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The microbiological quality of water in fish spas with *Garra rufa* fish, the Netherlands, October to November 2012

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In fish spas, clients may submerge their hands, feet or whole body in basins with *Garra rufa* fish, for dead skin removal. Skin infections may result from using these spas, transmitted from fish to clients, through either fish or water, or from client to client. The microbiological water quality was determined in 24 fish spas in 16 companies in the Netherlands through analysis of a single water sample per fish spa. Water samples were tested for the presence of *Aeromonas* spp., *Vibrio* spp., *Pseudomonas aeruginosa*, nontuberculous mycobacteria, and faecal indicator bacteria by using standard culture methods. The majority of the examined fish spas contained *Aeromonas* spp. (n = 24), *P. aeruginosa* (n = 18), *Vibrio* spp. (n = 16) including *V. cholerae* non-O1/O139 and *V. vulnificus*, and several rapid growing *Mycobacterium* spp. (n = 23) including *M. fortuitum*, *M. conceptionense*, *M. abscessus* and *M. chelonae*. Faecal contamination of the fish spa water was low. Based on the detected concentrations of *Aeromonas* spp., *Vibrio* spp., and *P. aeruginosa*, the detected *Mycobacterium* spp., and the health implications of these bacteria, the health risk from using fish spas is considered limited for healthy people with an intact skin and no underlying disease.

Introduction

Originating from Turkey, fish spas are increasingly popular and available throughout the world. In fish spas, clients submerge their feet, hands, or their whole body, in basins with *Garra rufa* fish that nibble dead and thickened skin from the submerged body parts during a 15 to 30 minutes treatment. *Garra rufa* are small toothless fish that belong to the carp family (*Cyprinidae*). The use of fish spas is mostly considered a cosmetic and relaxing treatment, but it is also offered to relieve skin disorders such as eczema and psoriasis [1-3]. Studies performed in Turkey and Austria suggested a beneficial effect of fish spa therapy, or ichthyotherapy, on psoriasis. However, several factors could have contributed to this outcome, including limited follow-up of patients, selenium in the therapy water, and simultaneous ultraviolet light A (UVA) treatment [2,3].

Since the same water and fish are used for several simultaneous and subsequent clients, and the fish are potential carriers of pathogens, the most important health risk from fish spas is the possible transmission of infections [1]. The water temperature in fish spas is kept at 25–30 °C thus providing opportunities for many bacteria to thrive. Pathogens may be transmitted from fish to man, from water to man, and from man to man with water and/or fish. An appropriate water quality is important to reduce the risk of infection for clients. Conventional water treatment and disinfection are, however, not possible, because these processes would kill the fish [1]. Commonly, the water is filtered, but most applied filters do not remove micro–organisms and those that do, have little effect on micro–organisms in biofilms or on the fish skin [1]. Continuous partly refreshment of the water results in dilution of the microbial contamination and may have a beneficial effect on water quality when no fresh contamination is introduced. However, in daily practice, fish spas are continuously re-contaminated while in use [1].

The handling of fish, and keeping fish in crowded aquaria, may lead to chronic stress, reduced fish health, and poor fish immunity [4]. Apparently healthy fish may carry (human) pathogens without having visible symptoms. When such fish are exposed to unfavourable conditions, outbreaks of infectious diseases may occur among the fish, resulting in an increased number of waterborne bacteria in the spas, with an accompanying increased zoonotic risk of transmission to humans [5]. Recently, *Aeromonas sobria* was implicated as the cause of massive die–off in *Garra rufa* at

a breeding farm in Slovakia [6], and a batch of ill *Garra rufa* in England appeared to be contaminated with *Streptococcus agalactiae* [7].

Examination of several batches of *Garra rufa* that entered the United Kingdom (UK) from Indonesia and several other Asiatic countries, demonstrated the presence of, among others, *Aeromonas* spp., *Vibrio* spp., *Mycobacterium senegelense* and *Streptococcus agalactiae*. All of these bacteria are capable of causing disease in humans [7].

Concerns about possible transmission of infections from fish spas to humans have led to the publication of guidance [1] and risk assessment documents [8] in the UK and France respectively, and a negative advice against starting new companies or continuation of existing companies offering fish spa treatment in Belgium [9]. Fish spas have been banned in some provinces in Germany due to animal welfare considerations, and the German veterinary authority has drafted a requirements document for new fish spas [10]. Animal welfare and hygiene considerations have resulted in a ban of fish spas in several states in the United States and some provinces in Canada [1].

In this study, the water in a random selection of fish spas throughout the Netherlands was tested for the presence of *Aeromonas* spp., *Vibrio* spp., *Pseudomonas aeruginosa*, nontuberculous mycobacteria (NTM) and the faecal indicator bacteria *Escherichia coli* and intestinal enterococci, to assess the microbiological water quality. Possible implications for public health are discussed.

Materials and methods

Recruitment of participants and sampling of fish spas

A random selection of 25 companies that offered fish spa treatment was asked by letter to participate in the study in September 2012.

At each participating company, one fish spa was sampled, however, when several types of fish spas were present (hand, foot, body), one spa of each type was sampled. Whenever there was visible dirt on the fish spa walls, Enviro Swabs (3M) were used to take swab samples from these walls. Water samples of 1.5 L were taken according to ISO 19458:2006. All samples were transported to the laboratory in insulating containers with melting ice and analysed within 24 hours from sampling. Samples were taken in October and November 2012, during opening hours, almost always unannounced, and at different times during the sampling days.

Sample analyses

All water samples were examined for the number of *Escherichia coli* (in 10, and 40 mL volumes), intestinal enterococci (in 10, and 40 mL volumes), *Aeromonas* spp. (in 0.1, and 1.0 mL volumes), and *Vibrio* spp. (in 0.1, 1, 10, and 40 mL volumes) by membrane filtration of appropriate volumes of the samples according to ISO 9308–1:2000 (Rapid Test), ISO 7899–2:2000, Havelaar et al. [11], and incubation of the membrane filters on Thiosulphate Citrate Bile salts Sucrose agar (TCBS; Tritium Microbiologie, Eindhoven, the Netherlands) at 36 ± 2 °C for 24 ± 4 hour, respectively. *Vibrio* characteristic colonies on TCBS were subcultured onto Trypton Soy Agar (TSA; Oxoid, Badhoevedorp, the Netherlands) and incubated at 36±2 °C for 20–24 hours.

From each sample, a maximum of five presumptive *Aeromonas* spp., and ten presumptive *Vibrio* spp. (five blue and five green colonies) were confirmed by using Matrix Assisted Laser Desorption Ionization Time of Flight mass spectrometry (MALDI–TOF) [12]. Occasionally, e.g. when large amounts of background flora were present, presumptive *E. coli* and enterococci were confirmed by MALDI–TOF.

