Noora Hinkka

Salmonella infections acquired abroad and detected in Finland, 1995-2009

Master's thesis
University of Tampere
Medical School
Department of International Health
Health Sciences (International Health)
June 2011

University of Tampere

Medical School

Department of International Health

HINKKA, NOORA: SALMONELLA INFECTIONS ACQUIRED ABROAD AND DETECTED IN FINLAND, 1995-2009

Master's Thesis, 63 pages

Supervisor: Professor Hanna Nohynek, Veterinary Epidemiologist Ruska Rimhanen-Finne

Health Sciences (International Health)

June 2011

In Finland, the annual number of reported *Salmonella* infections has been approximately 2,000-3,000 during the past 10 years. The vast majority of the infections has been acquired abroad. Nowadays salmonellosis is the second most reported cause of gastroenteritis in Finland. All *Salmonella* infections are included in generally hazardous communicable diseases.

This register-based study aims to find out the trends of *Salmonella* infections that are most likely contracted from abroad, but detected in Finland during 1995-2009, and to examine how these trends are correlated with the number of Finnish travellers to these destinations. All the registered 30,977 *Salmonella* cases of foreign origin during 1995-2009 were received from the National Infectious Diseases Register. Passenger information was extracted from the public data of Statistics Finland. The analyses targeted countries that had been at least once among the ten most frequently reported source countries for salmonellosis during the follow-up period.

The vast majority of the *Salmonella* infections was detected among Finnish citizens (95.0%). More female (54.4%) than male cases were reported (p <.001). The mean age of the persons with registered salmonellosis of foreign origin (37.7 yrs) was not essentially changed during the study period, but, instead, reports on children (<20 yrs) with *Salmonella* infection increased at the end of the study.

Thailand, Spain and Turkey were the most frequently reported source countries. The overall risk of travel-related salmonellosis was 31.8 / 100,000 Finnish travellers per year (including one-day cruises). The highest risk countries were Thailand (679.8/100,000 travellers to the country), Tunisia (517.0), and India (415.1). In general, the trends of incidences seemed to decline in almost every studied country since year 2000. However, Thailand was the only country that increased the number of Finnish passengers but had a steady or even increasing incidence trend of salmonellosis among the Finnish travellers.

S. enteritidis (43.5%) was unambiguously the most frequently detected serotype in Finland, followed by *S. typhimurium* (7.8%), *S. virchow* (4.2%), and *S. stanley* (3.7%). The majority of some serotypes was almost solely connected with travellers to a single country: *S. stanley* to Thailand and *S. bareilly* to India.

Future research is needed to understand the increasing number of reported salmonellosis of foreign origin in children under 20 years. Also, the gender disposition of reported salmonellosis in various age categories is still unknown.

Sisällysluettelo

ABBREVIATIONS

CI	Confidence interval
EAEI	Enteroaggregative *Escherichia coli*
ETEC	Enterotoxigenic *Escherichia coli*
n	Sample size
OR	Odds ratio
p	p-value
PT	Phage type
RRR	Reporting rate rations
S.	*Salmonella*
spp.	Species (pluralis)
STAT	Statistics Finland
TD	Traveller's diarrhea
VFR	Visiting friends and relatives

1 INTRODUCTION

Infections caused by *Salmonella* bacteria (also known as salmonellosis) represent a considerable disease burden. It is estimated that every year *Salmonella* infections affect 93.8 million people globally with 155,000 deaths (Majowicz et al. 2010). Salmonellosis can cause a serious gastroenteritis in humans. However, like many other diseases, the infection can also be sub-clinical or asymptomatic. The disease is usually food-borne, but other routes (water or vector-borne) are also possible (Zoonoosikeskus; Korkeala 2007). An estimated 80.3 million people suffer from food-borne salmonellosis every year (Majowicz et al. 2010).

In Finland, the situation is different compared to most other countries in the world because of the considerably low incidence of *Salmonella* bacteria among farm animals due to long-term planning surveillance programmes. In result of that the incidence of domestically acquired salmonellosis in humans is low compared to those acquired abroad due to international travelling, on average, 15 and 80%, respectively (around 5 % of cases the information of a source country of the infection is lacking). The annual number of reported *Salmonella* infections to the National Infectious Diseases Register has been 2,000-3,000 during the past 10 years. Until the year 1999, *Salmonella* infections were the most frequently reported cause of human gastroenteritis in Finland. Since then salmonellosis has been on the second place after campylobacteriosis. (Zoonoosikeskus) According to Finnish legislation, *Salmonella* infections are included in generally hazardous communicable diseases (Tartuntatautilaki).

All the reported salmonellosis cases are laboratory confirmed in Finland. The most commonly reported serotypes in Finland are *S. enteritidis*, *S. typhimurium*, *S. stanley*, and *S. virchow* (Hulkko et al. 2010; Zoonoosikeskus). In 2009, the most frequently reported source countries for acquiring salmonellosis among Finnish travellers were Thailand (31%), Turkey (5%), Egypt (5%) and Spain (5%) (Hulkko et al. 2010). However, it is unknown, which countries in the long run have contributed the most to salmonellosis detected in travellers in Finland, and how much a single source country has affected on the serotype distribution. This study was designed to answer the questions. In addition, a study question is how many travel-related *Salmonella* cases detected in Finland belong to foreigners. The interest is also to find out, weather there has been any changes in incidences of salmonellosis in countries with the highest risk. In addition, we are eager to know if the change in Finnish travel pattern, e.g., increasing number of trips to Asia, has contributed to the observed serotype distribution. This thesis tries to answer these questions.

The first part of the thesis introduces a reader to some published research on traveller's diarrhea, including salmonellosis. Considerable research has been devoted to the main topic, rather less attention has been paid to one bacteria genus like *Salmonella* spp. In addition, only few studies have been related to incidences of traveller's diarrhea among Finnish passengers in various destination countries.

The second part presents the register-based study on *Salmonella infections acquired abroad and detected in Finland, 1995-2009.* This research is retrospective and utilizes quantitative data. The main research data is extracted from the National Infectious Diseases Register. It provides all the reported *Salmonella* cases that have been acquired abroad and detected in Finland during 1995-2009. The data include also some basic details, such as gender of the cases and a suspected source country. Information on Finnish passenger number to various destination countries is received from Statistics Finland and is used to estimate incidences to acquire salmonellosis when Finns are travelling abroad.

2 REVIEW OF LITERATURE

2.1 Sources and principles used for literature review

The literature review was carried out in PubMed-database using keywords “salmonellosis” or “*Salmonella*” in different combination with words “traveller's diarrhea”, “tourists”, “global”, “etiology”, and “Finnish”. The search was also continued with using reference list from those relevant articles found in PubMed. In addition, the internet pages of National Institute for Health and Welfare (THL), Statistics Finland (STAT), the Zoonosis Centre, and the Association of Finnish Travel Agents (AFTA) were used.

THL (www.thl.fi) is a public research and development institute in the area of health, wellness and welfare. It is also a public statistical authority and keeps up the register, e.g., on laboratory confirmed infectious diseases detected in Finland. STAT (www.stat.fi) is a public authority, which produces the vast majority of Finnish official statistics. It provides, e.g., the estimations on number of Finnish travellers. The Zoonosis Centre (www.zoonoosikeskus.fi) is a national network of professionals from THL and the Finnish Food Safety Authority Evira (www.evira.fi). It was officially founded in 2007. “The purpose of the Centre is to ensure efficient cooperation of control and research operations in the monitoring and prevention of diseases transmitted between humans and animals. The Centre also serves as the Finnish contact point towards EU and other international zoonosis experts.” AFTA (www.afta.fi) is formed by travel agents, tour operators and incoming agents. It provides travel-related information and statistics.

2.2 Introduction to traveller's diarrhea

A beloved child has many names. Traveller's diarrhea (TD), aka 'Bali belly', 'Delhi belly', 'Fanny Tammy', 'Montezuma's revenge', or 'tourist trot', is the most common illness of international travellers originating from industrialized countries (Steffen 1986; Steffen & Ericsson 2000). The classic definition for traveller’s diarrhea encounters three or more unformed stools in 24 hours with at least one accompanying symptom: fever, nausea, vomiting, abdominal cramps or pain, tenesmus, or bloody stools. Milder forms can be manifested with fewer than three stools with or without additional symptoms.

(DuPont and Khan 1994; Steffen et al. 2003)

Travellers can be exposed to a broad range of enteropathogens that they are not used to encounter at home. According to a local hygiene level, the world can be divided into three different sections: low, intermediate and high risk areas (see Figure 1). Generally speaking, the risk of TD increases significantly when moving from low-risk areas to intermediate or high-risk areas, whereas moving between low-risk areas maintains the risk low. (DuPont and Khan 1994) Indeed, TD occurs commonly in all mentioned groups regardless of the country of origin. The incidence of TD has been unchanged for more than 50 years among travellers from industrial countries going to high-risk areas (Shah et al. 2009).

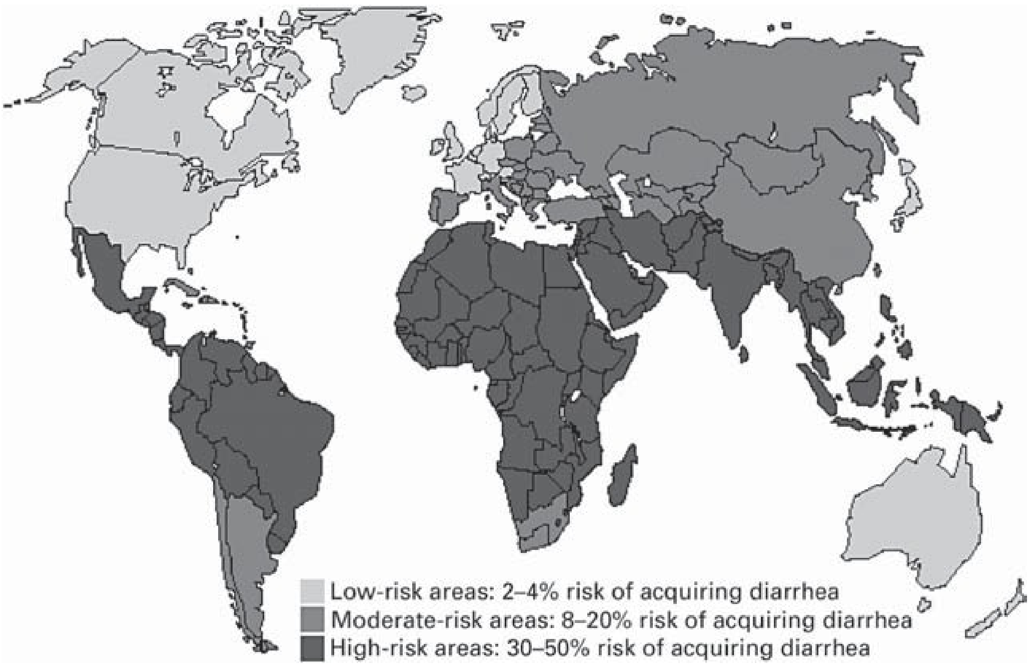

Figure 1: Incidence of TD by geographical area for travellers coming from low-risk regions. (DuPont 2005).

Traveller's diarrhea can originate from enteropathogenic bacteria, parasites or viruses (Gascon 2006). Incubation period varies depending on the pathogen (Table 1).

Enterotoxigenic *E. coli* (ETEC) has been detected to be the most common enteropathogen causing traveller's diarrhea globally (up to 33.6% of cases) (von Sonnenburg et al. 2000; Shah et al. 2009). *Salmonella* is also a fairly common cause of TD. It has been identified more often among travellers visiting in Asia (6.6-9.1% of the cases) than in Africa (5.5%), and in Latin America and the Caribbean (4.4%) (Shah et al. 2009).

Enteropathogen	**Incubation period**
ETEC	10-48 h
EAEC	8-48 h
Shigella spp.	1-3 days
Campylobacter jejuni	2-4 days
Salmonella spp.	12-24 h
Aeromonas spp.	1-2 days
Vibrio parahemolyticus	2-48 h
Yersinia enterocolitica	2-10 days
Rotavirus	1-3 days
Adenovirus	7-10 days
Giardia lamblia	3-40 days
Cyclospora cayetanensis	2-11 days

Table 1: Incubation period for some enteropathogens causing TD. (Gascon 2006)

2.3 High-risk versus low-risk regions

Classifying the world into three sections based on the level of local hygiene and rates of diarrhea in travellers and in infant population living in the region, the risk of acquired traveller's diarrhea can be presented in the following way: The expected low-risk countries, where the predicted risk of TD is around 4%, include the United States, Canada, Western Europe, Japan, Australia, and New Zealand, whereas often high-risk regions, where the predicted risk of TD is around 40%, include Latin America, Africa and souther Asia. The expected intermediate risk areas, where the predicted risk of TD is around 15%, include certain Caribbean islands (e.g. Jamaica), the Middle East, some northern Mediterranean areas, China, and Russia. (DuPont and Khan 1994; DuPont 2006)

Instead, using the data from GeoSentinel (www.geosentinel.org), which is a worldwide communication and data collection network for the surveillance of travel related morbidity established in 1995, Greenwood et al. (2000) calculated reporting rate rations (RRRs) for the travel-related gastrointestinal illnesses globally. It divides the world into four categories: very high, high, moderate and low RRRs' regions. RRRs can be used for the risk estimation of traveller's diarrhea. The divisions of hygiene level in former mentioned articles by DuPont & Khan and DuPont are quite similar with the study of Greenwood *et al.* as seen in Figure 2.

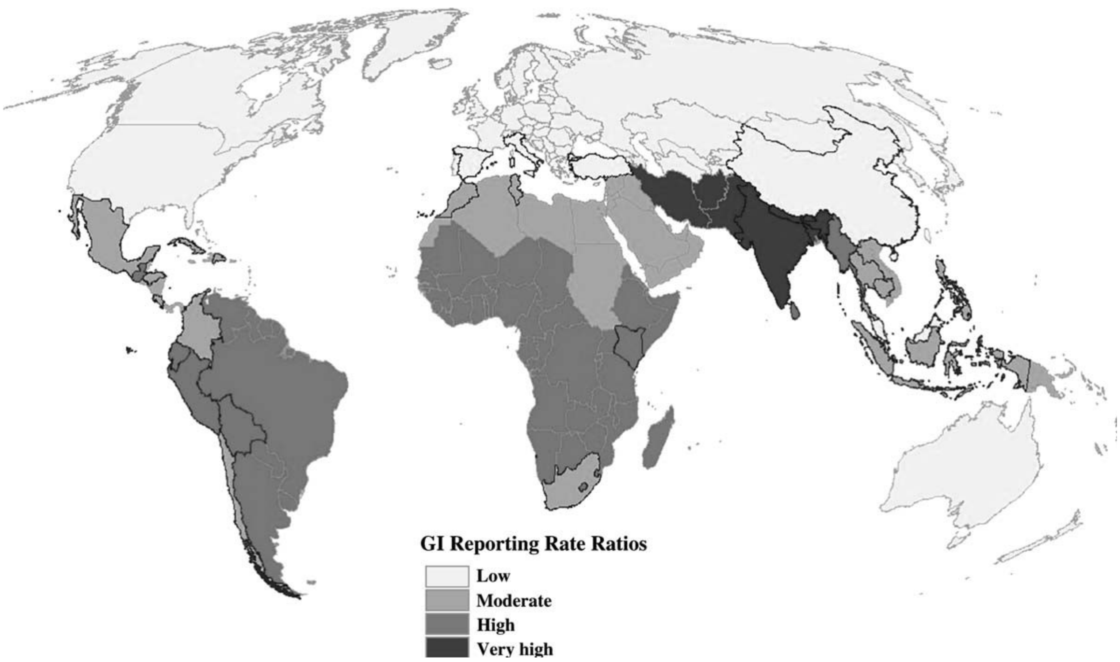

Figure 2: A profile map of reporting rate rations (RRRs) shows relative rate of acquired gastrointestinal infection by destination. A GeoSentinel reporting rate for gastrointestinal infection for a region = (a number of travellers reporting to GeoSentinel with an infectious gastrointestinal diagnosis after travel to the region) : (number of tourist arrivals to the region). RRR for gastrointestinal illnesses acquired in the destination region = (reporting rate for gastrointestinal infection for the region): (reference region's reporting rate). (Greenwood et al. 2008)*

*western and northern Europe were used as a reference region, because of the lowest rates of infections associated with oral ingestion of pathogens in travellers.

