Estimating the burden of acute gastroenteritis, foodborne disease and pathogens commonly transmitted by food; an international review

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Key Words
Acute gastroenteritis, foodborne illness, burden, global disease estimate, international review

Running Head
Burden of Acute Gastroenteritis

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Abstract

The burden of foodborne disease is not well defined in many countries, regions or on a global level. The World Health Organization (WHO), in conjunction with other national public health agencies, is coordinating a number of international activities designed to assist countries strengthen disease surveillance and determine the burden of acute gastroenteritis. This data can then be used to estimate (a) the burden associated with acute gastroenteritis of foodborne origin, (b) the burden due to specific pathogens commonly transmitted by food, and (c) the burden due to specific foods or food groups. Many of the scientists collaborating with WHO on these activities have been involved in quantifying the burden of acute gastroenteritis on a national basis. This paper reviews these key national studies, along with the international efforts that are providing the necessary information and technical resources to derive national, regional and global burden of disease estimates.
Introduction

Although a number of countries have conducted studies to determine the burden of foodborne disease, global estimates are lacking. The enormity of the problem is evident, however, from estimates of acute gastroenteritis in childhood, an important proportion of which are due to foodborne pathogens [1]. The globalization of the food supply has presented new challenges for food safety and has contributed to the international public health problem of foodborne disease. To initiate and sustain efforts aimed at preventing foodborne disease at a national and international level, the magnitude of the problem needs to be determined.

Estimating the burden of foodborne disease is complicated by the fact that very few illnesses can be definitively linked to food. Often it is only in outbreak situations that the link is made. Although acute gastrointestinal diseases are not all foodborne and foodborne diseases do not always result in acute gastroenteritis, food does represent an important vehicle for pathogens causing acute gastroenteritis. Studies determining the burden of acute gastroenteritis provide the basis for estimating the burden due to food and the burden of specific pathogens commonly transmitted by food. This paper reviews some of the national and international initiatives providing information and technical resources necessary to derive national, regional and global disease burden estimates. Countries included in this review were invited to participate via international research networks.

International initiatives
The World Health Organization (WHO) is involved in several initiatives designed to enhance laboratory-based surveillance and determine disease burden in countries and regions lacking estimates.

**WHO Global Salm-Surv:** Launched in January 2000, Global Salm-Surv is a capacity-building programme that strengthens laboratory-based surveillance and outbreak detection and response for diseases commonly transmitted by food. It is coordinated by WHO, the Danish Institute for Food and Veterinary Research, the United States Centers for Disease Control and Prevention (CDC), Reseau International des Instituts Pasteur, the Public Health Agency of Canada, Animal Sciences Group-Netherlands, United States Food and Drug Administration, Enter-net, and OzFoodNet–Australia [2]. The core elements include international training courses, an electronic discussion group, a website (http://www.who.int/salmsurv/en/), an external quality assurance system, a country databank of the top fifteen annual *Salmonella* serotypes, focused regional and national projects, and reference testing services. Through 2004, 26 training courses for microbiologists, epidemiologists, and managers have involved approximately 350 participants from over 90 countries. By enhancing laboratory-based surveillance, Global Salm-Surv is helping countries establish a foundation upon which to estimate the burden of foodborne disease.

**WHO Sentinel Sites Project:** In March 2002, WHO convened a consultation in Leipzig to discuss the feasibility of establishing sentinel sites to determine the burden of foodborne disease in regions lacking estimates. The meeting defined four surveillance categories based on the ability of the system to generate information on foodborne disease (Table 1) and
recommended using countries with category 3 or 4 surveillance for burden studies [3]. Jordan was selected as the first sentinel site for this project. A survey administered to clinical laboratories assessed routine laboratory practices and determined the number of specimens submitted and the number of laboratory-confirmed cases. A population survey administered via face-to-face interviews collected data on the number of persons ill with diarrhea or persistent fever, the number seeking medical care, and the number submitting stools and blood samples for analysis. Using data generated from these sources, multipliers were calculated to determine the burden of *Salmonella*, *Shigella*, and *Brucella*. In addition, a prospective health facility-based study was conducted to determine the proportion of pathogens commonly transmitted by food among patients seeking care in sentinel health facilities to validate burden estimates derived from the population and laboratory surveys. The Jordan study serves as a model for future sentinel sites.