P. aeruginosa was enumerated in 100 mL samples by using Pseudalert (IDEXX Laboratories Inc., Westbrook, ME, US) according to the manufacturer's instructions. A most probable number (MPN) table (provided by the manufacturer) was used to determine the *P. aeruginosa* concentration in the samples. Occasionally, the content of a fluorescent well was subjected to confirmation by MALDI–TOF.

For analysis of NTM, 1 L water samples were decontaminated by 30 minutes incubation with 0.005% cetylpyridinium chloride (CPC) at room temperature. Two 0.5 L fractions of the decontaminated samples were filtered through 0.45 µm pore size black membrane filters (Millipore, Amsterdam, the Netherlands). Subsequently, the two membrane filters were washed with 300 mL sterile distilled water, dissected, and placed onto the moderately selective sides (7H10) and the antimicrobial-supplemented highly selective sides (7H11) of two Middlebrook 7H10/7H11 agar bi–plates (Becton Dickinson, Erembodegem, Belgium). The plates were sealed in air permeable bags; one plate was incubated at 30 °C and the other at 36 °C for up to three weeks, with weekly inspection for growth of colonies with characteristic morphology. Presumptive mycobacterial colonies were picked, to a total of 10 per sample, and subcultured onto Middlebrook 7H10 agar plates supplemented with Delvocid (Tritium Microbiologie, Eindhoven, the Netherlands) at 30 °C and 36 °C, and identified by sequencing of the *rpoB* gene [13,14].

Water temperature of all samples was determined on site, whereas pH, turbidity, and conductivity were determined in the laboratory, using standard laboratory equipment.

Table 1

Physical–chemical and microbiological parameters in the water of 24 fish spas in 16 companies, the Netherlands, October–November 2012

Sample date (2012)	Company	Spa type and capacity	Water temperature (°C)	pH	Conductivity (µS/cm)	IE (n/100 mL)	*Aeromonas* spp. (n/100 mL)	*Vibrio* spp. (n/100 mL)	*Pseudomonas aeruginosa* (MPN/100 mL)
22 Oct	A	Foot, 1 person	29.5	8.43	451	0	30,000	0	124
22 Oct	A	Foot, 1 person	29.5	7.72	449	1	19,500	0	137
22 Oct	B	Foot, 2 persons	28.1	8.19	379	0	24,000	0	42
22 Oct	C	Foot, 2 persons	29.0	8.14	552	1	82,000	411	178
30 Oct	D	Foot, 4 persons	27.8	8.03	483	2	4,036	648	59
30 Oct	E	Body, 1 person	31.2	8.49	294	0	32	5.4	<1
30 Oct	F	Body, 1 person	31.3	8.48	296	3	5,491	87	6.4
30 Oct	F	Foot, 6 persons	31.3	8.59	251	0	4,145	270	150
30 Oct	G	Foot, 2 persons	25.0	8.15	225	0	109,000	0	144
06 Nov	H	Foot, 2 persons	26.8	8.49	348	0	5,864	2	1
06 Nov	H	Hand, 2 persons	26.8	8.53	357	0	2,909	3	<1
06 Nov	I	Foot, 4 persons	28.6	8.09	483	0	32,700	4,290	<1
06 Nov	J	Foot, 4 persons	28.1	8.29	356	0	20,000	0	24
06 Nov	K	Foot, 2 persons	27.8	8.32	513	18	30,500	0	>200
06 Nov	K	Hand, 2 persons	27.8	7.83	632	13	3,955	0	<1
06 Nov	L	Foot/hand, 1 person	33.0	7.36	1,083	0	18,500	6,900	>200
06 Nov	L	Body, 1 person	33.0	7.46	1,423	310	20,500	1,652	>200
06 Nov	L	Body, 2 persons	33.2	7.70	929	1	1,500	1,908	>200
13 Nov	M	Foot, 1 person	27.6	6.86	453	0	3,182	11	<1
13 Nov	M	Hand, 1 person	27.6	7.82	395	0	355	14	<1
13 Nov	N	Foot, 2 persons	28.6	6.98	416	0	16,500	850	1
13 Nov	N	Body, 1 person	28.6	8.23	333	0	2,800	34	14
13 Nov	O	Foot, 2 persons	27.6	7.74	218	0	44,000	11	2
14 Nov	P	Foot, 1 person	27.8	8.11	470	0	100	0	88
Minimum values			25.0	6.86	218	0	32	0	<1
Maximum values			33.2	8.59	1,423	310	109,000	6,900	>200
Median values			28.4	8.12	432	0	11,182	11	33

IE: intestinal enterococci; MPN: most probable number.

Results

Participants and samples

Fifteen companies positively responded to the request to participate in the study, a sixteenth company was included through intervention of the local public health service. The sixteen participating companies included wellness centres (n = 4), beauty salons (n = 1), and companies that solely offered fish spa treatment (n = 11). A total of 24 samples were collected: 15 samples from foot spas, five samples from body spas, three samples from hand spas, and one sample from a combined hand–foot spa. None of the fish spas had visible dirt on the spa walls, and therefore swab sampling of the spa walls was not done.

Physical-chemical water quality parameters

The water temperature in the spas ranged from 25.0 to 33.2 °C, with a median of 28.4 °C (Table 1). In body spas, the water temperature was generally higher than in foot and hand spas. In four of five body spas, the water temperature was above 31 °C. The pH value of the fish spa water ranged from 6.9 to 8.6, with a median value of 8.1. In all fish spas, water turbidity values of 0.00 Formazine Turbidity Units (FTU) were measured, indicating that the turbidity was very low and below the detection limit of the equipment used. The conductivity ranged from 218 to 1,423 µS/cm, with a median of 432 µS/cm. The highest conductivity values were exclusively found in the three spas of one company (Table 1).

Microbiological water quality

In most fish spas, faecal contamination based on the faecal indicator parameter intestinal enterococci was limited (Table 1). The *E. coli* analyses were seriously hampered by abundant growth of *Plesiomonas shigelloides*, which may have masked *E. coli* colonies. We therefore consider the *E. coli* data unreliable. *Aeromonas* spp. were present in all samples from all

Table 2

Water treatment and management in 16 fish spa companies, the Netherlands, 2012

Parameter/management	Number of companies	
	Yes	No
Water filter present	16	0
Water filter per fish spa	13	3
One water filter for several fish spas	3	13
UVC treatment of the water only	5	11
Ozone treatment of the water only	4	12
UVC and ozone treatment of the water	6	10
Neither UVC nor ozone treatment of the water	1	15
Monitoring of water temperature	15	1
Microbiological water testing	5	11
Keeping a log of water quality	11	5
Complete water replacement[a]	6	9
Partial water replacement[b]	9	6
No water replacement, only replenishment	1	15

UVC: ultraviolet light C.