2.4 Risk factors related to traveller's diarrhea

A Swedish study (Ahlm et al. 1994) of 442 travellers revealed that 49% of the travellers experienced some travel-related health problem (infectious or non-infectious disease, accident or injury, insect bites) during their trip, and 14% had symptoms for more than one illness. Most travellers (81%) were visiting in a high risk area for acquiring diarrhea. The most frequently reported health problems were diarrhea (36%) and upper respiratory infections (21%). TD was the only experienced health problem in 23% of the cases, whereas 12% had also other health problems during the trip. As one can expect, the overall incidence of illness was significantly higher among travellers going to high risk than to low risk areas (55% vs. 26%), and among those going on adventure tours compared to recreational tourists (74% vs. 41%). The incidence of illness was higher among young travellers than among the elderly (65% vs. 33%). Also, the longer the trip, the bigger the risk of falling ill. This was also the case with acquiring diarrhea. The study showed that as many as every other Swedish travelling to tropical and subtropical areas experienced some kind of travel-related, often incapacitating health problem. The mean duration of travel in the study was four weeks (median 3 weeks, range 1 week to 26 weeks) and the mean age 37 years (range 10 to 79 years). (Ahlm et al. 1994)

Travellers are exposed to a broad range of enteropathogens that they are not used to encounter at home. The risk of TD increases significantly when moving from low-risk areas to intermediate or high-risk areas, 10% and 40-60% respectively, whereas moving between low-risk areas the risk is only 2 to 4%. Of course, TD is not only a problem for travellers coming from low-risk areas, but also visitors from intermediate or high-risk areas suffer from TD. For those travellers the risk has been discovered to be 8-18%. (DuPont and Khan 1994) However, after longer stay in a new surrounding will diminish the risk of TD in spite of the origin of a traveller as some immunity develops (Steffen et al. 2003).

The average length for a package holiday trip is 1-2 weeks. One study (von Sonnenburg et al. 2000) found that almost two thirds of the tourists developed TD during a two week stay at high-risk destinations of India and Kenya. Also, large differences in infection rates were detected between hotels which were classified as high-risk and low-risk hotels.

Persons with impaired gastric-acid barrier are included in the group of particularly high risk for acquiring TD (Steffen et al. 2003; von Sonnenburg et al. 2000). Young age is also a significant risk factor for TD and salmonellosis, with the individual risk decreasing with increasing age. Infants, toddlers, and young adults of 15–30 years are particularly prone. (Ekdahl, de Jong, Wollin, et al. 2005; Steffen et al. 2004; Pitzinger et al. 1991) Also, small children often have particularly severe and long-lasting course of TD (Pitzinger et al. 1991). The elevated risk in the youngest part of the population is associated with increased faecal or oral contamination (e.g., poor hand hygiene of children, crawling and playing on the floor) in combination with poorer immunity than in adults. High risk in young adults is associated probably with ingestion of larger volumes of potentially contaminated food and an adventurous lifestyle. (Steffen 2005; Ekdahl, de Jong & Andersson 2005) In addition, one study found statistically significant ($p < .001$) differences in travel-associated morbidity between the sexes. Women were proportionately more likely than men to present not only with acute diarrhea (OR, 1.13; 95% CI, 1.09–1.38), but also chronic diarrhea (OR, 1.28; 95% CI, 1.19–1.37). Nevertheless, if taken a closer look at the numbers of acute diarrhea only caused by bacteria, the sex differences seem to disappear: OR 1.06; 95% Cl, 1.0-1.11. (Schlagenhauf et al. 2010) Many studies have not detected a gender difference for total diarrhea rates (Ekdahl, de Jong & Andersson 2005; Steffen et al. 2004; von Sonnenburg et al. 2000). The main risk factors related to acquiring traveller's diarrhea are represented in Figure 3.

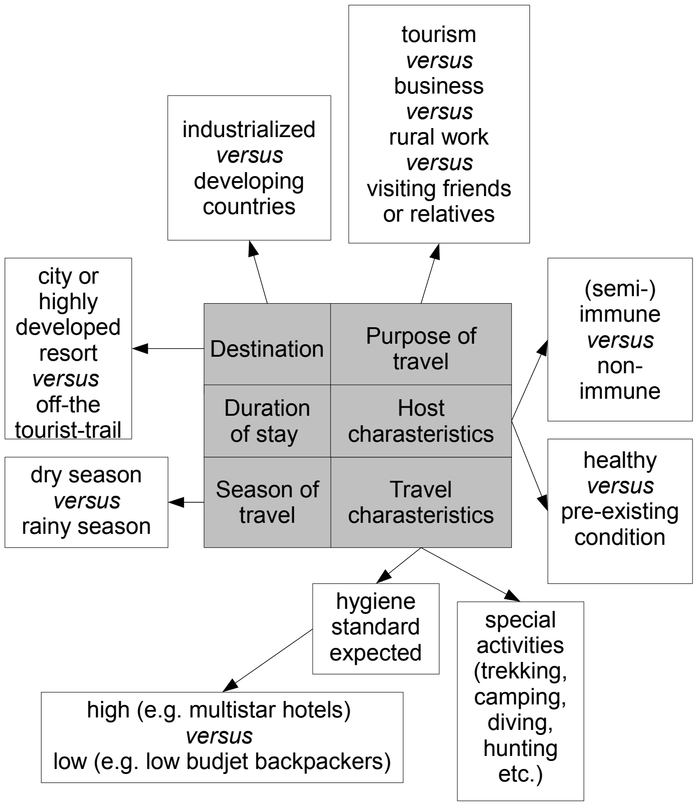

Figure 3: Travel health risks vary greatly depending on destination, season of travel, duration of stay, purpose of travel, and travel and host characteristics (modified from Steffen et al., 2003).

Some studies have found that seasonality has an effect on the etiology of TD (Mattila et al. 1992; Ekdahl, de Jong, Wollin, et al. 2005), but not all (von Sonnenburg et al. 2000). A Finnish study (Mattila et al. 1992) compared the findings of TD cases between the two Finnish traveller groups visiting Agadir, Morocco, in winter and fall of 1989. The total of 579 adults were participating in two package holidays to Morocco in winter (n = 233) and fall (n = 346). The results showed statistically significant differences between the groups. There were at least one pathogen found in 62% out of all 60 diarrheal cases in winter, and in 58% out of all 111 cases in fall. In addition, multiple pathogens were more often detected in winter (21%) than in fall (8%). Also *Salmonella enterica* showed seasonal variation. In fall, it was almost as common as ETEC (25% of diarrheal cases), but instead rare in winter (10%). Thus, the etiology of TD varied according to the season in the same tourist destination.

Genetic factors may also explain differences in morbidity between travellers, but that area needs more research (von Sonnenburg et al. 2000; DuPont 2009).

2.5 Importance of detecting traveller's diarrhea

The study of Nygård et al. (2002) discusses the possible importance of surveillance of infections among returning travellers. Surveillance would help detect emerging infections and outbreaks of infectious diseases in tourist destinations. It could be used to evaluate the characteristics of pathogens of the destination country, such as trends of antimicrobial resistance patterns and pathogenic changes. The destination country may lack the surveillance system or the surveillance system is deficient, or laboratories have limited capacity for testing. In addition, local public health authorities are not necessarily aware of infections or outbreaks among tourists if the local residents are not affected. (Nygård et al. 2002)

2.6 Studies on some popular source countries for acquiring TD

The Association of Finnish Travel Agents has listed the top-ten package holiday destinations for Finns in 2010 (→ Perspective for world tourism). As the list shows, the most popular destinations were mostly countries in Europe and around the Mediterranean see. In the list, there is only one Far East destination: Thailand.

Thailand is considered as a high risk country for acquiring TD (see the map in Figure 1 or 2). However, it is estimated that during the past 20 years the incidence rate of traveller's diarrhea has decreased in Thailand reaching now as low a proportion as 10% in Chiangmai and 20% in Phuket (Gushulak et al. 2007).

There are several TD-related studies conducted in Thailand. One study concentrated on pointing out the risk of TD by eating in tourist restaurants in Bangkok, Thailand. The study group collected samples from 35 restaurants (randomly chosen) out of 121 restaurants that were recommended by the two best selling tourist guide books on Amazon's book store. In chosen restaurants, samples from two meals were collected: one meal was ordered according to recommendation from a guide book and the other meal according to the likelihood to contain pathogens (e.g., dishes with raw meat or fresh salad). Still, only three pathogens were studied, *Salmonella*, *Campylobacter* and

Arcobacter (a *Cambylobacter*-like organism). The reason for that was that those bacteria were considered to be the most common source of TD in Thailand according to the authors. (Teague et al. 2010)

As a result of the study, eight restaurants out of 35 places had a positive dish and one restaurant had both dishes positive. Only one dish (2%) was positive to *Salmonella* (group E) and no traces for *Campylobacter* was found. Instead, *Acrobacter butzleri* was found from nine dishes (13%). Thus, the study indicated that having a meal in a restaurant recommended for tourists in Bangkok resulted in the risks of acquiring salmonellosis or *A. butzleri* infection 2 and 13%, respectively. Following binomial distribution probability rules, this means that the risk of exposure to more prevalent *A. butzleri* rises up to 75% when having 10 meals in those recommended restaurants. The price level of the restaurant was not a protective factor. (Teague et al. 2010)

One TD related study from Thailand (Chongsuvivatwong et al. 2009) used interviews of foreign tourist departing airports near the tourist destinations of Phuket and Chiang Mai. More than 22,000 tourists completed questionnaires. In addition, stool samples were collected from a subgroup of 56 people who had acquired TD in Phuket. Based on completed questionnaires the attack rate for TD among Europeans was 8%, whereas those from the United States and Australia / New Zealand it was 7 and 16%, respectively. In addition, those with stool samples revealed that 8 persons (14%) carried *Aeromonas sobria,* 7 persons (13%) enterotoxigenic *Escherichia coli* (ETEC), 7 persons (13%) *Vibrio spp* (two with *V. cholerae*), 2 persons (4%) *Campylobacter*, and 2 persons (4%) *Salmonella* spp. There were 3 persons (5%) who had more than one pathogen in their sample. The samples from the rest 33 persons (59%) were negative despite the symptoms of TD. None of the stool samples contained any signs of parasite infection. The mean duration of the stay in Thailand was less than 12 days.

Eating behaviours were studied among travellers. The most hotels provided a free breakfast. In addition, an equal proportion of visitors ate at the hotel or had their meals and beverages outside the hotel. Eating outside the hotel was an important risk factor for TD, which indicates that the overall hygiene level was better in hotel restaurants. The dose-response relationship between eating outside the hotel and the development of diarrhea was clear. Instead the study did not show increased incidence of diarrhea for people with putative risky eating behaviour such as eating meat, raw oysters or fish, salad, and uncooked vegetables. In addition, even though tap water was relatively rarely consumed among travellers, drinking tap water in these two Thai cities seemed to be a protective factor against TD according to the study. The reason for that remained unclear. Consequently, the study indicates that at least these two popular tourist destinations in Thailand do not belong to the high-risk regions of acquiring TD for Europeans and, also, that it is more important where tourists eat than what food items they eat. (Chongsuvivatwong et al. 2009) This is actually in consistency with the study of Rack et al. (2005), which argued that despite the lowest compliance with food hygiene among travellers to Thailand compared to other studied destinations, they had also the lowest incidence of illness.

Rack et al. (2005) studied the risk for travel-related diseases, symptoms and accidents in Germans who travelled to five popular tropical regions or countries: Kenya / Tanzania, Senegal / the Gambia, India / Nepal, Thailand, or Brazil. Only travellers with the age of over 18 years were studied. Other exclusion criteria were duration of the travel to more than two months, and major acute or chronic diseases. A total of 658 travellers, who visited the travel clinic of the Berlin Institute of Tropical Medicine prior to departure during 2003 and 2004, were followed up. Overall, an illness was reported by 43% of travellers and 10% reported more than one adverse health event. The most frequently mentioned symptom was gastrointestinal problems (35%). The mean duration of a disease was 5.9 days (ranging from 0 to 12.5 days). More details are seen in Table 2.

In the studied population, 56 % of those who travelled to India or Nepal became ill (OR 1.7; 95% CI 1.3-2.2; $p < .01$). The risk of becoming ill was significantly elevated in those two countries compared to other studied destinations, e.g., in Thailand 35% (OR = 0.71; 95% CI 0.6–0.9; $p < .01$) got sick. Still, there were no differences in age or travel characteristics among visitors to different destinations, especially between India and Thailand. Thailand and India / Nepal were the most popular back-packing destinations. (Rack et al. 2005)

Characteristic	
Mean age (yr)	40.3
Age range (yr)	18-80
Destination	
Brazil	12.5%
India / Nepal	24.9%
Kenya / Tanzania	25.4%
Senegal / the Gambia	5.2%
Thailand	32.0%
Mean duration of travel (d)	23.9
Duration range (d)	3-62
Travel conditions	
Basic (backpacker)	43.6%
Good (hotel)	56.4%
Previous travel to tropical countries	61.4%
Behaviour	
Food risk	78.9%
Tap water	11.7%
Raw vegetables / salad	75.9%
Raw milk	6.4%
Raw meat / fish	30.3%
Animal contact (except mosquito bites)	5.5%

Table 2: The upper part shows characteristics of study population and travel demographics, and the lower part the proportion of travellers taking part in risky behaviour. (Rack et al. 2005)

Shared factors for those reported having an illness were young age ($p < .05$), travel under basic conditions ($p < .01$) and long duration of travel ($p < .01$). However, there is a tendency for younger people to have longer-term (back-packing) travels compared to an average middle-age tourist. This could explain the connection of these two factors and also the risk for acquired illness, because longer time spent abroad can simply accumulate the risk over time. In addition, the longer the time spent travelling, the more difficult it is to keep up the manner of avoiding risky food items, e.g., fresh salad or ice cream. Anyway, according to the study it seemed that there were no association between illness and gender or travel experience. (Rack et al. 2005)

Interestingly, the study did not find an association between low food hygiene and morbidity, except in India. Of all studied travellers, only 20% followed the traditionally recommended dietary restrictions (shown in Figure 4) with the exception of India, where nearly 50% of travellers followed the recommendations. The lowest compliance with food hygiene was among travellers to Thailand and Brazil but, surprisingly, they had also the lowest incidence of illness. Instead, those who did not follow the traditionally recommended dietary restrictions in India showed a double-fold risk of illness (OR = 2.04; 95% CI 1.09–3.81; $p < .05$). There were no age or travel characteristics differences in travellers to India or Thailand or other countries in the study. Thus, according to the study sticking to food restrictions may be useful and protective in travellers going to a high-risk area, such as India, but that is not the case in all regions of low food hygiene. (Rack et al. 2005)

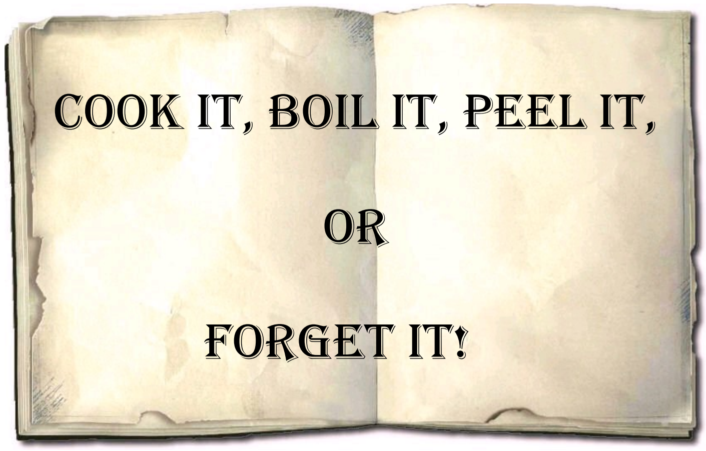

Figure 4: Traditionally recommended dietary restrictions.