**International Collaboration on Enteric Diseases ‘Burden of Illness Studies’**: In response to worldwide interest in studies to estimate the burden of acute gastroenteritis and foodborne disease, an international meeting, hosted by the CDC and chaired by WHO, was held in Atlanta in 2004 with representatives from 16 countries. The main outcome of this meeting was the establishment of an international collaboration which aims: (a) to foster communication between researchers via a list-server, conference calls, and an annual face-to-face meeting; (b) to create a forum for sharing information on the design, implementation and analysis of burden of illness studies; (c) to provide advice to countries wishing to conduct burden of illness studies; and (d) to contribute to global foodborne disease burden estimates. Currently, over 30 countries participate in the collaboration. One of the outputs of this group has been the
publication of a study comparing the prevalence of acute gastroenteritis in Australia, Canada, Ireland and the United States using a standardized case definition [4].

**National Initiatives**

England, the Netherlands and the United States [5, 6, 7, 8, 9] were among the first countries to embark on specific studies to understand the burden of diseases commonly transmitted by food. Following this first generation of studies, a number of other countries, including Australia, Canada and Ireland, launched similar studies [10, 11, 12]. These studies fall into two general designs: (a) prospective cohort studies with community etiology components and (b) cross-sectional surveys with or without supporting targeted studies.

Although prospective cohort studies are relatively expensive and complex, they have the advantage of providing community incidence rates by pathogen. Enhanced laboratory testing increases the proportion of cases with a laboratory confirmed diagnosis and provides an opportunity to screen for pathogens not usually included in routine surveillance. In cross sectional surveys, investigators ascertain the prevalence of self-reported acute gastroenteritis among persons in the community during a set period of time (e.g. one month). The advantage of this design is its relative simplicity and lower cost making it easily repeatable in different populations or time periods. The six countries reviewed highlight the different approaches taken to determine the burden of acute gastroenteritis (Table 2). Some countries have also completed burden estimates for specific pathogens commonly transmitted by food and/or the fraction of acute gastroenteritis transmitted by food or food groups.
**England:** A collaborative population-based study was conducted in England between 1993 and 1996 [5, 6]. Two of its principal objectives were: (a) to estimate the number and etiology of acute gastroenteritis cases in the population, presenting to general practitioners, and having stool specimens sent routinely for laboratory examination and (b) to compare the numbers and etiologies with the national laboratory reporting surveillance system.

Cohorts of individuals drawn from 70 general practices were recruited and stool specimens examined for bacteria, viruses and parasites. Data from these practices were also used to determine presentation and reporting rates. It was estimated that 20% of the population of England suffered from acute gastroenteritis each year (9.4 million cases) and that the most common etiologic agents were Norovirus (606,700); *Campylobacter* (422,200); Rotavirus (344,600) and non-typhoidal *Salmonella* (106,800). Data from this study were used in conjunction with data from national surveillance and special studies to estimate trends in the burden and etiology of foodborne illnesses [13]. Investigators estimated that domestically acquired foodborne illnesses resulted in 2.9 million cases in 1992 and 1.3 million cases in 2000. *Campylobacter* infection accounted for most health service usage while salmonellosis caused most deaths. More recently, the Health Protection Agency Communicable Disease Surveillance Centre developed a model to examine the burden and risk of domestically acquired foodborne disease associated with different food types [14]. Outbreaks traced to a single source of food were classified into broad food groups and the percentage of outbreaks due to each food type was calculated for each pathogen. This information was combined with pathogen specific estimates to produce pathogen specific burden by food type. Food consumption data was used to derive food-specific risks. It was estimated that consumption of
contaminated chicken meat and eggs accounted for nearly half of all hospitalizations and nearly a third of all cases and deaths due to indigenous foodborne illnesses.

The Netherlands: Two key studies of acute gastroenteritis have been conducted in the Netherlands, a general practitioner-based study and a community-based study [7, 8]. The objectives were: (a) to estimate the overall incidence and the rate of general practitioner consultations for acute gastroenteritis, (b) to identify the pathogens responsible for illness, (c) to assess the factors associated with general practitioner presentations and (d) to identify risk factors for acute gastroenteritis caused by specific pathogens.

