59–43.01)        | 1.32      |
| MacDonald et al. (1996)  | 83  | 8                                | 9.64 (4.97–17.88)         | 4.49      |
| McDonell et al. (1997)   | 23  | 2                                | 8.70 (2.42–28.60)         | 1.79      |
| Chaimers et al. (1999)   | 415 | 17                               | 4.10 (2.87–6.46)          | 8.50      |
| Fischer et al. (2001)    | 97  | 11                               | 11.34 (6.65–19.37)        | 4.91      |
| Beutin et al. (2002)     | 156 | 15                               | 9.62 (5.91–15.26)         | 6.20      |
| Beutin et al. (2004)     | 608 | 21                               | 3.45 (2.27–5.22)          | 9.15      |
| Ethelberg et al. (2004)  | 343 | 21                               | 6.12 (4.04–9.18)          | 8.12      |
| Liptakova et al. (2004)  | 9   | 3                                | 33.33 (12.06–84.58)       | 0.80      |
| Laine et al. (2005)      | 10  | 1                                | 10.00 (1.79–48.42)        | 0.88      |
| Afzal et al. (2006)      | 20  | 1                                | 5.00 (0.89–23.61)         | 1.60      |
| Gould et al. (2009)      | 3464| 218                              | 6.29 (5.33–7.15)          | 10.99     |
| Hedican et al. (2009)    | 206 | 2                                | 3.49 (1.66–6.85)          | 6.93      |
| Lathrop et al. (2009)    | 111 | 5                                | 4.50 (1.94–10.11)         | 5.27      |
| Mag et al. (2010)        | 33  | 2                                | 6.06 (1.68–19.61)         | 2.39      |
| Hadler et al. (2011)     | 663 | 46                               | 6.94 (5.24–9.13)          | 9.28      |
| Lienemann et al. (2012)  | 5   | 1                                | 20.00 (3.62–62.45)        | 0.48      |
| Pooled prevalence        | 6578| 422                              | 6.13 (4.61–7.82)          | 100.00    |

CI: confidence interval.

Notes: Heterogeneity, $I^2$: 63.4%. Freeman-Tukey double arcsine transformation was used to test effect size $z = 12.19; P = 0.000$. 

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