[a] Once to twice a week.

[b] Daily to once to twice a week, for 10 to 80%.

fish spas, although in varying numbers, ranging from 32 to 1.10^5 colony forming units (CFU) per 100 mL (Table 1). The median value of 1.10^4 CFU per 100 mL indicates that most numbers were on the high end of the range.

P. aeruginosa was detected in 18 of the 24 examined fish spas, while in six of 24 spas the most probable number was below the Pseudalert lowest detection limit of 1 per 100 mL. In four of the 18 positive spas, the most probable number was above the Pseudalert highest detection limit of 200 per 100 mL (Table 1). MALDI–TOF confirmed the presence of *P. aeruginosa* in positive wells, in those samples (n = 4) where it was applied.

Vibrio spp. were present in 16 of 24 fish spas; in positive samples, the *Vibrio* numbers ranged from two to 6,900 CFU per 100 mL, but most concentrations were low (Table 1). Species identification with MALDI-TOF demonstrated the presence of *V. cholerae* in all positive fish spas. PCR of the *toxR* and *ctxA* genes according to Schets et al. [15] confirmed that the isolates were *V. cholerae* and demonstrated that they were non-toxigenic. *V. vulnificus* was found in one full body spa only. PCR of the *vvhA* gene according to Canigral et al. [16] confirmed the MALDI-TOF identification.

Incubated samples could only be read for the presence of rapid growing mycobacteria (RGM). Reading the plates for the presence of slow growing mycobacteria was not possible due to the growth of large amounts of disturbing background flora. RGM were present in 23 fish spas; the incubated sample from the 24th fish spa could not be read due to overgrowth by fungi. *Mycobacterium* species that were frequently found included *M. fortuitum* ($n_{\text{fish spa}} = 21$), *M. conceptionense*/*M. senegalense* ($n_{\text{fish spa}} = 16$), *M. abscessus* ($n_{\text{fish spa}} = 15$), and *M. chelonae* ($n_{\text{fish spa}} = 13$). Less abundant were other *M. chelonae* complex isolates ($n_{\text{fish spa}} = 7$), *M. abscessus* subsp. *bolletii* ($n_{\text{fish spa}} = 8$), and *M. phocaicum* ($n_{\text{fish spa}} = 6$). *M. alvei*, *M. peregrinum*, *M. porcinum*, *M. wolinski*, and three novel, yet unknown environmental mycobacteria, were only incidentally isolated.

Management

The investigated companies had fish spas from various suppliers, whereas some of them constructed their own spas. Most companies purchased the fish from the same supplier.

All companies filtered the fish spa water, using biological filters with zeolite; the majority had one filter per fish spa installed. Additionally, most companies treated the water with ultraviolet light C (UVC), ozone or both. Almost all companies checked the water temperature on a regular basis, and many of them used a test kit designed for aquarium and pond owners to test a basic set of chemical parameters, including pH value, hardness, ammonia, nitrite, nitrate, phosphate, iron, and copper. Keeping a log was not a standard procedure. Five of the 16 companies had the microbiological water quality checked by a laboratory. Refreshment policies varied from total replacement of the water once to twice a week, to partial replacement of the water with a daily to weekly frequency (Table 2).

Discussion

All bacteria the fish spa water was tested for, were detected, although not in all spas and in varying concentrations. Whether or not *Aeromonas spp*. *Vibrio spp*., *P. aeruginosa* or RGM were found, could not be related to a specific type of spa (foot, hand, or body), a specific water treatment process (filtration with UVC, ozone or both), or a specific regime of water refreshment (total or partly, with varying frequency). Physical-chemical parameters did also not relate to presence or absence of bacteria or high or low bacterial counts. It is plausible that the small number of fish spas contributed to the inability to determine a possible correlation with microbiological water quality. Also, the presence of bacteria may depend on occasional contamination of the water by clients and the subsequent expansion of the contamination for prolonged time periods. Most owners could, however, not provide clear figures on spa use in terms of number of users per day; so a

relation between intensity of fish spa use and microbiological water quality could not be established.

When comparing the *Vibrio* spp. concentration in fish spas (0 – 6,900 CFU/100 ml, median 11 CFU/100 ml) with the numbers detected in various surfaces water in the Netherlands during summer (0 – $4.2.10^5$ MPN/100 ml, median 37 MPN/100 ml [15], the numbers in fish spas were mostly lower, or sometimes in the same order of magnitude, even though the water temperature in fish spas was ca 5 to 10 °C higher than the surface water temperature during summer [15]. Current *Vibrio* spp. concentrations in surface water led to a limited number of reported cases of illness in the Netherlands, which were mostly cases of ear complaints as a result of *V. alginolyticus* infections [15]. This suggests that the *Vibrio* spp. numbers in fish spas do not pose a major health risk. However, the presence of *V. cholerae* non–O1/O139 and *V. vulnificus*, which are a well–known cause of wound infections in humans [15,17], may pose a risk for people with a damaged skin. Moreover, the high water temperatures in fish spas can allow *Vibrio* spp. to proliferate to numbers higher than those observed in the sampled fish spas, resulting in an increased risk.

In chlorinated pools, *P. aeruginosa* should be absent in 100 ml samples of the pool water [18]; a requirement that was not met in 75% of the fish spas. There are no requirements for *P. aeruginosa* in recreational surface waters. Comparing the *P. aeruginosa* concentrations in fish spas (range 1 – 178 MPN/100 ml, median 33 MPN/100 ml) with those previously found in Dutch surface waters, generally shows lower concentrations in the latter (0 – 9 CFU/100 ml) [19], also in recreational water related to outbreaks of otitis externa (0.4 CFU/100 ml) [20]. In the swimming pool environment, *P. aeruginosa* commonly causes folliculitis through infection of disrupted follicles, and although dose response relationships for dermal exposure are unclear, the suggested levels of concern for healthy individuals are $>10^5$ per 100 ml [21]. Concentrations in that range were not found in the examined fish spas, suggesting that the health risk related to *P. aeruginosa* in fish spas is limited for people with an intact skin. *P. aeruginosa* may however pose a greater risk for people with a damaged skin, and in spas where numbers largely exceed 10^5 per 100 ml.