Keskimäki et al. (2000) studied the incidence of TD and the prevalence of bacterial enteropathogens, viruses and parasites in faeces of 204 Finnish travellers, who made a round-the-world trip in 16 days. They travelled from Finland to China, Malaysia, Australia, Fiji, Chile and Brazil and then back to Finland. During the trip 75 persons (37%) suffered from TD that seemed to occur in two phases. The first peak of diarrhea occurred during the first days after departure and the second peak during the last days before returning to Finland and after homecoming. In this study, the most commonly identified non-*E. coli* pathogens were strains of various *Salmonella enterica* serotypes, which were isolated either alone or with another bacterial pathogen in samples from 24% (n = 14) of the diarrheal episodes and 3% (n = 4) of the healthy returnees (p = 0.003). The study suggests that travellers are commonly exposed to multiple bacterial pathogens, such as *S. enterica*, and those can be even more common cause of TD than *E. coli*. (Keskimäki et al. 2000)

2.7 Salmonellosis

The genus *Salmonella* belongs to the family of *Enterobacteriaceae*. *Salmonella* bacteria are classified according to the Kauffman and White classification scheme based on *Salmonella* bacterial surface O- and H-antigens. There are around 2,500 serotypes in the genus. Serotypes can be divided into two species called *Salmonella enterica* and *S. bongori*. *S. enterica* has six subspecies: *S. enterica* subsp. *enterica, S. enterica* subsp. *salamae*, *S. enterica* subsp. *arizonae, S. enterica* subsp. *diarizonae, S. enterica* subsp. *houtenae, S. enterica* subsp. *indica.* Because many of the pathogenic serotypes of the *S. enterica* species are in the subspecies of *enterica,* it can be said that all the most important *Salmonellae* belong to *S. enterica* subsp. *enterica.* This subspecies is also the biggest one; it has as many as 1,500 different serotypes. (Korkeala 2007)

The usual growing temperature for *Salmonella* range from 7 to 47°C, but the optimal temperature is about 37°C. The optimal pH is around 6.5-7.7 ranging from 4.5 to 9.5. *Salmonella* can be destroyed easily by high cooking temperatures. Instead, it survives well when the contaminated food item is frozen or dried, all though the bacteria cannot grow in such extreme conditions. When the food is thawed or moistened the bacteria start to grow again. (Korkeala 2007)

The infective dose for salmonellosis is usually 10^5–10^8 cells (Gascon 2006; Korkeala 2007). However, if a food item contaminated by *Salmonella* is greasy (e.g. chocolate), it protects the bacteria from gastric acid so that even few *Salmonella* cells in the gut can create the infection (Blaser & Newman 1982; Korkeala 2007). Usually, the digested number of *Salmonella* bacteria is directly correlated to the clinical symptoms and inversely correlated to the incubation period. In other words, those patients who have a short incubation period (less than 22 hours) are more likely to have stronger stomach pain, higher fever and longer-lasting symptoms. Also, those patients are more likely to need hospitalization. The incubation period for salmonellosis usually varies from 8 to

72 hours and the infection normally lasts less than 6 days. (Korkeala 2007)

An infection caused by *Salmonella* bacteria belongs to the most important bacterial zoonoses (Gascon 2006). It is estimated that the infection affects globally 93.8 million people every year with 155,000 deaths (Majowicz et al. 2010). Salmonellosis can cause a serious gastroenteritis in humans. Usually, the disease is food-borne, but it can also be water or vector-borne (see Figure 5). (Korkeala 2007; Zoonoosikeskus). An estimated 80.3 million people suffer from food-borne salmonellosis every year (Majowicz et al. 2010).

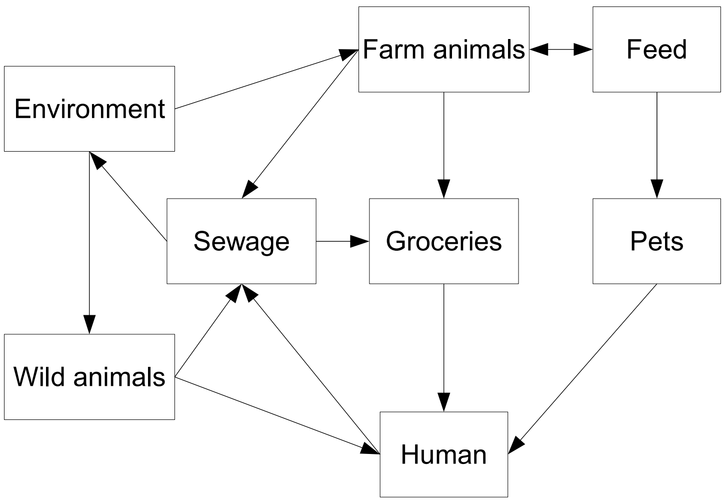

Figure 5: The cycle of Salmonella *bacteria in our surroundings (Korkeala 2007).*

In Finland, the total number of yearly detected and reported *Salmonella* infections has been around 2,000-3,000 during the past 10 years (Table 3) (Zoonoosikeskus). However, it is estimated that the real yearly number of infections would have been as many as 30,000, because only a minor proportion of cases ends up to be detected and reported (Korkeala 2007). Anyway, the proportion of reported domestically and internationally acquired salmonellosis has been stable at least for 20 years in the way that 70-90% of infections are travel-related (Kyyhkynen et al. 2004; Hulkko et al.

2009). For example, in 2008 the total number of reported salmonellosis in Finland was 3129, whereas in 2009 it was 2329. Still the proportion of domestically acquired salmonellosis was approximately the same in both years (13% of the cases). (Hulkko et al. 2010)

	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009
Foreign origin															
S. enteritidis	1033	976	929	951	893	1052	1243	904	887	758	834	879	735	1066	658
S. typhimurium	141	176	168	137	104	205	143	115	155	183	194	141	246	198	166
S. virchow	80	155	88	83	76	50	79	55	67	74	88	80	135	115	90
S. hadar	56	66	63	81	113	125	96	69	58						
S. newport										53		66		76	
S. infantis	179	62		69											
S. braenderup			35		38	49									
S. stanley							63	65	67	105	113	116	175	136	111
S. corvallis											60		59		68
Other	820	897	735	812	678	747	757	636	628	665	654	745	923	1014	846
Total	2309	2332	2018	2133	1902	2222	2376	1844	1862	1839	1943	2027	2273	2605	1939
Domestic origin	1096	481	808	512	656	325	390	406	310	336	443	397	372	374	309
Unknown origin	159	140	232	301	476	224	145	102	107	86	111	151	92	150	81
Total number of reported cases	**3564**	**2953**	**3058**	**2946**	**3034**	**2771**	**2911**	**2352**	**2279**	**2261**	**2499**	**2575**	**2737**	**3129**	**2329**

Table 3: In upper part, the number of internationally acquired Salmonella infections and the distribution of the most common serotypes between years 1995-2009. In lower part, the number of domestically acquired salmonellosis, the number of cases with unknown source country, and the total number of reported salmonellosis detected in Finland 1995-2009. S. typhi *and* paratyphi *are excluded. (Hulkko et al. 2010)*

For many years in Finland, the most common *Salmonella* serotype for domestically acquired infection was *S. typhimurium*, whereas *S. enteritidis* was the most common travel-related serotype for Finns (Kyyhkynen et al. 2004; Hulkko et al. 2010). During 2001–2002, Finns acquired salmonellosis from 102 countries. The biggest risk countries were Malaysia (incidence of 1,600 / 100,000), followed by India (1,237 / 100,000), Tunisia (671 / 100,000), Egypt (440 / 100,000), Thailand (436 / 100,000), Bulgaria (288 / 100,000), Turkey (125 / 100,000), and Spain (97 / 100,000). If the distribution of infected travellers from Spain and Thailand are compared, notable differences between these two countries are discovered. Infected traveller from Spain had *S. enteritidis* as the most prevalent serotype (77% of the findings), whereas those from Thailand had *S. stanley* and *S. hadar* as the most prevalent (16 and 10% of the findings, respectively). *S. enteritidis* was responsible only for 8% of the findings in Thailand. Furthermore, there were differences between *S. enteritidis* phage types (PTs). For travellers from Spain, PT 4 covered 34% and PT1 26% of all discovered 20 different *S. enteritidis* phage type findings. Instead, only six different PTs were detected among travellers from Thailand. (Kyyhkynen et al. 2004)

In 2009, the most commonly reported source countries for Finnish to acquire salmonellosis were Thailand (31% of strains), Turkey (5%), Egypt (5%), and Spain (5%) (Hulkko et al. 2010). In comparison, the most common source countries in 2008 were Thailand (35% of strains), Greece (9%), Egypt (5%), and Turkey (5%) (Hulkko et al. 2009). In 2009, *S. enteritidis* was the most common serotype responsible for 34% of all travel-related *Salmonella* findings, followed by *S. typhimurium*, *S. stanley*, *S. virchow,* and *S. corvallis.* The most common phage types of *S. enteritidis* were PT 1 (16%), PT 21(14%) and PT 4 (11%). The same for *S. typhimurium* were PT NST (19), PT 120 (12%) and PT 195 (9%). (Hulkko et al. 2010)

2.7.1 *Salmonella typhi* and *Salmonella paratyphi*

There are two *Salmonella* serotypes that cause systemic infection in humans, *S. typhi* and *paratyphi*. Both serotypes are spread mainly via contaminated groceries and water. Because *S. typhi* and *S. paratyphi* B do not occur in animals, the systemic infections in humans are always caused by direct or indirect feco-oral contamination of food or water due to human acting. (Korkeala 2007) The mortality of untreated *S. typhoid* is around 20%, whereas with appropriate treatment less than 1%. *S. paratyphi* causes usually a less severe syndrome even though the symptoms are quite similar. Nowadays, these infections are rare in developed countries mainly due to pasteurization of milk and improved purification of drinking water. (Korkeala 2007; Kyyhkynen et al. 2004) Generally, when talking about salmonellosis, *S. typhi* and *paratyphi* are excluded or pointed out separately (then called typhoid or paratyphoid salmonellosis), because of their capability of causing systemic infection which is less frequent for the other serotypes.

However, typhoid salmonellosis can still form a problem also in developed countries. For example, according to Day and Lalloo (2004) malaria and typhoid are the two most commonly imported life threatening tropical infections in the United Kingdom (UK). There are up to 300 imported cases of typhoid each year in the UK and the majority is originating from South Asia. However, the number of typhoid cases is relatively low if compared to the total number of travellers in the UK: over 22 million visitors from abroad came to the UK and 58 million overseas trips were made by the UK residents in 2001. (Day & Lalloo 2004)

In Finland, typhoid and paratyphoid salmonellosis are very rare. In recent years, these cases have been notified only occasionally, and the source of infection has almost always been related to international travelling. (Kyyhkynen et al. 2004) For example, there were four detected cases of *S. typhi* and five *S. paratyphi* in 2009. All the cases were linked with travelling abroad. (Hulkko et al. 2010).

2.7.2 *Salmonella* legislation in Finland

In Finland, the *Salmonella* situation is different compared to most other countries in the world. Here the occurrence of *Salmonella* bacteria among farm animals is considerably low due to long-term planning surveillance programmes. Furthermore, all *Salmonella* infections are included in generally hazardous communicable diseases in Finnish legislation (Tartuntatautilaki). As a result, the incidence of domestically acquired salmonellosis in humans is low compared to those acquired abroad due to international travelling, on average, 15 and 80%, respectively (around 5 % of cases the information of a source country of the infection is lacking).

Less than 1% of farm animals are carrying *Salmonella* in Finland (EVIRA 2006) and Sweden (National Veterinary Institute 2008). When becoming a member of the EU, Finland and Sweden received specific *Salmonella* guarantees, which, e.g., states that fresh meat (beef, veal, pork, poultry) should be tested for the presence of *Salmonella* bacteria before importation. If a cargo is tested *Salmonella* positive, importation is not allowed. These guarantees have contributed to the maintenance of the excellent *Salmonella* situation in these states. For maintaining this unique situation continuous control programmes are needed in the area of agriculture and food production. (EVIRA 2006)

The Communicable Diseases Act (583/1986) and Decree (786/1986) prescribe how to operate in the health care sector in the case of suspected or confirmed human *Salmonella* infection. According to the Communicable Diseases Decree typhoid fever, paratyphoid fever and other diseases caused by *Salmonella* bacteria are included in generally hazardous communicable diseases. Physicians make a communicable disease notification (physician's communicable disease notification) in the case of typhoid fever or paratyphoid fever. Otherwise, laboratories make a communicable disease notification of findings of pathogens of generally hazardous and notifiable communicable diseases and other microbial findings subject to registration. The National Institute for Health and Welfare (www.thl.fi) keeps a national communicable disease register for the purpose of combating communicable diseases and preventing and monitoring their spread and compilation of statistics and research on them. (Tartuntatautilaki; Tartuntatautiasetus)

A physician's communicable disease notification includes, besides the identification data of the patient, data on the patient's sex, municipality of residence and nationality, care place, course of infection, date of emergence of symptoms, and grounds for the diagnosis. The communicable disease notifications of laboratories include, besides identification data, information on the place of care, date of taking the specimen, test findings made, method of detecting a microbe, quality of the specimen and the name of the laboratory making the notification. In the question of *Salmonella*, also the place of infection has to be reported. (Tartuntatautiasetus)

2.7.3 Studies on travel-related salmonellosis

A comprehensive systematic review (Shah et al. 2009) considers the identification of *Salmonella* in various geographical areas by combining study results from all TD related articles from 1973 to 2004. The article finds following occurrence for the infection: 4.4% for Latin America and the Caribbean, 5.5% for Africa, 6.6% for South Asia, and 9.1% for South-East Asia. This indicates that salmonellosis is more often related to traveller's diarrhea in Asia than in Africa, Latin America or the Caribbean region.

Sweden is a proper country to compare the incidence of travel-related salmonellosis to Finland, because domestically acquired salmonellosis is rare in both countries. In 2008, there were 4,183 reported *Salmonella* cases in Sweden of which only 16% were domestically acquired. In recent years, Thailand has been the most frequently noted as a source country for those Swedish infections (approximately every third case). (National Veterinary Institute 2008) Likewise, Thailand has become a popular tourist destination for Finns. The number of passengers has more than doubled there during the last ten years (Statistics Finland). Since 2002, Thailand has indeed been the most frequently reported source country of travel-related salmonellosis also in Finland (366-922 cases per year). (Hulkko et al. 2010).

Using the data from the Swedish Travel and Tourist Database, Ekdahl et al. (2005) estimated that Swedish travellers made 68 million over-night journeys to different countries or regions during the period of 1997 to 2003, of those 78% were holiday trips and 22% business trips. According to the study, the most reported *Salmonella* infections (78%) were associated with travels to 151 different countries. The overall risk of salmonellosis was 36.5 ⁄ 100,000 travellers. The lowest risk was seen in the Nordic countries (1.7 ⁄ 100,000 travellers), which was also used as a reference value (OR 1). Instead, the highest individual risk was seen in the developing countries, specifically in East Africa (471 / 100,000 travellers, OR 405; 95% CI 249–658), India and neighbouring countries (OR 310; 95% CI 212–453), East Asia (OR 198; 95% CI 172–228), and West Africa (OR 176; 95% CI 112–277). The risk of salmonellosis decreased with increasing passenger age, whereas gender did not have an effect on the risk in this study. (Ekdahl, de Jong & Andersson 2005)

Out of the 24,358 Swedish cases (98.2% of all the reported cases) 202 different serotypes were represented, and distinct regional variations in serotype distribution was seen. *Salmonella enteritidis* was the most common serotype in most regions of the word, also in Europe where the dominance of this serotype was more than two-thirds of all cases. Instead, in Africa, Asia and America the variety of other circulating serotypes was greater. Also, some seasonal variety was seen, e.g., the highest risk of salmonellosis existed from June to September in Europe and from November to December in East Asia. (Ekdahl, de Jong & Andersson 2005)

An other Swedish study (de Jong & Ekdahl 2006a) has shown a clear causal relationship between the prevalence of *Salmonella* bacteria in egg production and human salmonellosis by using the data from the European Food Safety Authority

(EFSA) report on the prevalence of *Salmonella* in laying hen flocks, and the authors' former study (de Jong & Ekdahl 2006b) that estimated the burden of salmonellosis in various European countries. The later mentioned study (de Jong & Ekdahl 2006b) used the Swedish notification database on travel-related salmonellosis and randomly selected returning Swedish travellers coming from inside the EU region during the study period of 1997-2003. Using the data from the commercial Tourist Database the authors estimated the number of journeys to each European country (no data on illnesses is available in this dataset). According to the estimates Swedish travellers had 60 million overnight journeys to other European countries. The travels consisted of leisure trips (78%) and business trips (22%). Altogether 15,864 patients were notified positive to *Salmonella* after their journey to Europe, which means that the total risk was 26.2/100,000 travellers. Two-thirds of these infections were caused by *S. enteritidis,* and phage type (PT) 4 and 1 accounted for 35 and 22% of these cases, respectively. The lowest risk of salmonellosis was associated with journeys to Norway (incidence 0.2/100,000) and Finland (0.4/100,000). No cases of salmonellosis were reported among travellers from Luxembourg and Liechtenstein. The five topmost countries in Europe with the highest estimated burden of salmonellosis among Swedish travellers were Bulgaria, Turkey, Malta, Portugal and Poland (Table 4).