In the general practitioner-based study, a nationally representative network of approximately 60 practitioners reported the number of consultations for acute gastroenteritis each week. Approximately 75% of these general practitioners also participated in a case-control study, in which they invited the consulting cases and an age-matched control to complete a questionnaire and submit a stool sample for bacteria, parasite and virus testing. An age-stratified random sample from the registers of the same general practitioner network was selected for a community-based cohort study called ‘Sensor’. Two consecutive cohorts were followed for six months by weekly reporting of symptoms of acute gastroenteritis. Individuals developing symptoms according to the case definition, and a matched control from the cohort, were included in a case-control component. Cases and controls submitted stool samples and completed a questionnaire and cases also completed a medical diary. The standardized community incidence of acute gastroenteritis for the Netherlands was 283 per 1000 person-years and the general practitioner incidence 14 per 1000 person years [7, 8].
**United States:** Established in 1996, the Foodborne Diseases Active Surveillance Network (FoodNet) is the principle foodborne illness component of the CDC’s Emerging Infections Program [9]. In 2004, the total population in FoodNet sites was 43.3 million, or 15% of the U.S. population. The objectives of FoodNet are to determine the burden of foodborne disease and monitor trends over time.

To determine the burden of foodborne disease, FoodNet conducts active surveillance at >450 laboratories [15]. Active surveillance is complemented by surveys of clinical laboratories [16] and physicians [17] which describe diagnostic practices. Cross-sectional telephone surveys of the general population have also been conducted to investigate the burden of acute gastroenteritis in the community and determine the proportion of cases seeking care and submitting a stool specimen for testing [18]. The rate of acute gastroenteritis was estimated at 0.72 episodes per person-year which suggests 195 million episodes nationally [18].

Based on FoodNet data, the burden due to specific pathogens and food has been estimated. The burden of illness due to *Salmonella* was estimated by calculating the expected number of laboratory-confirmed *Salmonella* (based on FoodNet active surveillance data) and applying multipliers (based on the FoodNet population survey) for bloody and non-bloody diarrhea to adjust for cases not captured in laboratory–based surveillance. It was estimated that *Salmonella* account for 1.4 million illnesses, 15 000 hospitalizations and 400 deaths each year [19]. In a separate study, pathogen-specific burden estimates for a wide range of bacteria, parasites and viruses were calculated using FoodNet data. Multipliers of 20 for bloody
diarrhea, 38 for non-bloody diarrhea and 2 for pathogens causing severe disease were used. This study also estimated the proportion of acute gastroenteritis due to food based on outbreak data, targeted studies and expert opinion. It was estimated that 76 million cases of foodborne disease occur each year, of which 82% are of unknown etiology [20].

**Northern Ireland and the Republic of Ireland:** Two studies of acute gastroenteritis have been conducted in Northern Ireland and the Republic of Ireland. The objectives were to determine the incidence of acute gastroenteritis in the community and described physician management of patients with acute gastroenteritis.

A population-based, cross-sectional telephone survey of 9,903 people was conducted to determine the incidence of acute gastroenteritis and the health seeking behaviors of those ill [12]. The rate of acute gastroenteritis was estimated at 0.60 episodes per person-year, which if extrapolated to the population, amounts to 3.2 million episodes each year. During 2002 and 2003, a postal survey completed by 679 general practitioners was conducted to better understand the management of patients with acute gastroenteritis.

**Australia:** In late 2000, the Australian Government Department of Health and Ageing established OzFoodNet, a collaboration of foodborne disease epidemiologists, to more accurately determine the burden of foodborne illness in Australia. To achieve this, the National Centre for Epidemiology and Population Health in collaboration with OzFoodNet conducted a nationwide community survey to estimate the burden of acute gastroenteritis and analysed data from notifiable surveillance, outbreak summaries, community surveys,
laboratories and other sources to estimate the burden of illness from sixteen pathogens known to cause acute foodborne gastroenteritis [10].