Aeromonas spp. are ubiquitous in the aquatic environment, in a broad range of concentrations [22], and have also been detected in all examined fish spas. Concentrations in fish spas were in the order of magnitude as those typical for rivers receiving sewage discharge [22]. A health risk from the isolated *Aeromonas* spp. cannot be fully ruled out, but it may be limited for healthy individuals with an intact skin and no underlying disease or reduced immunity, since human skin and soft tissue infections with *Aeromonas* spp. are commonly associated with wounds after water related trauma, or occur in persons with underlying disease [23].

RGM, that have been detected in all examined fish spas, are known environmental opportunistic pathogens that are increasingly recognised as causative agents of human and fish disease, both in sporadic cases and outbreaks [24,25]. Their transmission to humans from an environmental source, with subsequent clinical disease, is however rarely proven, except for cases in hospital settings [24]. Most of the species isolated from fish spas have previously been found as the cause of illness in immune competent persons after exposure to various water sources, including whirlpool footbaths in a nail salon (*M. fortuitum*) [26], a fish tank after contact with broken glass (*M. senegalense*) [27], and therapy pool water (*M. phocaicum*) [28]. In the Netherlands, RGM have been isolated from tap and shower water without a direct link to illness [14]. *M. chelonae*, *M. abscessus*, and *M. fortuitum* are frequently found in clinical samples whereas the other species recovered from fish spas are less frequently observed [25]. The three yet unclassified environmental *Mycobacterium* species have not previously been isolated from human samples in the Netherlands and have not been found in the BLAST database.

The low level of faecal contamination confirmed the expected low input of intestinal enterococci with human faeces through hands and feet, as well as the limited contribution of the fish [29]. Dilution and regular cleaning policies probably enhance these low levels. A higher level of faecal contamination could be expected in full body spas, but was not observed. *Pl. shigelloides*, which appeared to be present in most fish spas and hampered the *E. coli* detection, is naturally present in warm surface water and causes human gastroenteritis [30]. *Pl. shigelloides* is known to disturb *E. coli* enumeration in samples from warm surface waters while using the Rapid Test in ISO 9308–1:2000 [30]. Although the presence of *Pl. shigelloides* in fish spas was not foreseen, it appeared that the bacterium is often part of the microbial flora in aquariums [31].

This study provided insight in the microbiological condition of fish spa water, albeit the number of data are too limited to suggest ranges for acceptable microbiological contamination. Fish spas do, however, require their own set of microbiological parameters and guide values. Swimming pool and recreational water guidelines are not particularly appropriate, since they focus on an environment with a residual effect of disinfectants, or apply to surface waters with different contamination sources.

The detected concentrations of *Aeromonas* spp., *Vibrio* spp., and *P. aeruginosa* in the water of the examined fish spas, in combination with the health implications of these bacteria at such levels, and the detected *Mycobacterium* spp. and their health implications, suggest a low health risk from fish spas. The data from this study support the opinion of Health Protection Agency (now Public Health England) and the French

Agency for Food, Environmental and Occupational Health and Safety (ANSES) that the health risk from using fish spas is limited for healthy people with an intact skin and no underlying disease. Persons with underlying disease affecting the immune system, such as diabetes, and skin conditions, such as psoriasis and eczema, and persons with a damaged skin, may be at a greater risk. Transmission of infection through ingestion of intestinal pathogens in contaminated water is of limited importance in hand and foot spas, but it may play a role in body spas. Moreover, head immersions in body spas, may lead to ear infections with *P. aeruginosa* or *Vibrio* spp. In all spa types, pathogens can be transmitted through hand–mouth contact. This transmission route is likely to be more relevant when the water is heavily contaminated [32].

In addition to establishing microbiological guidelines for fish spas, drafting a code of practice on hygiene in fish spas and risk communication to clients is recommended.

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Conflict of interest

None declared.

Authors' contributions

FMS and HHvdB designed the study, HHvdB and RdZ carried out microbiological analyses, FMS performed data analysis and drafted the manuscript, FMS, DvS and AMdRH interpreted data, and all authors reviewed and revised the first and final drafts of this manuscript.

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Phylogeographical pattern of *Francisella tularensis* in a nationwide outbreak of tularaemia in Norway, 2011

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In 2011, a nationwide outbreak of tularaemia occurred in Norway with 180 recorded cases. It was associated with the largest peak in lemming density seen in 40 years. *Francisella tularensis* was isolated from 18 patients. To study the geographical distribution of *F. tularensis* genotypes in Norway and correlate genotype with epidemiology and clinical presentation, we performed whole genome sequencing of patient isolates. All 18 genomes from the outbreak carried genetic signatures of *F. tularensis* subsp. *holarctica* and were assigned to genetic clades using canonical single nucleotide polymorphisms. Ten isolates were assigned to major genetic clade B.6 (subclade B.7), seven to clade B.12, and one to clade B.4. The B.6 subclade B.7 was most common in southern and central Norway, while clade B.12 was evenly distributed between the southern, central and northern parts of the country. There was no association between genotype and clinical presentation of tularaemia, time of year or specimen type. We found extensive sequence similarity with *F. tularensis* subsp. *holarctica* genomes from high-endemic tularaemia areas in Sweden. Finding nearly identical genomes across large geographical distances in Norway and Sweden imply a life cycle of the bacterium without replication between the outbreaks and raise new questions about long-range migration mechanisms.

Introduction

Tularaemia is a zoonotic infection caused by the bacterium *Francisella tularensis*, a pathogen with extreme infectivity and a potential biothreat [1]. Several subspecies have been recognised, of which *F. tularensis* subsp. *holarctica* (or type B) is present in Europe. Tularaemia is a rare disease in a global context, making the experience with outbreak investigations very limited. The Scandinavian countries, however, quite regularly experience outbreaks in humans involving tens to hundreds of patients. In Norway, several outbreaks have been attributed to *F. tularensis* contamination of water wells by dead rodents. The exposure to infection by drinking water results in an oropharyngeal clinical form of tularaemia in humans and this is the most common form reported in Norway [2-4]. For unknown reasons, the incidence rate of tularaemia in humans is lower in Norway than in the two other Nordic countries Finland and Sweden. While a mean annual number of 34 (range: 11–66) tularaemia cases were reported in Norway 2006 to 2010, Finland and Sweden reported during the same period a mean annual number of 298 and 305, respectively [5]. The mode of transmission to humans is also different because tularaemia in Finland and Sweden is generally transmitted by the bite of an arthropod taking a blood meal resulting in the ulceroglandular form of tularaemia [6,7]. The reasons for the epidemiological differences in incidence and clinical form of tularaemia between the three countries are unknown.