Country	Risk per 100,000 travellers	Percent *S. Enteritidis* among Swedish travellers	Percent *S. Typhimuriu m* among Swedish travellers	Reported incidence per 100,000 inhabitant	Under-detection index	Estimated incidence per 100,000 inhabitant
Norway	0.2	30	40	3.77	1.0 (ref.)	4
Finland	0.4	29	39	13.1	0.6	8
Iceland	2.2	25	75	129	0.4	47
Estonia	2.6	85	2	40.6	1.3	54
Ireland	3.2	33	25	16.0	4.3	69
Denmark	3.8	67	15	44.4	1.8	81
Netherlands	4.6	71	29	12.6	7.7	98
United Kingdom	5.6	83	7	27.9	4.3	119
Germany	8.3	59	13	21.5	8.3	177
France	8.4	79	13	96.1	1.8	178
Austria	12.0	83	2	85.6	3.0	255
Italy	12.8	54	18	20.6	13.1	271
Belgium	13.5	86	10	153	1.9	286
Lithuania	15.3	94	0	32.5	10.0	325
Latvia	23.9	98	1	43.4	11.7	507
Greece	39.2	70	8	8.5	97.7	833
Croatia	40.1	85	8	27.9	30.6	852
Slovenia	40.1	50	20	85.1	10.0	852
Hungary	41.8	71	34	163	5.5	888
Czech Republic	54.8	77	5	391	3.0	1161
Slovakia	54.8	94	0	336	3.5	1165
Cyprus	66.0	37	15	19.7	71.2	1403
Romania	68.6	40	31	4.4	332	1457
Spain	72.0	79	7	14.9	103	1531
Poland	76.5	77	3	100	16.2	1626
Portugal	79.9	82	7	4.5	378	1697
Malta	101	60	13	23.1	92.6	2141
Turkey	110	48	4	39.2	59.8	2344
Bulgaria	129	68	17	10.1	271	2741

Table 4: Comparison of the risk of salmonellosis among Swedish travellers to nationally reported incidence and estimated incidence of salmonellosis. (de Jong & Ekdahl 2006b)

According to the study the burden of salmonellosis in Europe was geographically distributed so that the lowest burden was in the north and the highest burden in the south. In the Northern Europe, Poland was the only exceptional country where the burden of salmonellosis was high. In addition, countries in the eastern parts of Europe tended to have a higher burden than the countries in the western parts of Europe. Serotype distribution varied among the European countries so that the most common *S. enteritidis* (average of 67%) accounted for the minimum of 25% in Iceland, but the maximum of 98% in Latvia. The second most frequent serotype was *S. typhimurium* accounting for 9% of the cases on average. (de Jong & Ekdahl 2006b)

2.8 Perspective for world tourism

There has been a substantial growth of tourism activity in the past 60 years. An average annual growth rate for international arrivals has been approximately 6.5% between 1950-2005: starting from 25 million and ending to 806 million. Despite the impact of financial crisis at the end of the 2000s, the estimated number of international tourists was 880 million in 2009. The development of international travel has been particularly strong in Asia and the Pacific, where the average growth rate has been 13%, followed by the Middle East with 10%. In the Americas and in Europe the growth has been slower and below the world's average growth, 5 and 6% respectively. By 2020, the estimate of international arrivals is expected to reach 1.6 billion. (UNWTO 2010)

In 2009, the ten top tourism destinations in the declining ranking were: France, United States, Spain, China, Italy, United Kingdom, Turkey, Germany, Malaysia and Mexico. Generally, reasons for the international travel were divided into four sectors:

1) leisure, recreation and holidays (represent 51% of causes),
2) visiting friends or relatives, health, religion or other reason (27%),
3) business and professional (15%), and
4) and not specified (7%). (UNWTO 2010)

In Finland, there is no official travel register that routinely would keep up the total number of travellers going outside the country borders. That is why it is impossible to get exact numbers of package holidays, business travel and self made backpacking trips. However, there are several instances that keep up travel-related statistics.

According to the Association of Finnish Travel Agents (AFTA) Finns made approximately 944,700 free-time package holidays by air plane in 2010. A year earlier, the number was 961,400. In 2010, the most popular destination was Europe: 635,000 travellers (67% of the package trips). Finns favour especially for Spain (39% of package holidays to Europe), followed by Greece (17%). However, most travels to Spain were actually headed to the Canary Islands: a total of 206,000 travellers. In addition, the Middle East and the North Africa have also been increasingly popular tourist destinations for Finns. In 2010, altogether 185,000 persons made a package holiday there, which accounted for more than 19% rise compared to 2009. The highest rises were seen for Egypt and Turkey. At the same time, 124,000 Finns made a package holiday to the Far East. The trend of package holidays to the Far East have been decreasing in 2009 and 2010. (AFTA 2010)

AFTA has listed the top ten package holiday destinations for Finns in 2010:

1. Spain/the Canary Islands/the Balearic Islands: 247 866 travellers
2. Greece: 160 238 travellers
3. Turkey: 81 559 travellers
4. Egypt: 70 544 travellers
5. Thailand: 69 496 travellers
6. Portugal/Madeira/the Azores: 42 342 travellers
7. Bulgaria: 30 889 travellers
8. Cyprus: 29 883 travellers
9. Italy: 28 347 travellers
10. Tunisia: 15 645 travellers

However, AFTA's statistics are only one part of the total travels made by Finns. The estimate of Statistics Finland for international travels was 6,693,000 trips in 2009. The total number includes all forms of travelling abroad, also one day trips and cruises (Table 5). (Statistics Finland)

	Free-time travel				*Business travel*				*All travel abroad*
	One-day trip	**Cruise**	**Over-night trip**	**Total**	**One-day trip**	**Cruise**	**Over-night trip**	**Total**	**Total**
2009	739	1 262	3 596	5 597	122	97	877	1 096	6 693
2008	584	1 263	3 328	5 175	128	116	1 146	1 391	6 566
2007	553	1 282	3 230	5 065	111	147	1 090	1 348	6 413
2006	555	1 469	3 147	5 172	117	123	1 017	1 257	6 428
2005	639	1 570	3 112	5 321	121	157	1 062	1 341	6 662
2004	489	1 693	3 022	5 204	126	134	949	1 209	6 413
2003	409	1 914	2 601	4 925	100	186	884	1 170	6 094
2002	395	2 099	2 662	5 156	87	188	908	1 183	6 339
2001	430	2 087	2 645	5 162	86	231	861	1 178	6 339
2000	408	2 387	2 397	5 192	103	229	902	1 234	6 426

Table 5: The estimated number (x1000) of performed free-time and business travels from 2000 to 2009 among Finnish citizens at the age of 15-74 years. Free-time travel includes package holidays and self-made backpacking trips. (Statistics Finland)

3 AIMS AND HYPOTHESES

3.1 Aims of the study

The objectives of the study are to find trends of salmonellosis that are most likely contracted from abroad, but detected in Finland during 1995-2009, and examine how these trends are correlated with the number of Finnish travellers to these destinations. The more specific aims are to determine:

1. whether the number of *Salmonella* infections acquired abroad change yearly,
2. which countries are reported as a source of salmonellosis most frequently,
3. whether the increased number of travellers to some countries have contributed proportionally more to the total number of *Salmonella* cases,
4. whether there is an association between a country and a *Salmonella* serotype, and
5. the frequency of non-Finnish citizens reported with *Salmonella* infection.

3.2 Hypotheses to be tested

1. Travelling rates are positively correlated to the number of reported *Salmonella* cases in Finland.
2. Some countries are more frequently reported as a source than others when compared to the absolute numbers of Finnish tourists to these destinations.

4 RESEARCH SECTION

4.1 Materials and methods

Salmonella infections detected in Finland are reported to the National Infectious Diseases Register. The reported infections can be divided into domestically acquired cases and cases of foreign origin according to a source country. In this context, cases of domestic origin refer to those acquired in Finland, and cases of foreign origin refer to those acquired abroad due to international travelling. An infection is defined as acquired abroad if the symptoms of the case started within seven days after returning abroad.

The number of salmoellosis of foreign origin and of domestic origin in Finland between 1995-2009 was received from the Report of Infectious Diseases in Finland 1995-2009 (Hulkko et al. 2010). Also, the yearly number of *Salmonella* cases with uninformed source countries was received from the Report.

The data used in this study was quantitative and was received from the National Infectious Diseases Register. All the *Salmonella* cases identified in Finland that has been reported to be of foreign origin due to international travelling between 1995 – 2009 were accepted to the study. Information included case identity number, registration date for the *Salmonella* infection, sample type, serotype, person's age, gender, nationality (whether Finnish or non-Finnish), reported source country and the place of residence (if Helsinki, Espoo, Vantaa, Turku or Tampere).

All the cases linked with travelling to more than one country before the beginning of symptoms of salmonellosis had a mention of all those countries. Still, the most likely country was named and this information was used in the study. This procedure was done, because it was assumed that a person would probably have mentioned that country as a source of which he or she felt to be the most likely one (e.g., maybe eaten some risky food items there), or maybe by knowing some basics of the typical incubation period of the traveller's diarrhea, a health care professional together with a patient had concluded the most likely source country. However, there were an exception of six cases which had not pointed out the main suspected source country of their infection, but instead had a list of more than one suspected country. Therefore, the data from the main suspected source countries of these cases could not be used, because the missing information of only one suspect country.

In Finland, there is no official travel register that routinely collects the exact number of travellers going abroad for package holiday, business and self made backpacking trips. Travel-related information of outbound trips made by Finns was received from the public data of Finland Statistics (STAT). STAT classifies outbound trips into leisure trips involving overnighting in destination country, cruises, same-day visits, and business and professional visits. The results are gathered from sample-based computer assisted telephone interview survey made every month since the year 2000. The monthly sample size is approximately 2,200 persons. STAT states that the samples are drawn by systematic sampling from the central population register, and the population comprises persons aged 15 to 74 with the permanent residence in Finland. (Statistics Finland) Because the methods of conducting travel information were changed several times during 1990s, the data of outbound trips made by Finns before year 2000 was excluded from the study.

The statistics on Finnish and non-Finnish citizens with a permanent residence in Finland were received also from STAT. These statistics on the structure of the population are gathered at the turn of every year. (Statistics Finland 2).

The most commonly reported source countries to acquire *Salmonella* were examined in two different ways. Firstly, all 147 countries that were reported as a source for detected salmonellosis in Finland during 1995 to 2009 were ranked. The ranking gave twenty topmost source countries (without knowing the number of passengers to those countries at this stage). Secondly, again all 147 countries were looked at the same way as in the first phase with two exceptions. Instead of looking the reported cases over the 15-year follow-up period, the follow-up went on only one year. Besides the time limitation, now only ten most reported countries were selected. According to the reported cases, this annual list of the ten topmost source countries for acquiring salmonellosis over 15 years period was named as *the top-10 list* and the name is used further in the text, too.

Because of the vast number of different source countries in the data and the specific interests to study only the most frequently reported source countries for salmonellosis (aim no. 2), the result section concentrates on following countries that had been included at least once in the top-10 list during years 1995-2009.

Travel information was used to calculate an incidence to acquire salmonellosis in a certain country (Table 6). The risk of acquiring the disease per 100 000 travellers was calculated using notification data as the numerator, and the total numbers of travellers from STAT as the denominator. The countries on focus were the most risk source countries, i.e., those countries which had been on the top-10 list of the most frequently reported source countries for acquiring salmonellosis at least once during the study period. Some countries had incomplete travel information (because information was not carried or it was too uncertain to share), which excluded them from incidence calculation. Incidence was not calculated if there were missing values in travel information for more than two years. Otherwise, if there were one or two missing years in the number of travellers, incidence for those years were filled in by using the mean incidence of those years around the gap. All incidences could be calculated only for the interval 2000-2009, because travel information included only those years.

											Means	
	2000	**2001**	**2002**	**2003**	**2004**	**2005**	**2006**	**2007**	**2008**	**2009**	**2000-2004**	**2004-2009**
Thailand	55	53	44	49	66	54	92	130	91	121	53	98
Turkey	39	63	63	49	61	67	65	46	56	107	55	68
Spain	725	705	686	656	741	698	798	787	799	813	703	779
Greece	143	163	136	134	161	136	151	158	158	168	147	154
Tunisia	17	19	12		11	16	20	21	20	13	15	18
Estonia	2190	2131	2177	1970	2002	2050	1830	1673	1772	1793	2094	1824
India	10		13			17	13	20	20	19	12	18
Russia	393	373	370	297	354	353	286	254	258	235	357	277
Bulgaria	17	22	29	54	50	64	65	43	68	34	34	55
Egypt	18	21	18	26	55	36	23	27	46	53	28	37
Hungary	35	50	52	34	60	52	59	74	44	59	46	58
Brazil					15	23	18		11	11	N	16
Cyprus	20	37	26	17	29	16	27	23	42	21	26	26
Morocco	11		10								11	N
Portugal	57	55	54	52	52	46	55	61	57	63	54	56
Malaysia	11									11	N	N
Denmark	76	78	85	103	71	74	79	118	122	88	83	96
Italy	82	103	122	130	119	156	163	169	200	193	111	176
Latvia	32	33	81	109	72	113	82	86	88	64	65	87

Table 6: Finnish passengers (x1000) to the countries that have included at least once in the top-10 list during the years 1995-2009. Means are calculated for the periods of 2000-2004 and 2005-2009. N=not calculated because of too many missing values. Source: STAT.

The analysis of the data was done by using the following programmes: Open Office Excel 3.1, SPSS Statistics 19 and Stata 11.2. Age values were categorized into seven to have a table for age distribution: under 5, 5-9, under 20, 20-39, 40-59, 60-79, and over 80 years. Frequencies on reported salmonellosis cases in these age categories were calculated using three time intervals: 1995-1999, 2005-2009 and 1995-2009. Poisson confidence intervals for incidence densities and their ratios were calculated. Within-yearly incidence density ratios were combined using Mantel-Haenszel procedure.

Yearly exact confidence intervals for incidence rate (density) ratios between the genders with reported salmonellosis were calculated with the help of binomial probability (STATA ir command, c.f. Breslow&Day: Statistical methods in cancer research, Volume II, pp. 93-94). Within-yearly incidence density ratios were then combined using Mantel-Haenszel procedure to evaluate the statistical significance between the genders with reported salmonellosis (STATA ir command, c.f. Breslow&Day: Statistical methods in cancer research, Volume II, pp. 109-113).

Exact confidence intervals for the incidence (density) rate ratios between the first five years interval and the final five years were calculated for the three youngest age categories. Also to get the actual *p*-value, the "midp" two-sided exact significance test for the (density) rate ratios between the first five years interval and the final five years was calculated as the binomial in those three youngest age categories. The same results as above is possible to get using Poisson regression.

4.2 Ethical considerations

Notification data in the National Infectious Diseases Register is regulated by the Communicable Disease Act, and contain full personal identification. For receiving the data, it is mandatory the make an official request in which a researcher needs to name the reasons for using the data. After the request, the data was received within two weeks.

Extracted data from the notification database for this study does not contain any information that could be linked to a specific person. Other databases used in the study are from public sources and either these do not contain any information that could be linked to a specific person.

4.3 Results

The results of the study on *Salmonella infections acquired abroad and detected in Finland, 1995-2009* are divided into three sections according to 1) demographic determinants of the cases, 2) source countries, and 3) serotype distribution.