The number of illnesses due to foodborne transmission was estimated for each of the sixteen pathogens commonly transmitted by food and the proportion of all acute gastroenteritis due to foodborne transmission was calculated. As such estimates have an inherent degree of uncertainty, due largely to a paucity of appropriate quality data about each of the known pathogens, a plausible distribution of data values, rather than a single estimate, was used in the calculations. Real data was used to inform the parameters of the simulated distribution of all elements wherever possible. The plausible interval estimates are credibility intervals with an interpretation akin to credibility intervals in Bayesian inferences. The surveillance and outbreak data were adjusted for under-ascertainment using information from the community survey and other sources. For each pathogen, the proportion of acute gastroenteritis caused by foodborne transmission was derived for Australia from the literature and a Delphi process. Diseases that were potentially foodborne but did not cause acute gastroenteritis or were not acquired in Australia were not included in the estimation. It was estimated that 5.4 million cases of foodborne gastroenteritis occur in Australia each year, with a 95% credible interval of 4.0–6.9 million cases. Foodborne transmission accounts for approximately 32% (95% Credible Interval 24%–40%) of 17.2 million cases of gastroenteritis from all causes annually in Australia [10].

**Canada:** The National Studies on Acute Gastrointestinal Illness were developed in 1999 with the aim of estimating the incidence of acute gastroenteritis and quantifying under-
ascertainment at key interfaces in Canada’s national surveillance program. Four studies were implemented to address these objectives; the population, physician, laboratory and public health reporting studies.

The incidence of acute gastroenteritis was ascertained through a telephone survey conducted in four health regions and nationally. The rate of acute gastroenteritis was estimated at 1.3 episodes per person-year [11]. The physician survey, administered to general practitioners and paediatricians in the same health regions, determined that 3.4% of patients seen by physicians were diagnosed with acute gastroenteritis each month, of which 22.3% were requested to submit a specimen for laboratory testing [21]. The laboratory survey was designed to quantify pathogen yields and examine inter-laboratory variation in practices or policies that may influence pathogen yield. In 2000, there were 459,982 stools specimens tested for enteric pathogens, of which 5%, 15%, 8% and 19% were positive for enteric bacteria (excluding C. difficile), C. difficile, parasites and viruses respectively [22]. The public health reporting study focused on reporting practices at the Health Unit level. Based on these studies, it was calculated that each case of acute gastroenteritis reported to the Provincial Health Authority represented between 105 and 1389 community cases, with a mean of 313 [23].

**Discussion**

By enhancing laboratory-based surveillance and determining the burden of gastroenteritis in regions lacking such estimates, the global initiatives coordinated by WHO and the national studies described in this paper represent important steps towards estimating the global burden of foodborne disease. When national estimates are determined, they must take into account the burden of illness that is not ascertained by routine surveillance. As many patients with acute
gastroenteritis do not visit a health care provider or submit a specimen [5, 23], clinician and laboratory diagnosed cases greatly underestimate the burden of illness in the community. Once the burden of acute gastroenteritis is known, then food- and pathogen-specific estimates can be calculated. The most accurate way to assign burden to specific pathogens is through prospective cohort studies. As patient and physician behaviour is influenced by factors related to an infectious agent, using multipliers based on a syndrome from a retrospective survey may lead to an under-estimation (e.g. noroviruses that cause mild self-limiting illnesses) or over-estimation (e.g. rotaviruses that affect young children) of pathogen-specific burdens. Future studies could be enhanced by taking into consideration the role of immunity when deriving pathogen-specific burden estimates.