Distinct genetic subpopulations (major phylogenetic clades) have been identified among *F. tularensis* subsp. *holarctica* strains [8]. High-resolution molecular methods including whole genome sequencing distinguish four major genetic clades denoted B.12, B.6, B.4 and B.16 [9-11]. The clades occur with different frequency in different geographical areas [12-15]. Recent studies in Sweden have indicated phylogeographical patterns both in local outbreaks and across larger geographical distances. These studies from Sweden also identified areas where *F. tularensis* persisted over several years and spatial associations of certain genetic subpopulations [16]. Little is known about phylogeographical patterns of *F. tularensis* in Norway.

In 2011, a large outbreak of tularaemia occurred in Norway with a total of 180 cases coinciding with the highest density of lemmings recorded in the last forty years [17]. Although the high incidence lasted

Table

Genetic clade and subclade of human *Francisella tularensis* subsp. *holarctica* isolates in relation to type of specimen, clinical classification, time of infection and geographical distribution, Norway, 2011 (n = 18)

Strain ID	Type of specimen	Clinical classification	Time of year	Geographical region	Genetic clade/ subclade	NCBI accession number
NO-1/2011	Blood	Typhoidal	January	Central	B.7	JPPDoooooooo
NO-2/2011	Blood	Respiratory	February	Central	B.12	JPMMoooooooo
NO-3/2011	Blood	Respiratory	February	South	B.7	JPPEoooooooo
NO-4/2011	Blood	Typhoidal	March	Central	B.7	JPMJoooooooo
NO-5/2011	Aspirate	Ulceroglandular	May	South	B.12	JPPFoooooooo
NO-6/2011	Exudate from ulcer	Ulceroglandular	July	South	B.7	JPMKoooooooo
NO-7/2011	Exudate from ulcer	Ulceroglandular	August	North	B.12	JPMLoooooooo
NO-8/2011	Exudate from ulcer	Ulceroglandular	August	South	B.12	JPPGoooooooo
NO-9/2011	Exudate from ulcer	Ulceroglandular	August	South	B.7	JPPIoooooooo
NO-10/2011	Tissue biopsy	Ulceroglandular	August	South	B.7	JPPHoooooooo
NO-11/2011	Tissue biopsy	Respiratory	August	South	B.7	JPPJoooooooo
NO-12/2011	Exudate from ulcer	Ulceroglandular	August	South	B.12	JPMNoooooooo
NO-13/2011	Aspirate	Ulceroglandular	August	South	B.7	JPMOoooooooo
NO-14/2011	Blood	Typhoidal	September	North	B.7	JPPKoooooooo
NO-15/2011	Blood	Respiratory	November	North	B.4	JPMPoooooooo
NO-16/2011	Exudate from ulcer	Ulceroglandular	November	Central	B.7	JPMQoooooooo
NO-17/2011	Exudate from ulcer	Ulceroglandular	October	North	B.12	JPMRoooooooo
NO-18/2011	Blood	Glandular	November	North	B.12	JPMSoooooooo

NCBI: National Center for Biotechnology Information.

throughout the year, there were clear differences in epidemiology between seasons, both in the incidences in different geographical areas and in the clinical forms of tularaemia recorded. The outbreak started in January 2011 in central Norway (Sør-Trøndelag and neighbouring counties) with mainly cases of oropharyngeal tularaemia linked to the use of drinking water from private wells [18]. This part of the outbreak lasted until April. In the period from May to September, sporadic cases occurred scattered throughout the country with increasing frequency of the ulceroglandular form of tularaemia linked to insect bites [17]. From October to December, many cases of tularaemia were reported from the north of Norway, equally distributed between the oropharyngeal, glandular, typhoidal and respiratory forms of tularaemia. For comparison, the number of tularaemia cases reported in 2011 in Sweden was 349, slightly above the annual average of the period 2006 to 2010 [5,19].

The aim of this project was to use whole genome sequencing for genotyping of *F. tularensis* cultured from human specimens during the outbreak in 2011 to investigate the genotype distribution of tularaemia in Norway. We also wanted to analyse associations of genotype with epidemiological characteristics and disease presentation and identify patterns of spread of the bacterium.

Methods

Isolation of clinical strains

F. tularensis was cultured from 18 of the 180 patients diagnosed with tularaemia in Norway in 2011. All these isolates were included in the study. *F. tularensis* was cultured from four of 57 tularaemia cases during the period January to April, from 10 of 40 cases in the period May to September (seven of these in August), and from four of 83 cases in the period October to December. The isolates were from blood (n = 7), skin ulcer (n = 7), tissue biopsy (n = 2) and aspirate (n = 2) specimens from patients living in nine different counties (Table).

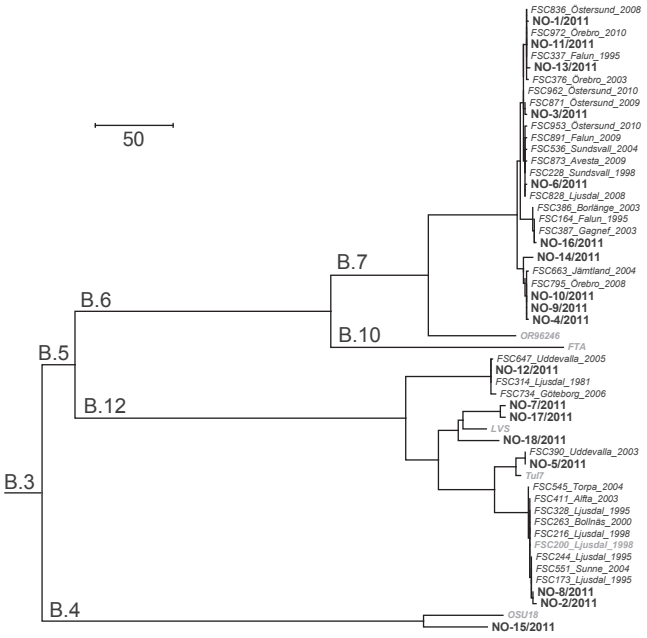
The study, which was based on informed written consent from each patient, was approved by the Regional Committee for Medical and Health Research Ethics, central Norway (project 2012/867).

Genome sequencing and assembly

Genome sequencing was performed using 100 bp paired-end libraries on an Illumina HiSeq 2000 machine (Illumina, San Diego, CA). The reads were assembled de novo using the ABySS [20]. The raw sequence reads were mapped back against the draft genome using Bowtie 2 [21] allowing identification of uncertain positions in the genome with VarScan 2 [22]. Positions reported having a second variant with frequency higher than 20% were subsequently masked. The overall genome coverage was ca 850-fold.

Figure 1

Neighbour-joining phylogenetic tree based on whole genome alignment of *Francisella tularensis* sequences (n = 53)



The tree is based on alignment of 1 ,613,828 shared nucleotide positions and rooted using FSC022, a B.16 strain (not shown), and drawn to scale with branch length representing the number of nucleotide changes.