4.3.1 Determinants of cases with *Salmonella* infection acquired abroad

A total of 30,977 *Salmonella* cases of foreign origin were reported in Finland between 1995 and 2009 (yearly changes are seen in Figure 6). Out of them 16,851 (54.4%) were female and 14,126 male (45.6%). Of the cases, 29,434 (95.0%) were Finnish and 349 (1.1%) non-Finnish. In addition, there were 1,194 (3.9%) cases without a note of citizenship.

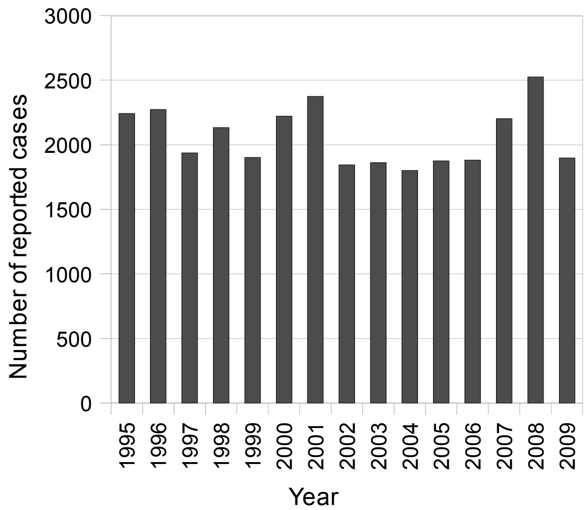

Figure 6: Detected salmonellosis of foreign origin in Finland between 1995-2009.

Age of the persons with acquired salmonellosis of foreign origin was normally distributed. Over the whole study period, the mean age was 37.7 years (yearly mean ranged from 36.7 to 38.4 years). Infection was represented in every age category starting from newborns (age marked as 0). Differences in reported morbidity between seven age categories are shown in Table 7. The table also shows morbidity among the age categories at the first five and at the final five years of the study. Comparing these five year intervals, a statistically significant (*p* <0.01) increase (increases in the incidence density ratios 34%, 27%, 14% respectively) was seen in the incidence densities of reported cases in all age categories under 20 years (<5, 5-9, and <20).

Age	Frequency (1995-1999)	Percent (1995-1999)	Frequency (1995-2009)	Percent (1995-2009)	Frequency (2005-2009)	Percent (2005-2009)
<5	246	2.3	816	2.6	308	3.0
5-9	290	2.8	698	2.9	327	3.1
<20	1324	12.6	4165	13.4	1435	13.8
20-39	4060	38.7	11990	38.7	3984	38.4
40-59	4190	39.9	12213	39.4	4096	39.4
60-79	897	8.6	2548	8.2	843	8.1
>80	18	0.2	61	0.2	25	0.2
Total	10489		30977		10383	

Table 7: Distribution of age among persons, who acquired salmonellosis abroad during 1995-1999 (in the left), 1995-2009 (in the middle), and 2004-2009 (in the right).

Differences on reported salmonellosis cases between genders were examined. There were statistically significant difference (*p* <0.001) on morbidity: every year more female than male cases were reported (Figure 7). Incidence (density) rate ratios between males and females were statistically homogeneous through the years (Test of homogeneity (Mentel-Haenswel) chi2(14)=19,53 Pr>chi2=0.1457). The combined incidence rate ratio between males and females over the years was 0.88 (95% CI (0.86,0,90)).

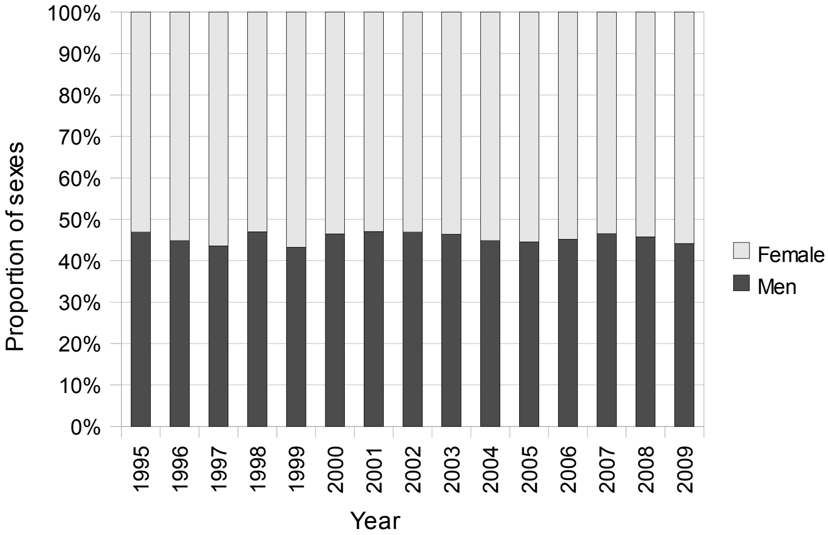

Figure 7: Variation of reported genders per year.

Nationality of the persons whose salmonellosis were registered in Finland during the study period was divided into three categories. The largest proportion consisted of persons whose nationality was Finnish; other nationalities were marked to be either as a 'foreigner' or under the status 'unknown'. In total, there were 29,434 cases of Finnish nationality, whereas 349 were categorized as foreigners and 1,194 had an unknown nationality (Figure 8). Since 2002, nationality has been missing only occasionally. Table 8 shows the proportion of foreigners with registered *Salmonella* infection compared to the proportion of foreigner with permanent residence in Finland during 1995-2009.

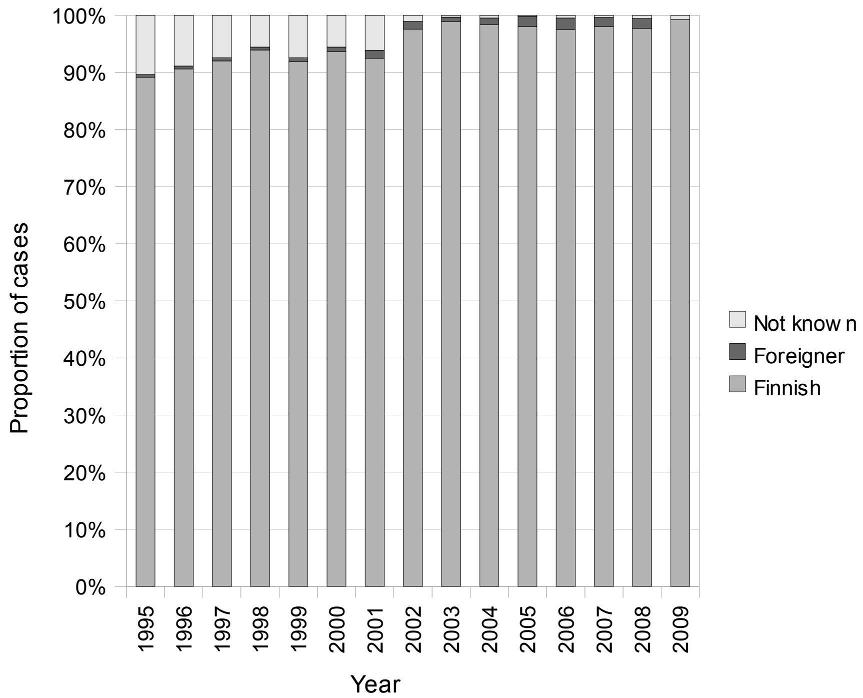

Figure 8: The distribution of reported nationalities during 1995-2009.

Year	Reported *Salmonella* infections in foreigners (%)	Proportion of foreigners in Finland (%)
1995	0.6	1.4
1996	0.6	1.5
1997	0.6	1.6
1998	0.5	1.7
1999	0.7	1.7
2000	0.8	1.8
2001	1.5	1.9
2002	1.4	2.0
2003	0.8	2.1
2004	1.2	2.1
2005	1.8	2.2
2006	2.1	2.4
2007	1.7	2.6
2008	1.8	2.8
2009	1.7	3.0

Table 8: The yearly proportion of reported Salmonella *infections among non-Finnish citizens in Finland compared to the proportion of non-Finnish citizens in the whole population in Finland, 1995-2009. Source for the data on nationalities: STAT.*

4.3.2 *Salmonella* infections according to source countries

In total, there were 147 different countries marked as a source for travel-related salmonellosis. During 1995-2009, the most frequently reported source countries for salmonellosis acquired abroad were Thailand, Spain and Turkey (Table 9). These countries were included among the most frequently reported source countries (the top-10 list) each year (Table 10). Altogether 19 countries were on the top-10 list during the 15 years time. This means that there have been some yearly changes among the reported source countries, e.g., Denmark, Italy and Latvia have been on the top-10 list only once.

Source country	Number of cases	Proportion (%)
Thailand	6210	20.0
Spain	3793	12.2
Turkey	1970	6.4
Greece	1808	5.8
Tunisia	1580	5.1
Estonia	1438	4.6
Bulgaria	1355	4.4
India	1220	3.9
Egypt	989	3.2
Russia	980	3.2
Hungary	808	2.6
Morocco	663	2.1
Portugal	612	2.0
Cyprus	530	1.7
Malaysia	401	1.3
Brazil	383	1.2
Latvia	357	1.2
China	335	1.1
Germany	328	1.1
Italy	306	1.0
Total	26066	84.1

Table 9: The most frequently reported source countries for acquired salmonellosis. The total number of the cases and their percentage proportions of all the reported cases in Finland shows how many travellers have officially suffered from Salmonella *infection due to international travel to these countries during 15 years follow-up.*

	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009
Thailand	112	188	237	317	307	292	307	380	398	366	377	502	795	922	712
Turkey	198	362	217	211	78	81	97	100	74	99	79	56	67	126	124
Spain	191	283	352	306	375	424	531	263	202	210	187	145	118	100	106
Greece	196	114	(50)	95	123	111	175	100	154	142	88	89	85	232	54
Tunisia	176	159	112	156	121	186	101	77	88	(59)	59	61	94	91	58
Estonia	169	117	188	87	108	170	75	70	46	42	125	(44)	(47)	90	60
India	75	143	95	(58)	(44)	62	(61)	(29)	(39)	76	74	93	170	116	85
Russia	151	61	54	(40)	(39)	116	91	95	78	52	(31)	(38)	(35)	54	45
Bulgaria	(9)	(10)	(15)	(36)	(52)	(30)	94	135	200	156	194	170	105	113	(36)
Egypt	(5)	(20)	(7)	(11)	(19)	(50)	140	(41)	73	136	127	48	59	133	120
Hungary	(72)	86	71	89	67	(57)	90	42	(42)	(27)	(29)	(34)	55	(24)	(23)
Brazil	(3)	(2)	(1)	(4)	(0)	(4)	(11)	(15)	(38)	51	86	70	53	(21)	(24)
Cyprus	106	(28)	(26)	78	68	61	(55)	(36)	(12)	(6)	(7)	(8)	(10)	(16)	(13)
Morocco	(58)	174	66	67	78	(46)	(42)	(23)	(17)	(11)	(13)	(17)	(17)	(17)	(17)
Portugal	(60)	(44)	50	(52)	61	(43)	(31)	(27)	49	(26)	(28)	59	(38)	(32)	(12)
Malaysia	(17)	(12)	(12)	(22)	(48)	80	(21)	(35)	(15)	(13)	(17)	(34)	(19)	(19)	37
Denmark	133	(7)	(8)	(39)	(9)	(3)	(5)	(2)	(2)	(2)	(0)	(2)	(2)	(4)	(2)
Italy	(20)	(14)	(14)	62	(22)	(20)	(25)	(17)	(23)	(15)	(18)	(9)	(13)	(21)	(13)
Latvia	(8)	(5)	(15)	(11)	(16)	(40)	(48)	57	(19)	(9)	(25)	(45)	(16)	(27)	(16)

Table 10: The top-10 list. Numbers (print in bold) of yearly reported Salmonella *cases from the ten topmost source countries to acquire the infection. Italicized numbers with brackets are reported cases from the country when it did not belong to the top-10 list.*

The overall risk of being notified with travel-associated salmonellosis was 31.8 / 100,000 Finnish travellers per year during the 10 years time. Yearly incidences of salmonellosis for the highest source countries are shown in Figure 9 a-c. The first figure (Figure 9a) represents the incidences from the most risk source countries, and the final one (Figure 9c) represents incidences from the countries that were on the tail of the list in Table 10. Because of inadequate passenger values, three top-10 list countries are missing: Brazil, Malaysia and Morocco. Denmark is not shown, because it was on the top-10 list only in 1995 and travel information starts from the year 2000. After the year 1995, the mean of reported salmonellosis in Denmark has been 6.2 and median 2.5. Therephore, it is not any more the country of interest concerning the most risk countries of travel-related salmonellosis. Precise yearly incidences and mean incidences of the countries are seen in Table 11, which also presents numbers of reported cases.

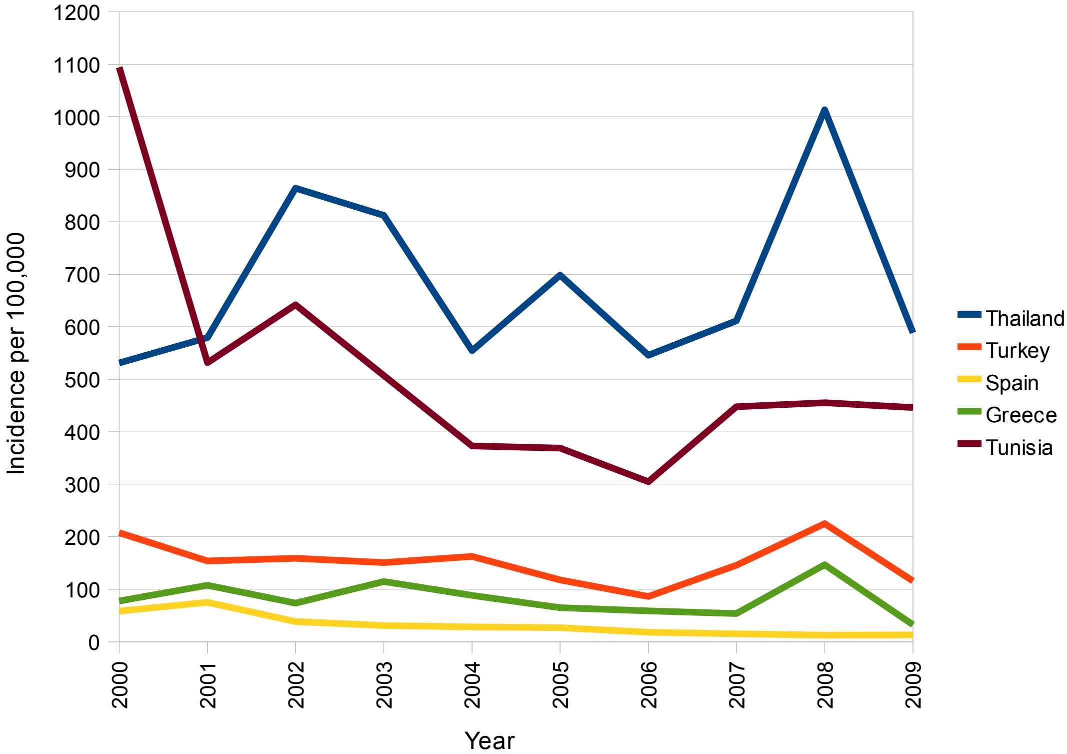

Figure 9a: Incidence of salmonellosis per 100,000 Finnish passengers (to the country in question) in five countries that have been 14 or 15 times on the top-10 list as a source country for traveller's salmonellosis during 15 years. The value 2003 in Tunisia is a mean from the cases in 2002 and 2004 because of the missing passenger information from the data of STAT.