Estimating the proportion of acute gastroenteritis due to food requires researchers to combine information from multiple sources and often rely heavily on expert opinion [20, 24]. Using a plausible distribution of values, instead of a point estimate, allows researchers to convey the inexact nature of these assessments. Estimating the proportion of acute gastroenteritis due to food is more challenging in countries without good outbreak data and in developing countries where the role of food as a vector and the spectrum of pathogens causing acute gastroenteritis are not well understood. Improved surveillance and response capacity, both of which are addressed through Global Salm-Surv, are critical to developing these estimates. Studies to better understand the causes of acute gastroenteritis in the high proportion of patients with negative stool cultures will avoid relying on the assumption that the proportion foodborne is similar for cases of known and unknown etiology and further improve foodborne estimates. The impact of dietary differences on foodborne disease estimations also needs to be assessed.
When data from various countries is pooled to derive regional or global estimates, the impact of the study design and existing surveillance systems need to be considered. Prospective and retrospective studies yield different disease estimates. In the English study, when respondents were surveyed retrospectively, prior to prospective study, an incidence of 5.5 cases per person year was calculated, nearly three times that of the prospective study [5]. This retrospective estimate was similar to previous estimates from retrospective studies conducted in the United Kingdom [25, 26] Australia, Canada, Ireland and the United States [4]. Conversely, the prospective estimates from the Netherlands are similar to prospective estimates from the English study [5, 8]. Reasons for the differences have largely been attributed to recall bias or telescoping [5]. However, a more thorough examination of the effect of study design on disease estimates would be beneficial prior to comparing data from national studies. Efforts are underway to develop a model case definition for acute gastroenteritis to further facilitate international comparability of data. Attributes of surveillance systems generating data used in burden estimates (such as sensitivity, representativeness, and predictive value positive) are also important variables to consider when comparing data between countries and regions.

While researchers continue to improve estimates of the burden of foodborne disease, numerous studies are also attempting to attribute disease to specific food-animal sources. Approaches to food attribution include the use of data from outbreaks [5] and sporadic case-control studies [9]. Molecular source tracking methods have been used where subtype information is available from humans and animal-food sources [27]. With more accurate information on the relative contribution of different foods to the total disease burden and more
precise estimates of the burden of foodborne illness, these studies support the overall goal of reducing the socio-economic burden of essentially preventable diseases.
Acknowledgements

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References


<table>
<thead>
<tr>
<th>Surveillance Category</th>
<th>1. No formal surveillance</th>
<th>2. Syndromic surveillance</th>
<th>3. Laboratory-based surveillance</th>
<th>4. Integrated food-chain surveillance</th>
</tr>
</thead>
</table>
| Expected Outcomes     | Non-specific disease     | Non-specific disease     | Etiology-specific, including etiology-specific, including etiology-specific, including etiology-specific, including etiology-specific, including etiology-specific, including etiology-specific, including etiology-specific, including etiology-specific, including etiology-specific, including etiology-specific, including etiology-specific, including etiology-specific, including etiology-specific, including etiology-specific, including etiology-specific, including etiology-specific, including etiology-specific, including etiology-specific, including etiology-specific, including etiology-specific, including etiology-specific, including etiology-specific, including etiology-specific, including etiology-specific, including etiology-specific, including etiology-specific, including etiology-specific, including etiology-specific, including etiology-specific, including etiology-specific, including etiology-specific, 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| Contribution of Surveillance System to Burden of Foodborne Disease | None | Limited | Potentially significant | Significant |

<p>| External Support Required to Conduct Burden of Foodborne Disease Assessment | High | Moderate | Minimal | None |</p>
<table>
<thead>
<tr>
<th>Ability of Surveillance System to Attribute Disease to Specific Food Sources</th>
<th>None</th>
<th>None</th>
<th>Moderate</th>
<th>High</th>
</tr>
</thead>
<tbody>
<tr>
<td>Usefulness of Surveillance Data to Contribute to Risk Analysis</td>
<td>None</td>
<td>Limited</td>
<td>Potentially significant</td>
<td>High, allows validation of models</td>
</tr>
</tbody>
</table>

*Table adapted from ‘Methods for Foodborne Disease Surveillance in Selected sites, WHO’ (WHO/CDS/CSR/EPH/2002.22)*
Table 2. Characteristics of key studies on community burden of acute gastroenteritis