Bold: Norwegian isolates; italics: Swedish strains within a distance of two nucleotide polymorphisms from any Norwegian strain; grey: reference strains.

In silico screening of *Francisella* strains

Genome sequences were initially in silico screened by the CanSNPer software [23] using published canonical SNP *Francisella tularensis* subsp. *holarctica* markers [9-13]. To select a suitable set of reference strains, the 18 draft genomes were aligned with Swedish *F. tularensis* subsp. *holarctica* genomes from the same genetic clades, as determined by CanSNPer (n=313). Using this alignment, reference strains that were within a distance of two single nucleotide polymorphisms (SNPs) from any Norwegian sequence were selected for further analysis.

Genome alignment and phylogenetic tree construction

A multiple genome alignment of 53 strains was generated by concatenation of a number of pairwise alignments where each strain was aligned against the reference strain FSC200 [24] using progressive MAUVE [25]. In addition to the 18 Norwegian and 29 selected Swedish strains, six common reference genomes were included (OR96246, FTNF002–00 [26], LVS, Tul7 [13], FSC200 [24], OSU18 [27], and the tree was rooted in FSC022 [28]. The phylogenetic tree was constructed in MEGA6 [29].

Results

All 18 isolates of *F. tularensis* cultured from patients in Norway in 2011 were identified as *F. tularensis* subsp. *holarctica* based on whole genome sequence genotyping. The distribution of the isolates in genetic clades and subclades is shown in the Table and Figure 1. Seven of the isolates were assigned to the major genetic clade B.12, one to clade B.4 and 10 isolates to a subclade denoted B.7 belonging in the major clade B.6.

Type of specimen

Among the seven isolates cultured from blood, four belonged to subclade B.7, while two belonged to B.12 and one to clade B.4 (Table). Four isolates from skin ulcers belonged to subclade B.7 and three to B.12. The two isolates from aspirates belonged to B.12 and B.7, respectively, while both isolates from tissue biopsies belonged to subclade B.7.

Clinical form of tularaemia

Ten of the *F. tularensis* isolates were from cases of ulceroglandular tularaemia (Table). Five of these isolates belonged to subclade B.7; the other five strains belonged to clade B.12. Two of the four isolates from patients with a respiratory form of tularaemia belonged to subclade B.7, while the other two belonged to B.12 and B.4. The three isolates recovered from patients with typhoidal tularaemia all belonged to subclade B.7. Finally, the isolate from a patient with glandular tularaemia was of clade B.12.

Mode of infection

Three of the six *F. tularensis* isolates cultured from ulcers caused by insect bite belonged to subclade B.7 while the three others belonged to subclade B.12. The three isolates recovered from patients with typhoidal tularaemia who reported to have drunk water from a private well, belonged to subclade B.7. Inhalation (clade B.12), outdoor work in a farm (subclade B.7), handling of a dead rabbit (subclade B.7), stab wound while handling fish (clade B.12), and hunting and other outdoors activities (clade B.12) were reported as likely mode of infection for five other isolates. For the four remaining isolates, information on the likely mode of infection was not available.

Seasonal distribution

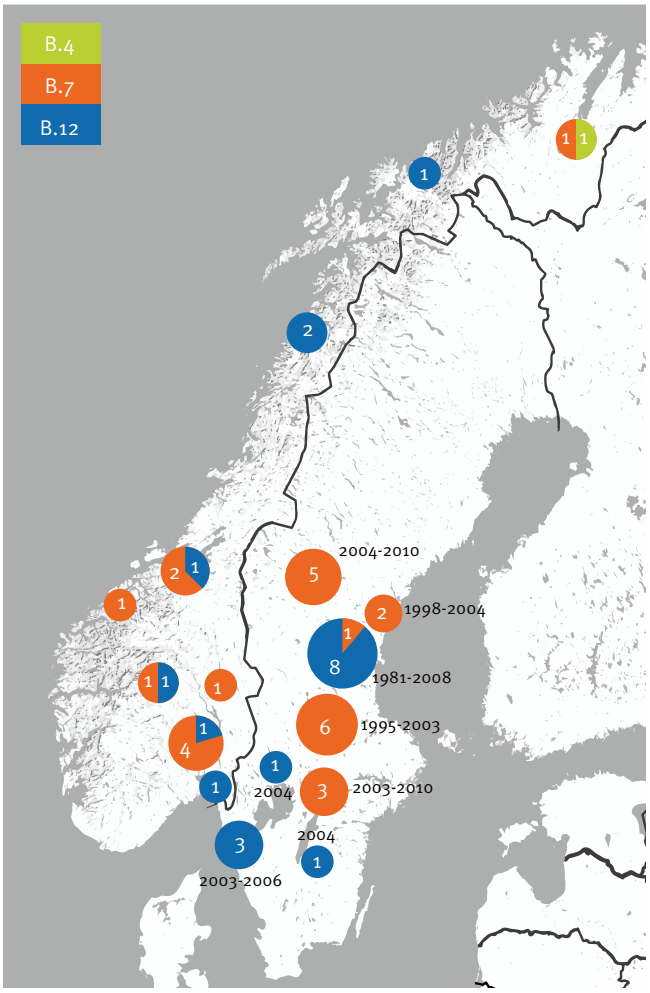
Three of the four *F. tularensis* isolates cultured in the period January to April belonged to subclade B.7 and one belonged to clade B.12 (Table). In the period May to September, 10 cases were culture-positive, eight of whom had the ulceroglandular form of tularaemia. Six of the isolates from this period belonged to subclade B7, and four to clade B.12. Among the four isolates recovered during the period October to December, two belonged to subclade B.12, one to clade B.4 and one to subclade B.7.

Geographical distribution

Among the nine isolates recovered from patients in southern Norway, six belonged to subclade B.7 and

Figure 2

Geographical distribution of near-identical (within a distance of two single nucleotide polymorphisms across the genome) *Francisella tularensis* strains in Norway (n = 18) and Sweden (n = 29)



Strains included on the map are the same as those listed in the different clades and subclades (B.7, B.12 and B.4) in the Neighbour-joining tree in Figure 1.

three to clade B.12 (Figure 2). In comparison, three of the four isolates from central Norway belonged to subclade B.7 and one belonged to clade B.12, while one of the five isolates from patients living in northern Norway belonged to subclade B.7, three belonged to B.12 and one to clade B.4. Two patients living in southern Norway provided information that they may have contracted the infection while walking in the mountains or working on a farm without specifying where. For a third patient, information on the place of infection was not available. One patient living in northern Norway reported infection after an insect bite while travelling in Sweden (strain NO-7/2011).