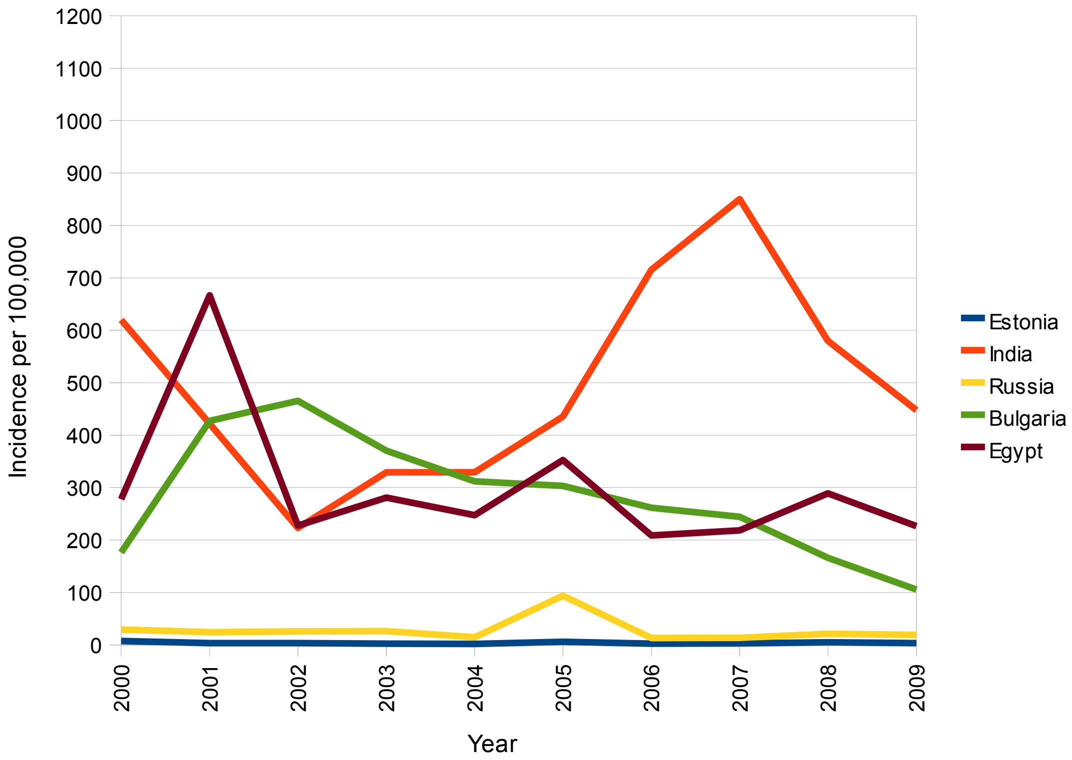

Figure 9b: Incidence of salmonellosis per 100,000 Finnish passengers (to the country in question) in five countries that have been 8 to 13 times in the top-10 list as a source country for traveller's salmonellosis during 15 years. The values 2003 and 2004 in India are means from cases in 2002 and 2004 because of the missing passenger information from the data of STAT.

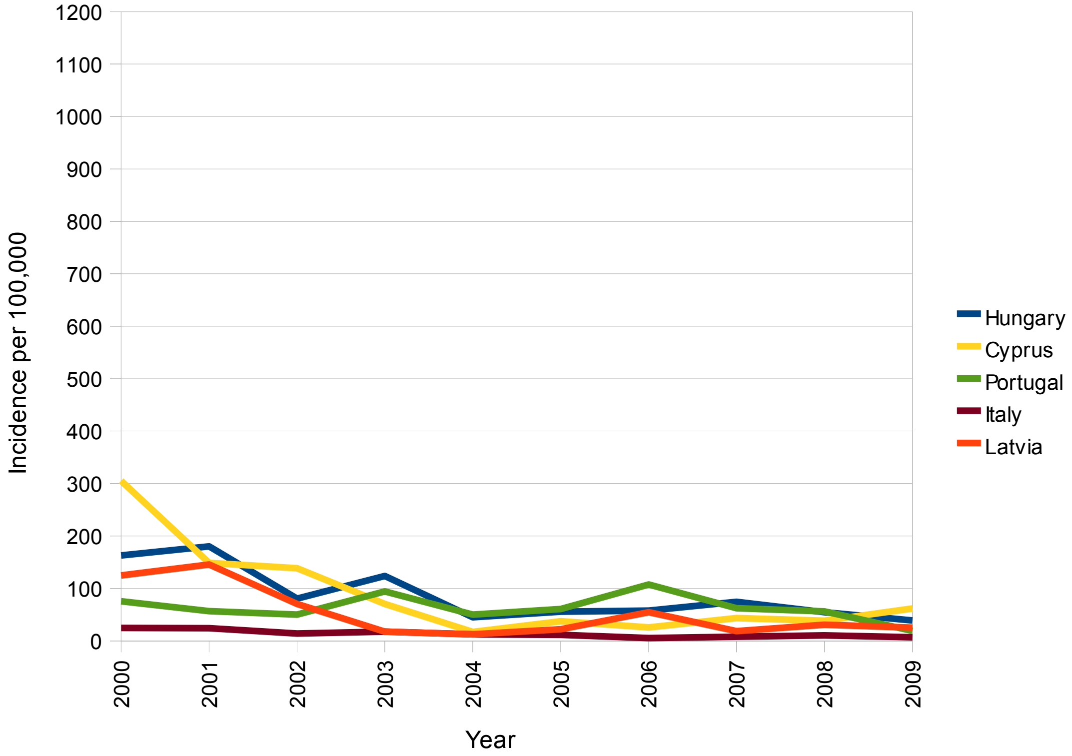

Figure 9c: Incidence of salmonellosis per 100,000 Finnish passengers (to the country in question) in five countries that have been 1 to 7 times in the top-10 list as a source country for traveller's salmonellosis during 15 years.

		2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	Mean / year
Thailand	No. of cases	292	307	380	398	366	377	502	795	922	712	505.1
	Incidence / 100,000	530.9	579.2	863.6	812.2	554.5	698.1	545.7	611.5	1013.2	588.4	679.8
Turkey	No. of cases	81	97	100	74	99	79	56	67	126	124	90.3
	Incidence / 100,000	207.7	154.0	158.7	151.0	162.3	117.9	86.2	145.7	225.0	115.9	152.4
Spain	No. of cases	424	531	263	202	210	187	145	118	100	106	228.6
	Incidence / 100,000	58.5	75.3	38.3	30.8	28.3	26.8	18.2	15.0	12.5	13.0	31.7
Greece	No. of cases	111	175	100	154	142	88	89	85	232	54	123.0
	Incidence / 100,000	77.6	107.4	73.5	114.9	88.2	64.7	58.9	53.8	146.8	32.1	81.8
Tunisia	No. of cases	186	101	77	88	41	59	61	94	91	58	85.6
	Incidence / 100,000	1094.1	531.6	641.7	507.2	372.7	368.8	305.0	447.6	455.0	446.2	517.0
Estonia	No. of cases	170	75	70	46	42	125	44	47	90	60	76.9
	Incidence / 100,000	7.8	3.5	3.2	2.3	2.1	6.1	2.4	2.8	5.1	3.3	3.9
India	No. of cases	62	61	29	39	76	74	93	170	116	85	80.5
	Incidence / 100,000	620.0	421.5	223.1	329.2	329.2	435.3	715.4	850.0	580.0	447.4	495.1
Russia	No. of cases	116	91	95	78	52	331	38	35	54	45	93.5
	Incidence / 100,000	29.5	24.4	25.7	26.3	14.7	93.8	13.3	13.8	20.9	19.1	28.1
Bulgaria	No. of cases	30	94	135	200	156	194	170	105	113	36	123.3
	Incidence / 100,000	176.5	427.3	465.5	370.4	312.0	303.1	261.5	244.2	166.2	105.9	283.3
Egypt	No. of cases	50	140	41	73	136	127	48	59	133	120	92.7
	Incidence / 100,000	277.8	666.7	227.8	280.8	247.3	352.8	208.7	218.5	289.1	226.4	299.6
Hungary	No. of cases	57	90	42	42	27	29	34	55	24	23	42.3
	Incidence / 100,000	162.9	180.0	80.8	123.5	45.0	55.8	57.6	74.3	54.5	39.0	87.3
Brazil	No. of cases	4	11	15	38	51	86	70	53	21	24	37.3
	Incidence / 100,000	N	N	N	N	340.0	373.9	388.9	N	190.9	218.2	302.4
Cyprus	No. of cases	61	55	36	12	5	6	7	10	16	13	22.1
	Incidence / 100,000	305.0	148.6	138.5	70.6	17.2	37.5	25.9	43.5	38.1	61.9	88.7
Morocco	No. of cases	46	42	23	17	11	13	17	17	17	17	22.0
	Incidence / 100,000	418.2	N	230.0	N	N	N	N	N	N	N	324.1
Portugal	No. of cases	43	31	27	49	26	28	59	38	32	12	34.5
	Incidence / 100,000	75.4	56.4	50.0	94.2	50.0	60.9	107.3	62.3	56.1	19.0	63.2
Malaysia	No. of cases	80	21	35	15	13	17	34	19	19	37	29.0
	Incidence / 100,000	727.3	N	N	N	N	N	N	N	N	336.4	531.8
Denmark	No. of cases	3	5	2	2	2	0	2	2	4	2	2.4
	Incidence / 100,000	3.9	6.4	2.4	1.9	2.8	0.0	2.5	1.7	3.3	2.3	2.7
Italy	No. of cases	20	25	17	23	15	18	9	13	21	13	17.4
	Incidence / 100,000	24.4	24.3	13.9	17.7	12.6	11.5	5.5	7.7	10.5	6.7	13.5
Latvia	No. of cases	40	48	57	19	9	25	45	16	27	16	30.2
	Incidence / 100,000	125.0	145.5	70.4	17.4	12.5	22.1	54.9	18.6	30.7	25.0	52.2

Table 11: Yearly registered salmonellosis and incidences per 100,000 Finnish passengers and their means in the top-10 list countries. N=number not available.

4.3.3 Serotype distribution of salmonellosis cases

There were 228 different laboratory confirmed serotypes or serotype groups for the cases. Serotypes that formed more than 1% of all the *Salmonella* cases of foreign origin in Finland between 1995-2009 are presented in Table 12. In addition, Table 13 shows the serotype distribution between those source countries in which the number of a single detected serotype exceeded a hundred cases during the study period.

Serotype	**Frequency**	**%**
S. agona	438	1.4
S. anatum	377	1.2
S. braenderup	512	1.7
S. corvallis	473	1.5
S. enteritidis	13463	43.5
S. hadar	885	2.9
S. infantis	658	2.1
S. newport	662	2.1
S. group B	919	3.0
S. group C	739	2.4
S. group D	627	2.0
S. stanley	1144	3.7
S. typhimurium	2411	7.8
S. virchow	1300	4.2
Total	**24608**	**79.5**

Table 12: Laboratory confirmed serotypes or serotype groups, and their frequencies and percentage proportions (when % > 1.0) in detected Salmonella *cases in Finland, 1995-2009.*

	Austria	Bulgaria	China	Cyprus	Czech Republic	Germany	Denmark	Estonia	Egypt	Spain	Greece	Hungary	India	Italy	Latvia	Morocco	Poland	Portugal	Russia	Thailand	Tunisia	Turkey	All countries in total
S. agona																				113			438
S. anatum																				157			377
S. bareilly													160										215
S. braenderup																				159	133		512
S. corvallis																				213			473
S. enteritidis	106	750	143	184	250	212		1020	328	2664	1263	546	185	158	325	346	221	503	722	750	433	920	13463
S. hadar																				287			885
S. infantis							151																658
S. newport																				155			662
S. panama																				168			197
S. stanley																				969			1144
S. typhimurium		131						133	110	329	124		204							340	142		2411
S. virchow									101											438		223	1300
S. weltevreden																				124			178
S. group B																				505			919
S. group C																				148			739
S. group D										135													627

Table 13: Source countries with a single serotype having caused more than a hundred infections during 1995-2009 among Finnish travellers.

Number of passengers to various destination countries have an influence on salmonellosis cases of foreign origin detected in Finland. Therefore, Table 14 shows the percentage proportions of the most common serotypes in the top-10 list countries.

	Denmark	Russia	Estonia	Latvia	Hungary	Bulgaria	Greece	Italy	Spain	Portugal	Cyprus	Turkey	Morocco	Egypt	Tunis	India	Thailand	Malaysia	Brazil
S. enteritidis		73.7	70.9	91.0	67.6	55.4	69.9	51.6	70.2	82.2	34.7	46.7	52.2	33.2	27.4	15.2	12.1	21.7	
S. typhimurium		5.3	9.3			9.7	6.8	23.2	8.7			4.7		11.1	8.5	16.7	5.5		
S. virchow												11.3	8.7	10.2					
S. stanley																	15.6		
S. corvallis																		13.5	
S. hadar					7.9								11.6						
S. infantis	68.6					5.7													
S. blockley											11.3								
S. saintpaul																			22.2
S. newport																			25.1
S. braenderup															8.4				
S. bareilly																13.1			

Table 14: Serotype distribution for each top-10 list country with at least 50 reported cases caused by a single serotype during 1995-2009. Numbers represent percentage proportions of the reported cases from that country.

During 1995-2009, *Salmonella enteritidis* was clearly the most frequently reported serotype in all of the top-10 list countries except for Thailand, India, Denmark and Brazil (Table 15). Also *S. typhimurium* originated from several countries. It was even more frequently reported among passengers from India than *S. enteritidis*. *S. stanley* was, however, a significant serotype only in Thailand, and just a few occasional cases were detected from other source countries over the study period: 969 cases in Thailand out of the total of 1,144. Likewise, India was the main source for *S. bareilly* (160/215 cases).

THAILAND

	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	**Total**
S. corvallis									12	20	25	34	36	44	42	213
S. enteritidis	23	32	40	31	40	18	27	26	29	18	44	76	103	147	96	750
S. hadar	9	10	11	16	32	45	29	41	39	9	7	13	11	10	5	287
S. rissen	1	10	7	21	14	18	14	11	9	17	8	15	34	37	25	241
S. group B	9	15	18	23	13	22	10	13	17	25	19	27	68	137	89	505
S. stanley	13	16	21	33	29	26	48	58	59	101	103	102	150	118	92	969
S. typhimurium	2	8	19	7	5	4	3	5	5	7	18	31	72	76	53	315
S. virchow	2	10	6	14	17	10	23	22	40	23	39	41	64	70	57	438

INDIA

	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	**Total**
S. bareilly	5	27	15	5	4	6	17	4	7	2	15	14	15	17	7	160
S. braenderup	7	9	9	2	3	4	1	4	5	2	2	5	7	4	9	73
S. enteritidis	8	15	5	6	8	13	4	8	5	14	11	20	37	20	11	185
S. newport	3	11		1	3		2			4	8	7	7	6	7	59
S. oslo	1		1		3	10	8	4	1	5	4	4	11	7	2	61
S. group C	4	11	6	5	5	5	2		3	3	5	1	8	5	5	68
S. typhimurium	15	18	15	12	8	10	13	4	3	21	12	14	33	15	11	204
S. virchow	2	6	13	8	1	6	2	1	3	6	2	3	21	5	2	81

BRAZIL

	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	**Total**
S. newport	1			1			3	2	5	18	22	20	9	7	8	96
S. saintpaul						1	2	3	7	12	22	20	11	5	2	85

DENMARK

	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	**Total**
S. infantis	119			32												151

Table 15: The most frequently reported serotypes (i.e. > 200 cases in total in Thailand, and > 50 cases in other countries) among passengers from Thailand, India, Brazil, and Denmark during the study period of 1995-2009.

4.4 Discussion

In Finland, the yearly number of the reported *Salmonella* infections acquired abroad has been quite stable over the last 15 years; each year, on average 2,000 salmonellosis cases are detected. This also represents a major part of all reported *Salmonella* cases in Finland (Hulkko et al. 2010). Therefore, international travelling is the main reason for the salmonellosis in Finland.

Hulkko et al. (2010) claim that both domestically acquired and travel-related salmonellosis cases have been decreasing in the period 1995-2009. The falling trend is clear in the reported domestic cases (Table 3), but in order to see the decrease in the number of travel-related cases one has to ignore the years 2007 and 2008. However, only a limited number of diarrheal cases are ever investigated, which means that the yearly reported numbers show only the top of an ice berg of the suffered infections. In reality, the total number of salmonellosis cases, especially those acquired abroad, is most probably much higher. It has been estimated that there could be even 30,000 domestically acquired salmonellosis each year in Finland, but the majority do not end up in the register (Korkeala 2007).

Surely there are more *Salmonella* infections of foreign origin than are registered. The reasons for under-detection, among other thing, can be that the infection usually does not require any medical help (e.g., a short, sub-clinical or asymptomatic course of the infection). In addition, the infection can be considered as "a normal diarrhea that happens for everyone every now and then". Also, a sample detected by a laboratory can be falsely negative. An on-going antimicrobial therapy or advanced convalescence can be reasons for a negative laboratory result. Considering all suspected TD cases, even after a comprehensive microbiological evaluation, approximately every third case (20-40%) still remains without the evidence of a causative agent (DuPont 2009).