<table>
<thead>
<tr>
<th>Study Description &amp; (Study Period)</th>
<th>Sampling Method</th>
<th>Sample Size</th>
<th>Supporting/Related Studies</th>
<th>Name of Study and/or (Key Collaborators)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Australia</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cross-Sectional</td>
<td>Overall sample was respondents</td>
<td>6087</td>
<td>Laboratory survey; analytic study to determine burden of foodborne illnesses</td>
<td>OzFoodNet (Commonwealth Department of Health and Ageing; State and Territory health authorities; the Communicable Disease Network of Australia; the National Centre for Epidemiology and Population Health, Australian National University; Food Standards Australia; New Zealand; the Public Health Laboratory Network)</td>
</tr>
<tr>
<td>Population-based Survey (Sep 2001 - Aug 2002)</td>
<td>stratified by state</td>
<td>providing</td>
<td>determine</td>
<td></td>
</tr>
<tr>
<td>(7 states/territories in Australia) with households and respondents randomly selected</td>
<td>information on individuals gave details about their own experience and about gastroenteritis in other household members</td>
<td>16400</td>
<td>foodborne illnesses</td>
<td></td>
</tr>
<tr>
<td><strong>Canada</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Multiple Cross-Sectional</td>
<td>Random selection of households and respondents from</td>
<td>17500</td>
<td>Laboratory survey; analytic</td>
<td>NSAGI (Public Health Agency of Canada;</td>
</tr>
<tr>
<td>Study Type</td>
<td>Sampling Method</td>
<td>Sample Size</td>
<td>Study Design</td>
<td>Collaboration</td>
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<tr>
<td>Population-Based Surveys</td>
<td>respondents (next birthday in household) located in selected health regions and 3500 on a national level. Health regions selected to represent urban and rural conditions</td>
<td>4 selected health regions and 3500 on a national level. Health regions selected to represent urban and rural conditions</td>
<td>Physicians; local health unit survey; case definition analysis</td>
<td>Provincial Epidemiologists and Laboratory Directors; Department of Population Medicine, University of Guelph</td>
</tr>
<tr>
<td>England Cohort Study</td>
<td>Stratified random (by age and sex) sampling of cohort from GP registers</td>
<td>9776 enrolled in cohort</td>
<td>Physician based studies, nested case control study; analytic study to determine burden of foodborne illnesses and food-specific</td>
<td>IID Study: (Public Health Laboratory Service; the Medical Research Council General Practice Research Framework; the London School of Hygiene and Tropical Medicine)</td>
</tr>
<tr>
<td>Country</td>
<td>Study Type</td>
<td>Methodology</td>
<td>Sample Size</td>
<td>Survey Type</td>
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<td>-----------------------------------------------------------------------------</td>
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<td>-------------</td>
</tr>
<tr>
<td>Ireland</td>
<td>Cross-Sectional</td>
<td>Random dialling in the Republic of Ireland and Northern Ireland, random selection households and respondents (next birthday in household) per month in the Republic of Ireland and 400 per month in Northern Ireland</td>
<td>9,600</td>
<td>Physician</td>
</tr>
<tr>
<td>Netherlands</td>
<td>Prospective</td>
<td>Random selection of individuals within representatively selected GP catchments</td>
<td>4860</td>
<td>Physician based studies, nested</td>
</tr>
<tr>
<td>United States</td>
<td>Multiple Cross-Sectional Population-Based Surveys (1996 - 1997 [1st survey])</td>
<td>Random selection of households and individuals</td>
<td>A total of 52,605 respondents (9003 in 1st survey, 12,755 in 2nd survey, 14,647 in 3rd survey and 16,200 in 4th survey)</td>
<td>Laboratory surveys; active surveillance; case control studies; analytic study to determine burden of foodborne illnesses</td>
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<td>Population-Based Surveys (next birthday in household) in selected Counties or States (1998 - 1999 [2nd survey])</td>
<td>Random selection of households and individuals</td>
<td>(9003 in 1st survey and 16,200 in 4th survey)</td>
<td>Analytic study to determine burden of foodborne illnesses</td>
</tr>
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<td>[3rd survey] 2000 - 2001</td>
<td>Random selection of households and individuals</td>
<td>(14,647 in 3rd survey and 16,200 in 4th survey)</td>
<td>Analytic study to determine burden of foodborne illnesses</td>
</tr>
<tr>
<td></td>
<td>[4th survey] 2002 - 2003</td>
<td>Random selection of households and individuals</td>
<td>(14,647 in 3rd survey and 16,200 in 4th survey)</td>
<td>Analytic study to determine burden of foodborne illnesses</td>
</tr>
</tbody>
</table>
survey}