Comparison with Swedish strains

Among the 313 archived Swedish *F. tularensis* strains included in the analysis, the genomes of 29 strains differed at two or fewer SNPs compared with the outbreak genomes from Norway (Figure 1). All those 29 strains had been isolated during the period 1981 to 2010 in areas highly endemic for tularaemia in central Sweden (Figure 2). Since culture for *F. tularensis* was not routinely performed in Norwegian medical microbiology laboratories before 2011, archived genome sequences from Norwegian *F. tularensis* isolates from that period were not available for this study.

Discussion

In this study we have shown that 10 of 18 *F. tularensis* subsp. *holarctica* isolates from human tularaemia cases from the outbreak in Norway in 2011 belonged to the genetic subclade B.7, while seven isolates belonged to clade B.12 and one to clade B.4. Isolates from the clade B.12 showed higher genomic variability than those belonging to the subclade B.7. Comparison of the isolates from the outbreak in Norway with archived genome sequences from Sweden since 1981 revealed strong sequence identity between some Norwegian and Swedish isolates from high-endemic areas. Twenty-nine isolates from Sweden differed at two or fewer SNPs from one or several isolates from Norway (Figure 1). No information is available on the mutation rate for *F. tularensis* in general or during replication in hosts. Thus, the meaning of near-identical strains (a maximum of two SNPs across the genome) cannot be put into context of mutation rate. Because both countries are located on the Scandinavian Peninsula and share a long border, our results support a common ecology of *F. tularensis* on the Peninsula, although the incidence and mode of transmission of tularaemia differ between Norway and Sweden. Reasons for differences in the epidemiology of tularaemia between the two countries are not known, but one possible explanation of the higher proportion of oropharyngeal cases in Norway could be that private wells for drinking water might be more common in Norway [18]. Our data suggest that several of the genetic clades have moved long geographical distances and that near-identical genetic clones of the bacterium were found to be far apart both geographically and temporally. An alternative explanation may be that identical genotypes of *F. tularensis* have evolved by parallel evolution in many geographical regions of the Scandinavian Peninsula. Our results may be consistent with a life cycle of the bacterium that includes a state of quiescence (absence or very low level of replication) for long periods of time between outbreaks [30,31].

Both subclade B.7 and clade B.12 of *F. tularensis* subsp. *holarctica* were detected in tularaemia cases from all three regions of Norway. However, while subclade B.7 were mostly found in the southern and central regions of the country, the clade B.12 isolates were more evenly distributed between the regions (Figure 2).

Before the outbreak in 2011 and since the disease became a notifiable disease in Norway in 1977, only five cases of human tularaemia have been reported from the northernmost county Finnmark. Altogether 62 cases of tularaemia were reported from this county

during this outbreak which in Finnmark lasted until 2012. Considering the high sequence identity between the B.7 isolate from Finnmark (strain NO-14/2011) and other B.7 isolates both from southern Norway and central Sweden, the emergence of tularaemia in Finnmark was most probably caused by bacteria already present in the environment. Their activation and amplification may have required additional factors such as the large outbreak in lemmings that occurred in Finnmark in 2011. This raises questions about what mechanisms allowed these near-identical strains to spread across such large geographical distances. Birds have been implicated in the transportation of *F. tularensis* [32,33]. However, while occasional transportation by birds cannot be excluded, the general geographical pattern of near-identical strains found in this study is not characteristic of the north-south migration routes of migratory birds on the Scandinavian Peninsula. Many different mechanisms for dissemination could be envisaged, such as long-range aerosol transport by wind, carriage by arthropod vectors and/or infected migratory wild animals, or a combination of several mechanisms. Further research into this phenomenon is needed.

In this study we found no statistical association between the genotype of *F. tularensis* and type of specimen, clinical presentation, mode of transmission or time of the year when the specimen was collected, although the low number of bacterial strains may have obscured weak associations (Table). Our findings are in analogy with those reported in a recent genomic study of a respiratory tularaemia outbreak in Sweden [30]. In the latter study it was shown that the respiratory form of tularaemia was not tied to specific genotypes of *F. tularensis* and that outbreak genomes shared high sequence similarity with archived isolates originating from patients from distant geographical regions and collected up to 10 years apart [30]. Despite the mentioned lack of significant association in our study, it is worth noting that *F. tularensis* of clade B.12 was found mainly in patients with ulceroglandular tularaemia, and that all three isolates from patients with typhoidal tularaemia belonged to subclade B.7 (Table).

We were able to culture *F. tularensis* from only 10% of the tularaemia cases in 2011. Few reports are available on the sensitivity of culture in the diagnosis of tularaemia, but a low sensitivity has been reported in an outbreak of orpharyngeal tularaemia [34]. This, as well as the overrepresentation of the ulceroglandular form of the disease among culture-positive cases, make it difficult to assess the representativeness of the isolates for the whole outbreak. Another limitation is that for three of the isolates, we did not have data on where the patients had been infected.

In conclusion, 18 isolates of *F. tularensis* subsp. *holarctica* from a nationwide outbreak of tularaemia in Norway were genotyped by whole genome sequencing: among those, subclade B.7 was most frequent (10 isolates), followed by clade B.12 (seven isolates) and B.4 (one isolate). We found no association between genotype and clinical presentation of tularaemia, time of year of disease, or specimen type. Subclade B.7 was most common in southern and central Norway, while three of the five isolates from patients from northern Norway belonged to clade B.12. The isolates from this study showed near-identity with archived genomes from high-endemic areas in Sweden.

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Conflict of interest

None declared.

Authors' contributions

All of the authors collaborated in the presented work. JEA, MF, AS, AL, AJ defined the research theme. KWL, JEA and KB did the primary characterisation of the bacterial strains, applied for ethical approval of the study and collected patient data. JEA, MF, AS AL analysed data, interpreted results and wrote the draft manuscript. All authors have contributed to and approved the manuscript.

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Illness and injury of travellers abroad: Finnish nationwide data from 2010 to 2012, with incidences in various regions of the world

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The number of international tourist arrivals reached 1,000 million in 2012. Assessment of travellers' health problems has relied on proportionate morbidity data. Given the lack of data on number of visitors to each region, incidences have been impossible to calculate. This study, largest yet reporting travellers' health problems, is the first to present incidence of illness and injury. Data on Finnish travellers with health problems abroad during 2010 to 2012 were retrieved from the database of an assistance organisation, SOS International, covering 95% of those requiring aid abroad. The numbers were compared with those of Finnish travellers in the database of the Official Statistics of Finland. The SOS International database included 50,710 cases: infections constituted the most common health problem (60%), followed by injuries (14%), diseases of skin (5%), musculoskeletal system and connective tissue (5%), digestive tract (3%), and vascular system (2%). Gastroenteritis (23%) and respiratory infections (21%) proved the most frequent diagnoses. Overall incidence of illness or injury was high in Africa (97.9/100,000 travel days; 95% Bayesian credible interval (BCI): 53.1–145.5), southern Europe plus the eastern Mediterranean (92.3; 95% BCI: 75.4–110.1) and Asia (65.0; 95% BCI: 41.5–87.9). The data show significant differences between geographical regions, indicating the main risks and thus providing destination-specific tools for travellers' healthcare.