In the physician's communicable disease notification, it is mandatory to name the patient's nationality. In spite of that, until 2002 there were more than one hundred cases without the information each year. Since then, cases without any record on nationality have been only occasional. This study shows that almost all registered salmonellosis of foreign origin in Finland have been acquired by Finns. This means that foreigners who are living or visiting in Finland are not carrying *Salmonella* in the extent that it would govern the statistics. In other words, non-Finnish citizens do not form a notable proportion of salmonellosis detected in Finland. The low incidence of reported salmonellosis among foreigners was a slightly unexpected result, because it is known that immigrants are more prone to risk behaviours concerning infectious diseases: they make trips to visit friends and relatives (VFR travel). Therefore, if the hygiene level in the visiting area is lower than in Finland, VFR travellers are more likely to expose to pathogens than an ordinary holiday or business traveller. The reasons for the low incidence of non-Finnish citizens in salmonellosis reports might be due to uneagerness to seek medical care in contrast to Finnish citizens, or better developed gastrointestinal immunity against enteropathogens.

Still, Table 8 shows that as the proportion of foreign citizens living in Finland has increased during the 15 years period, also the proportion of *Salmonella* infections among this group has elevated. However, because of low total incidence of salmonellosis in foreign citizens, it is impossible to conduct more detailed specification of those cases. Instead, because the study shows that the vast majority of reported salmonellosis of foreign origin have been suffered by Finnish citizens, it is probably safe to use the term 'Finnish travellers' when talking about persons with detected salmonellosis in Finland due to international travelling during 1995-2009.

The average age of the persons with reported salmonellosis has not essentially changed during the study period, even though demographic change could, for instance, increase the proportion of travelling older people which would be reflected at the number of reported infections in the respective age categories. However, statistics do not support this presumption. Instead, the proportion of the youngest age categories (<5, 5-9, and <20 years) has been growing among the reported cases. Reasons for explaining the shift might be that children are taken abroad at earlier age, or they are taken to higher-risk countries for acquiring TD than a decade ago. It is also important to remember that not healthy adults or the healthy elderly, but youngsters are the ones who belong to the highest risk group for acquiring TD (and also salmonellosis), (Ekdahl, de Jong, Wollin, et al. 2005; Steffen et al. 2004; Pitzinger et al. 1991). In other words, the proportion of the reported salmonellosis of foreign origin in the youngest age categories is expected to increase slowly in the future, because more Finnish children are likely to travel abroad and are also likely to get sick easier than other age categories. Yet, the threshold for seeking medical assistance when having diarrhea is lower when talking about a child than an adult. This may also have some effect on the distribution of the reported cases as a whole.

A typical person with salmonellosis acquired abroad and detected in Finland, is Finnish by a nationality and around 40 years old. There is a statistically significant gender predisposition: more females seems to fall ill than males. This elevated proportion of women may be explained by the behaviour of women to seek medical care easier than men (Bunton 2002). In addition, according to the Infectious Diseases Legislation, those who work in certain jobs (grocery industry, health care sector, with drinking water purification or with small children) need to be *Salmonella* tested after a trip beyond the Scandinavian countries. This means that people who could spread their infection via work to a large population or to the most vulnerable ones need to be tested immediately after the journey even if they do not show any symptoms (Tartuntatautilaki). However, a notable proportion of people working in the health care sector (such as nurses) or in institutional kitchens (schools, hospitals, food industry etc.) are women, witch may also have a contribution to the higher proportion of female cases seen in the data.

The number of yearly detected salmonellosis of foreign origin has stayed quite stable over the past 15 years despite fluctuations in the number of Finnish travellers, their travel destination preferences and activities there etc. Globally, the number of international travellers has been increasing constantly, people are more eager to visit to exotic destinations, travelling has become easier and travelling has become cheaper and cheaper due to increased competition etc. Therefore, it is amazing how stable the detected number of salmonellosis of foreign origin has been in Finland. Even though Finns are not used to be afraid of *Salmonella* infection, because of its low prevalence in Finland, *Salmonella* bacteria are commonly present in human surroundings outside the Nordic countries. For all these reasons, it is most probable that *Salmonella* infections of foreign origin among Finnish citizens will not decline in the future. A different story is whether these cases end up in the Infectious Diseases Register or not.

There were 147 named source countries for salmonellosis in the Infectious Diseases Register. This covers 75% of the countries in the world, which shows that Finnish are travelling really widely. During 2000-2009, Finns made more than 6 million journeys abroad every year (Statistics Finland). The travel statistics include also one-day trips and cruises. But as it is known, the longer the trip the higher the risk of acquiring traveller's diarrhea (Steffen et al. 2003). The shortest trip outside the country borders can be as short as a couple of hours. For example, a day cruise to a neighbouring country, such as Estonia, Russia or Sweden, is very popular among Finnish recreational travellers. Also, business trips by plane can be as short as cruises. That is why it can be slightly problematic to evaluate incidences for acquiring salmonellosis from near-by countries among Finnish passengers. Let us think about an example. If someone has taken a part in a day cruise and then suffered from salmonellosis within 7 days, would that be an infection of foreign origin? Does the interpretation change whether a person is staying aboard all the time or disembarks for a couple of hours? How about if the person had not been eating anything while disembarked? Surely these questions will have an effect on the person's risk evaluation for acquiring salmonellosis abroad.

However, according to the division of salmonellosis for domestic origin and for foreign origin, all the above mentioned scenarios should be regarded as salmonellosis of foreign origin in the case that there is no other reason for different classification (i.e. a clear food poisoning related to some domestic event). Yet, this classification system can underestimate the risk of acquiring salmonellosis in the countries near-by Finland where a lot of one-day trips are made. A large number of passengers increases the denominator probably more than the number of falsely positive cases increases the numerator in the calculation of the incidence.

The ten most popular holiday destinations for Finns in 2008 in the declining order were: Estonia, Spain, Sweden, Italy, Greece, German, Russia, France, United Kingdom and Thailand. The same countries were on the list also in 2004, but not in the exactly same order. (Statistics Finland) This means that the same countries have been popular travel destinations for Finnish travellers already for years. That can also be seen in the list of the most frequently reported source countries for acquired salmonellosis. Instead, some countries have been on the top-10 list only once maybe because of an epidemic. For example in 1995, there was an *S. infantis* outbreak in Denmark (Wegener & Baggesen 1996). After the epidemic, the number of reported cases from Denmark has been extremely low even though the yearly numbers of Finnish passengers to Denmark is high.

Among the top-10 list of countries, the number of Finnish passengers has increased especially in Thailand and Italy, but also in Turkey, Spain, Greece, Tunisia, India, Bulgaria, Egypt, Hungary, Denmark and Latvia during the past 10 years. In contrary, travels to Estonia and Russia have clearly decreased (Table 6).

According to the registered cases and estimated travel information during 2000-2009, the overall risk of salmonellosis due to international travelling was 31.8 / 100,000 Finnish travellers per year. This is slightly smaller than the value Swedish researchers have estimated among Swedish traveller: 36.5 ⁄ 100,000 travellers (Ekdahl, de Jong, Wollin, et al. 2005). A reason to this difference between values could be at least partly explained by the vast amount of day cruises that Finnish are doing each year. These are included in the total number of passengers travelling beyond the country borders. Instead, the Swedish study takes into account only overnight travels outside Sweden.

Graphical incidence curves are shown for 15 travel destinations in Figure 9 a-c. The incidence curve shows how the risk for acquired salmonellosis has changed in each country during the study period. The highest decline was seen in Tunisia. Also Spain, Cyprus, Hungary, and Latvia were showing clear declining trends. A more moderate decline was seen in Portugal, Greece, Turkey, Egypt, and Bulgaria. Of course, yearly variation of incidences was seen in every country. However, in Thailand the yearly variation of incidence was extremely large. It almost looks like the highest peaks of incidences were in every third year. In Portugal, Greece, Turkey, and Egypt, yearly variations have been strong, but the main trend still seems to go down little by little. In Bulgaria, the incidence curve was a reverse U-shape, which means that the incidence was highest in the middle of the study period. In Estonia and Russia, the curves showed low and steady incidences, but in 2005 there seems to have been an outbreak in Russia. As was pointed earlier, these two neighbouring countries of Finland are among the most favourite travel destinations for Finns. Even though there were lots of registered *Salmonella* cases linked to both countries, given the high number of travellers, the incidences stayed at a very low level.

In India, there seems to be a huge yearly variation in incidence. However, travel information was missing for two years, which also makes the interpretation of the incidence trend slightly unreliable. Anyhow, incidences that could be calculated in India were still high compared to most of the other countries studied.

In general, the trends of incidences seemed to decline in almost every studied country except in Thailand and India. This means that the overall risk for acquiring salmonellosis among Finnish travellers has decreased in most of the studied countries since the beginning of year 2000 (except for Bulgaria with the lowest incidence at the beginning and at the end of the decade). Because of inadequate travel information on India, Thailand was the only country of those examined that showed an increase in the number of Finnish passengers and a steady or even an increased incidence trend of salmonellosis among Finnish travellers. In other words, Thailand can be seen as a country of increased number of Finnish travellers, but at the same time it has contributed proportionally more to the total number of *Salmonella* cases detected in Finland.

However, calculated incidences are only approximates, because there is no official travel register in Finland. Also, the data from STAT is gathered from interviewing persons aged 15-74 years and the survey does not include any details from the trips made by other persons in the household. Therefore, passenger information used in this study does not include the outbound trips made by children under 15 years or the elderly over 74 year. For this reason, the incidences shown in this study might over-exaggerate the risk of salmonellosis especially in destinations which are popular for children or the elderly, e.g., Thailand.

The mean incidences during the ten year period show that the most probable countries for Finns to acquire salmonellosis were Thailand (679.8), Tunisia (517.0), and India (415.1/100,000 travellers). The countries with the lowest risk were Denmark (2.7) and Estonia (3.9/100,000 travellers). This shows that Estonia, the most popular destination country for Finns to travel to (more than a million travels every year), was a fairly safe destination concerning salmonellosis.

Thailand was the most frequently reported source country for salmonellosis acuired abroad and detected in Finland, 1995-2009. Hence, annual variation in Thailand largely contributed to the changes in the total number of reported infections. A peak in the total number of cases in 2008 was also seen as a peak in the incidence curve of Thailand (Table 6, Figure 9a).

The annual lists of the most frequently reported *Salmonella* serotypes of foreign origin in Finland are presented by Hulkko et al. (shown on Table 3), but Table 12 sums the most frequently reported serotypes over the follow-up period of 15 years. *S. enteritidis* (43.5%) has been unambiguously the most frequently detected serotype in Finland, followed by *S. typhimurium* (7.8%), *S. virchow* (4.2%), and *S. stanley* (3.7%). Considering the most frequently reported serotypes in each studied country (Table 14), *S. enteritidis* has been the main pathogen in almost every listed country with the exceptions of Thailand, India, Denmark and Brazil. *S. enteritidis* has still been strongly present in Thailand and India, but not in Denmark and Brazil. Since 1996, registered salmonellosis among Finnish passengers from Denmark has been extremely low, which also explains why different serotypes have not been detected overall. Instead, the extremely low incidence of *S. enteritidis* among travellers from Brazil remains unknown. As expected, *S. enteritidis* strongly dominated in Europe (de Jong & Ekdahl 2006b). For example in Latvia, almost all reported *Salmonella* cases were that serotype, which agrees with the study of de Jong & Ekdahl (2006b). The inscidence of *S. enteritidis* remained high in the northern part of the Mediterranean sea, but appeared already lower on the other side of the sea. In Asia, the proportion of the serotype was even lower. These observations are supported by a Swedish study (Ekdahl, de Jong, Wollin, et al. 2005). Also, *S. typhimurium* was shown frequently in many countries. The Swedish researchers have found that the second most frequent serotype in Europe was *S. typhimurium* which accounted for 9% of the cases (de Jong & Ekdahl 2006b).

de Jong and Ekdahl (2006b) estimated the five topmost countries in Europe to have the highest burden of salmonellosis for Swedish travellers. These countries were Bulgaria, Turkey, Malta, Portugal and Poland. The researchers estimated the risk for acquiring *S. enteritidis* infection in Bulgaria to be 87.5/100,000 travellers, followed by Portugal with 66.4/100,000 travellers, and Turkey with 53.0/100,000 travellers. Our data shows that the mean incidence over the study period for the same countries were 283.3/100,000 travellers in Bulgaria, 63.2/100,000 in Portugal, and 152.4/100,000 in Turkey. The proportion of *S. enteritidis* was, of course, lower (percentage proportions are shown in Table 14): 156.9/100,000 in Bulgaria, 54.6/100,000 in Portugal, and 71.2/100,000 travellers in Turkey. When comparing our results to the Swedish studies, Bulgaria showed almost a double incidence rate in our study and also the incidence for Turkey was elevated among Finnish passenger. Instead, incidence for Portugal seemed to be quite at the same level in both studies.

In total, there were fewer detected *Salmonella* infections from Brazil than from Thailand and India. Also, serotype distribution between the countries was different. Compared to Thailand, travels to Brazil have been made considerably less often, which explains a lower number of detected cases in Brazil. Instead, the numbers of travellers to Brazil and India were almost at the same level. Still, there were huge differences in serotype distributions and also in the number of cases between these countries. One reason for the high number of cases and a wide range of different serotypes in India and Thailand might be explained by travel behaviour. These two Asian countries have been popular destinations for Finnish backpackers. Also, more low-price flighting tickets have traditionally been available from Finland to Asia than to South America. This makes Asia a more favourable destination for low budget travelling. However, economical travelling and backpacking expose travellers easier to low hygiene levels (such as sleeping in hostels and eating in street vendors) than package trips (sleeping in hotels and eating in restaurants) (Steffen et al. 2003). Thus, economical travelling and backpacking increases the risk of TD. In addition, backpackers tend to stay longer in their trips than people with business and package trips. The longer the stay, the bigger the risk for acquiring TD (Ahlm et al. 1994; Steffen et al. 2003).

S. typhimurium was the second most frequently reported serotype in Finland. Again, it was not a common finding among travellers from Brazil, but in many other countries it seemed to be a fairly common serotype. Interestingly, the majority of some of the detected serotypes was linked almost solely to passengers from one country: *S. stanley* from Thailand and *S. bareilly* from India. This does not necessarily indicate that these serotypes were strongly present only in these countries or areas, but rather that the notification data and travel data were limited. As it was said earlier, not only a small proportion of salmonellosis are reported, but also Finnish passengers are not presented regularly in every geographical area. A small group of Finns can travel to an exotic destination and get all sick. However, because there is no common register for every travel made by Finns, we do not find out these uncommon destinations, and, furthermore, get the incidence of salmonellosis there.

Thus, this study does not necessarily show the countries with the highest incidence of acquired salmonellosis among Finnish passengers. There is not yet a tool to find out that information. A limitation of this research is that only countries with a high reported number of cases are studied (Table 9 and 10). This also means that most probably only destinations with a high number of passengers are being selected, because of sufficient amount of cases to end up in the study. As it was seen in the comparison of the incidences between the selected top-10 list countries, incidence takes into account the absolute number of reported cases and the number of passengers. This reveals differences on risk for acquiring salmonellosis between the countries. However, we could also get interesting results, if there was a common travel register. Then we could select, for example, only countries with the smallest number of Finnish travellers and then find out the number of reported salmonellosis from those countries.

Our data did not include the serotypes of *S. typhi* or *S. paratyphi*, which cause a systemic infection unlike the other *Salmonella* serotypes normally do. However, typhoid and paratyphoid salmonellosis are rarely detected in Finland and almost all the cases have been related to international travelling (Hulkko et al. 2010; Kyyhkynen et al. 2004). Typhoid and paratyphoid fever can be common diseases in some parts of the world and also a threat for foreign visitors coming to that area. For example, the capital of Nepal, Kathmandu, has been named as the World Capital of Enteric Fever. Not only a big proportion of *S. typhi* and *S. paratyphi* form a problem, but also increasing antimicrobial resistance against *Salmonella* bacteria. (Karkey et al. 2008; Parry & Threlfall 2008) Even though many travellers also from Finland travel to these endemic areas, still, notably few typhoid and paratyphoid cases have been detected in Finland. A low yearly incidence of detected typhoid in Finland could indicate that Finns who are travelling to an endemic area are taking the vaccine, which is available against typhoid fever. There is no vaccine available against other *Salmonella* serotypes.

Because this was a register-based study based on laboratory confirmed findings of positive *Salmonella* tests, there is no doubt of reliability of the study cases. Laboratories performing these tests are under the regulation of Infectious Diseases Decree. According to the legislation, all positive cases need to be reported to the National Infectious Diseases Register (Tartuntatautilaki). Thus, all *Salmonella* infections detected in Finland are also registered and the causative stains are sent to THL for verification and further typing. However, one can suffer from salmonellosis without knowing it. These sub-clinical cases, of course, do not end up in the National Infectious Diseases Register unless these persons are not tested for some other reasons. Diarrhea is the most common symptom when travelling abroad and is often suffered without medical assistence. Hence, this also leads to under-reporting of salmonellosis. Duration of travel, medication, etc. may lead to nagative results in laboratory tests after homecoming. . Also cases that are diagnosed positive for *Salmonella* during their travel (i.e., those who are seeking hospital care), are unlike to enter for Finnish *Salmonella* register (if not tested again positive in Finland). All these circumstances can cause bias to the data received from the National Infectious Diseases Register. Still, the total of 30,977 *Salmonella* cases of foreign origin were studied in this thesis, which represents around 2,000 cases per each year. This is a considerably large sample size and therefore the results of the study can be generalised to describe *Salmonella* infections among Finnish travellers.

4.5 Public Health Implications

There are at least three important arguments that need to be taken into account when evaluating the importance of travel-related salmonellosis with the public health perspective.

Firstly, all *Salmonella* infections are laboratory confirmed and registered in Finland (Tartuntatautilaki). However, it is most likely that there are many times more acquired infections, but those do not end up in the National Infectious Diseases Register (Korkeala 2007), because of under-detection (do not require hospital care, sub-clinical infections, negative laboratory finding etc.). If there is no laboratory confirmed cause for diarrhea, a traveller just knows they have suffered from TD, which is the most common symptom when travelling abroad. However, certain risky countries, where the risk of salmonellosis is strongly elevated, should be followed more actively and also travellers should be informed more carefully on the infection. Finns are not used to think of *Salmonella* infections, because of its extremely low occurrence in groceries and animals in Finland. For example, the risk for acquiring salmonellosis in Spain (the most popular holiday destination according to AFTA) was 21 fold lower than in Thailand (the fifth popular destination) and in Turkey (the third popular destination) 4.5 fold lower than in Thailand.

Secondly, *Salmonella* infection can cause not only gastrointestinal symptoms but also secondary diseases, e.g., reactive arthritis and joint stiffness. Until now 10 per cent of Finns who have suffered from salmonellosis are also diagnosed with reactive arthritis. Therefore, *Salmonella* infections have a notable influence on the burden of human chronic diseases even in Finland. (Korkeala 2007)

Thirdly, the globally growing use of broad-spectrum antimicrobials has increased the resistance of *Salmonella* bacteria towards many drugs (Parry & Threlfall 2008). Multi-resistant bacteria are a serious problem for people who require antimicrobial care for any reason. Even a harmless infection of *Salmonella* bacteria can spread resistance factors to other bacteria in the gastrointestinal system and, thus, weaken the effect on future antimicrobial therapy for that person.

Therefore, *Salmonella* infections should have an important emphasis on public health work in Finland also in the future. Increasing international travelling, immigration and trade accelerates spreading of *Salmonella* pathogens, which need to be prepared. Prevention and early disease control processes need high inputs, among other thing, in training, education and surveillance, which are, of course, economically costly. At best, these measures would result in lower disease burden and better antimicrobial resistance, which would benefit many sectors in society, not only health care. Eventually, healthier people and animal are more productive, which is also the best alternative for the national economy.

5 CONCLUSIONS

The aims of the study were to find out trends of salmonellosis acquired abroad and detected in Finland during 1995-2009, and to examine how these trends were correlated with the number of Finnish travellers.

According to this study, the yearly incidence of *Salmonella* infections of foreign origin notified to the National Infectious Diseases Register has stayed quite stable over the 15 years follow-up period in Finland. Thailand, Spain and Turkey were the most frequently reported source countries for travel-related salmonellosis. Even though the overall risk of travel-related salmonellosis was as low as 31.8 / 100,000 Finnish travellers 15 years and above per year, there were several fold differences in incidences between the studied countries. The highest risk countries were Thailand (679.8/100,000 travellers), Tunisia (517.0), and India (415.1). Still, the risk for acquiring salmonellosis among Finnish travellers has been decreasing in most of the studied countries since the beginning of year 2000. Thailand was, however, the only country which showed an increasing number of Finnish travellers while at the same time contributed proportionally more to the total number of *Salmonella* cases detected in Finland. This study also shows that some *Salmonella* serotypes detected in Finland were typical findings among travellers from certain countries.

Despite the increasing number of immigrants in Finland, the vast majority of the infections were detected among Finnish citizens. This study did not identify reasons for low incidence of salmonellosis among non-Finnish citizens, even though it would be an interesting research area, because of the known risk behaviour of immigrants concerning infectious diseases: visiting friends and relatives. Due to increasing immigration also into Finland and the potential to spread infection upon return, the number of travel-related *Salmonella* infections among non-Finnish citizens should be followed up carefully on the public health side.

This study indicates that the proportion of children with travel-related salmonellosis is increasing, even though the mean age of the persons with the reported salmonellosis has not essentially changed. Future research is needed to understand the reasons for this increased number of salmonellosis among children under 20 years. Also, research for defining the countries that are more responsible for travel-related salmonellosis on children is needed. Certain countries are particularly popular for family holiday destinations, but whether the incidence of acquired salmonellosis in Finnish children varies among these countries is unknown. In addition, this study shows that females were significantly more often reported with salmonellosis than males (54.4 vs. 45.6%). However, the issue was not further studied, so whether this gender disposition is seen homogeneously in every age category or only over-represented in certain age categories, needs also further research.

Data collection methods have improved over the years. The Infectious Diseases Register has collected information on salmonellosis since the 1990s. However, a limitation of this study was a short follow-up of incidences due to difficulties in receiving travel information on Finnish passengers. A challenge for future studies is to solve the problem of collecting accurate travel information on Finnish travellers. It would also be interesting to see incidence trends in a longer time scale than 10 years.

This study identifies the highest risk countries for acquiring salmonellosis among the most popular destination countries for Finnish travellers. Even though some countries with a high incidence of salmonellosis may have remained outside of our focus, still, this study was able to show the main countries from a public health point of view, which should be taken into consideration when targeting travel related health advice.

AKNOWLEDGEMENTS

I would like to sincerely thank my supervisors Prof. Hanna Nohynek and Veterinary Epidemiologist Ruska Rimhanen-Finne for their guidance and valuable pieces of useful advice. Also, I would like to express my warm gratitude to the Statistician Jukka Ollgren for data managing guidance, and to Research Prof. Anja Siitonen for helpful comments and worthwhile advice.

I am grateful to many other people who have helped me, directly and indirectly, in the preparation of this Master's Thesis.

REFERENCES

AFTA, 2010. Association of Finnish Travel Agents. *http://www.smal.fi/index.php?139*. Available at: http://www.smal.fi/index.php?139 [Accessed March 10, 2011].

Ahlm, C. et al., 1994. Health problems and self-medication among Swedish travellers. *Scandinavian Journal of Infectious Diseases*, 26(6), 711-717.

Blaser, M.J. & Newman, L.S., 1982. A review of human salmonellosis: I. Infective dose. *Reviews of Infectious Diseases*, 4(6), pp.1096-1106.

Bunton, R., 2002. *Health promotion : disciplines, diversity, and development* 2nd ed., London ;;New York: Routledge.

Chongsuvivatwong, V. et al., 2009. Epidemiology of travelers' diarrhea in Thailand. *Journal of Travel Medicine*, 16(3), pp.179-185.

Day, J.N. & Lalloo, D.G., 2004. Neurological syndromes and the traveller: an approach to differential diagnosis. *Journal of Neurology, Neurosurgery, and Psychiatry*, 75 Suppl 1, pp.i2-9.

DuPont, H.L. and Khan, F.M. 1994. Travelers' Diarrhea: Epidemiology, Microbiology, Prevention, and Therapy. *Journal of Travel Medicine*, 1(2), pp.84-93.

DuPont, H.L., 2009. Systematic review: the epidemiology and clinical features of travellers' diarrhoea. *Alimentary Pharmacology & Therapeutics*, 30(3), pp.187-196.

DuPont, H.L., 2006. New insights and directions in travelers' diarrhea. *Gastroenterology Clinics of North America*, 35(2), pp.337-353, viii-ix.

DuPont, H.L., 2005. Travelers' diarrhea: antimicrobial therapy and chemoprevention. *Nature Clinical Practice. Gastroenterology & Hepatology*, 2(4), pp.191-198; quiz 1 p following 198.

Ekdahl, K., de Jong, B. & Andersson, Y., 2005. Risk of travel-associated typhoid and paratyphoid fevers in various regions. *Journal of travel medicine*, 12(4), pp.197-204.

Ekdahl, K., de Jong, B., Wollin, R., et al., 2005. Travel-associated non-typhoidal salmonellosis: geographical and seasonal differences and serotype distribution. *Clinical Microbiology and Infection: The Official Publication of the European Society of Clinical Microbiology and Infectious Diseases*, 11(2), pp.138-144.

EVIRA, 2006. Salmonella control and prevalence of salmonella 1995 – 2004. Available at: http://www.evira.fi/files/products/1285760453926_eviran_julkaisuja_3_2006.pdf [Accessed January 11, 2011].

Gascon, J., 2006. Epidemiology, Etiology and Pathophysiology of Traveler's Diarrhea. *Digestion*, 73(1), pp.102-108.

Greenwood, Z. et al., 2008. Gastrointestinal infection among international travelers globally. *Journal of Travel Medicine*, 15(4), 221-228.

Gushulak, B., Funk, M. & Steffen, R., 2007. Global changes related to travelers' health. *Journal of Travel Medicine*, 14(4), pp.205-208.

Hulkko, T. et al., 2009. *Tartuntataudit Suomessa 2008*, Helsinki: Terveyden ja hyvinvoinnin laitos.

Hulkko, T. et al., 2010. *Tartuntataudit Suomessa 1995-2009*, Helsinki: Terveyden ja hyvinvoinnin laitos.

de Jong, B. & Ekdahl, K., 2006a. Human salmonellosis in travellers is highly correlated to the prevalence of salmonella in laying hen flocks. *Euro Surveillance: Bulletin Européen Sur Les Maladies Transmissibles = European Communicable Disease Bulletin*, 11(7), p.E060706.1.

de Jong, B. & Ekdahl, K., 2006b. The comparative burden of salmonellosis in the European Union member states, associated and candidate countries. *BMC Public Health*, 6, p.4.

Karkey, A. et al., 2008. Kathmandu, Nepal: still an enteric fever capital of the world. *Journal of Infection in Developing Countries*, 2(6), pp.461-465.

Keskimäki, M. et al., 2000. Prevalence of diarrheagenic Escherichia coli in finns with or without diarrhea during a round-the-world trip. *Journal of Clinical Microbiology*, 38(12), pp.4425-4429.

Korkeala, H., 2007. *Elintarvikehygienia ympäristöhygienia, elintarvike- ja ympäristötoksikologia*, Helsinki: WSOY Oppimateriaalit.

Kyyhkynen, A., Korkeila, M. & Siitonen, A., 2004. Salmonella-infektioiden epidemiologiaa - tartunnat kotimaasta tai matkatuliaisina. *Suomen Lääkärilehti*, 59(44), pp.4273-4277.

Majowicz, S.E. et al., 2010. The global burden of nontyphoidal Salmonella gastroenteritis. *Clinical Infectious Diseases: An Official Publication of the Infectious Diseases Society of America*, 50(6), pp.882-889.

Mattila, L. et al., 1992. Seasonal variation in etiology of travelers' diarrhea. Finnish-Moroccan Study Group. *The Journal of infectious diseases*, 165(2), pp.385-388.

National Veterinary Institute, 2008. Zoonoses in Sweden 2008. Available at: http://www.sva.se/upload/pdf/rapport/Zoonosrapport_webb.pdf [Accessed January 11, 2011].

Nygård, K. et al., 2002. Detection of a previously uncommon salmonella phage in tourists returning from Europe. *Lancet*, 360(9327), p.175.

Parry, C.M. & Threlfall, E., 2008. Antimicrobial resistance in typhoidal and nontyphoidal salmonellae. *Current Opinion in Infectious Diseases*, 21(5), pp.531-538.

Pitzinger, B., Steffen, R. & Tschopp, A., 1991. Incidence and clinical features of traveler's diarrhea in infants and children. *The Pediatric Infectious Disease Journal*, 10(10), pp.719-723.

Rack, J. et al., 2005. Risk and spectrum of diseases in travelers to popular tourist destinations. *Journal of Travel Medicine*, 12(5), pp.248-253.

Schlagenhauf, P. et al., 2010. Sex and gender differences in travel-associated disease. *Clinical Infectious Diseases: An Official Publication of the Infectious Diseases Society of America*, 50(6), pp.826-832.

Shah, N., DuPont, H.L. & Ramsey, D.J., 2009. Global etiology of travelers' diarrhea: systematic review from 1973 to the present. *The American Journal of Tropical Medicine and Hygiene*, 80(4), pp.609-614.

von Sonnenburg, F et al., 2000. Risk and aetiology of diarrhoea at various tourist destinations. *Lancet*, 356(9224), pp.133-134.

Statistics Finland. Suomen virallinen tilasto (SVT): Suomalaisten matkailu [verkkojulkaisu]. Available at: http://stat.fi/til/smat/tau.html [Accessed January 20, 2011].

Statistics Finland 2. Statistics Finland - Statistics by topic - Population structure. Available at: http://stat.fi/til/vaerak/tau_en.html [Accessed May 31, 2011].

Steffen, R, 1986. Epidemiologic studies of travelers' diarrhea, severe gastrointestinal infections, and cholera. *Reviews of Infectious Diseases*, 8 Suppl 2, pp.S122-130.

Steffen, R., 2005. Epidemiology of traveler's diarrhea. *Clinical Infectious Diseases: An Official Publication of the Infectious Diseases Society of America*, 41 Suppl 8, pp.S536-540.

Steffen, R., deBernardis, C. & Baños, A., 2003. Travel epidemiology--a global perspective. *International Journal of Antimicrobial Agents*, 21(2), pp.89-95.

Steffen, R. & Ericsson, C.D., 2000. Special section:travel medicine. *Clinical Infectious Diseases: An Official Publication of the Infectious Diseases Society of America*, 30(5), pp.809-810.

Steffen, R. et al., 2004. Epidemiology of travelers' diarrhea: details of a global survey. *Journal of travel medicine*, 11(4), pp.231-237.

Tartuntatautiasetus. Communicable Diseases Decree 786/1986. Available at: http://www.finlex.fi/fi/laki/ajantasa/1986/19860786 [Accessed January 17, 2011].

Tartuntatautilaki. Communicable Diseases Act 583/1986. Available at: http://www.finlex.fi/fi/laki/ajantasa/1986/19860583 [Accessed January 17, 2011].

Teague, N.S. et al., 2010. Enteric pathogen sampling of tourist restaurants in Bangkok, Thailand. *Journal of travel medicine*, 17(2), pp.118-123.

UNWTO, 2010. UNWTO Tourism Highlights. Available at: http://www.unwto.org/facts/eng/pdf/highlights/UNWTO_Highlights10_en_HR.pdf [Accessed January 12, 2011].

Wegener, H.C. & Baggesen, D.L., 1996. Investigation of an outbreak of human salmonellosis caused by Salmonella enterica ssp. enterica serovar Infantis by use of pulsed field gel electrophoresis. *International Journal of Food Microbiology*, 32(1-2), pp.125-131.

Zoonoosikeskus. Zoonosis Centre in Finland. Available at: http://www.zoonoosikeskus.fi/portal/fi/zoonoosit/bakteerien_aiheuttamat_taudit/salmonella/ [Accessed February 7, 2011].