Introduction

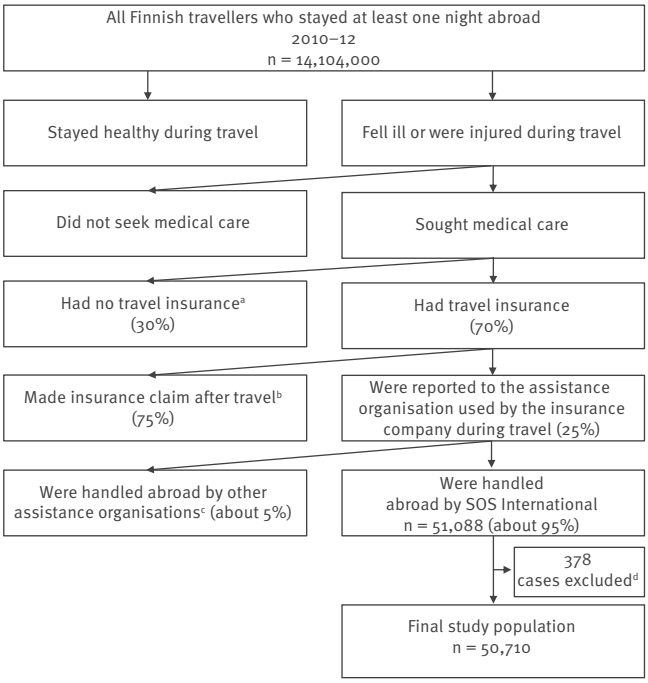
The annual number of international tourist arrivals globally exceeded 1,000 million in 2012 and is expected to reach 1,800 million by 2030 [1]. Of those travelling from developed to developing countries, over half have been reported to fall ill while abroad and 8% to require medical attention [2]. The growing volume of travel means an increased burden on healthcare both in host countries and at home.

Assessment of travellers' health problems has largely been based on calculations of proportionate morbidity of returning travellers as reported by specialised centres for travel and tropical medicine [3-6]. Data on illness or injury while abroad have been collected chiefly after travel from questionnaires, telephone surveys [2,7-14] and insurance claims [15,16], data recorded during actual travel are scarce. While a few studies have reviewed emergency-assistance services of individual insurance companies [17-19], comprehensive information on travellers' health problems abroad is non-existent. Furthermore, epidemiological data allowing calculation of the incidence of the whole spectrum of health problems in relation to number of travellers seem to be completely lacking [20].

The study presented here draws on the particular conditions found in Finland, a country with a population of 5.5 million [21]. Approximately 95% of those requiring help of an assistance organisation because of health problems while abroad are recorded in the database of SOS International (SOS), serving several insurance companies. In addition, Finland is among the few countries monitoring their annual number of travellers to various destinations. According to the Official Statistics of Finland (OSF) database [22], in 2012 Finns made 7.7 million visits abroad in which they stayed for at least overnight. Combining these two large datasets enabled determination not only of travellers' proportionate morbidity but, more importantly, also incidence of health problems.

Figure 1

Overview of course of Finnish travellers' health problems abroad and study population, 2010–12 (n = 50,710)



[a] Source: Federation of Finnish Financial Services. Vakuutustutkimus 2012. [Insurance survey 2012] [30].

[b] Source: Claims specialist Ilkka Valanne, Eurooppalainen, personal communication, 2 October 2013.

[c] Source: Medical director Ari Kinnunen, EMA Finland, and Medical Director Pauli Haapsaari, MedFlight Finland, personal communication, 3 September 2013.

[d] Excluded because of incomplete information.

Methods

Assistance organisation data

SOS, serving Nordic and Baltic insurance companies, provides travellers with 24-hour emergency assistance abroad: advice, medical evaluation, referral to treatment, cost coverage and arrangement of transportation if indicated for medical reasons. SOS covers approximately 95% of all Finnish cases (77% of inpatients, 99.8% of outpatients) handled abroad by assistance organisations (Figure 1); records for 2010 to 2012 were included in this analysis.

All SOS data are processed in a computerised database. Coordinating doctors are assigned to approximately 86% of inpatient and 1% of outpatient cases. They stay in contact with the patient and clinician abroad, examine medical reports, evaluate treatment and give orders for repatriation. Non-medical assistance coordinators see to the uncomplicated inpatient and outpatient cases, recording diagnoses provided by clinicians abroad.

Information available for our study comprised age, sex, time and country of illness or injury, inpatient or outpatient status, main diagnosis, repatriation and death. Research clearance was received from SOS.

Definitions

A case was defined as a Finnish traveller abroad with one episode of illness or injury, handled by SOS during 2010 to 2012. A person with several separate episodes was counted more than once. Classification as inpatient was based on information from the hospital abroad. Any case not recorded as an inpatient but who had at least one outpatient visit was classified as an outpatient case. Deceased travellers who had not been registered as inpatients were entered as outpatient cases, with their diagnoses being unavailable.

Repatriations were grouped by return: as planned, air ambulance, or other rearranged transport. The data collection procedure included as inpatients those outpatient cases whose flights had to be rescheduled.

To describe the study population and proportionate morbidity of all cases, countries were classified into the following geographical regions: southern Europe (the Balkan states, Cyprus, Greece, Italy, Malta, Portugal including Madeira, Spain including the Canary Islands); rest of Europe; the eastern Mediterranean (Israel, Turkey); North Africa; sub-Saharan Africa; western Asia; south-central Asia (from Pakistan to Bangladesh); south-east Asia; north-east Asia; Central and South America and the Caribbean; North America; Australia, New Zealand and Oceania. For incidence calculations, the geographical classification was modified to be compatible with the OSF classification [22].

Travel seasons were categorised by first date of symptom onset or injury, being divided into winter (October to March) and summer (April to September).

Diagnoses

Coordinating doctors encoded diagnoses applying the *International Statistical Classification of Diseases and Related Health Problems 10th revision* (ICD-10) [23]. Assistance coordinators recorded them as open text. For our study, a single coordinating doctor, one of the researchers (H.S.), encoded these diagnoses by applying ICD-10. The diagnostic categories were those of ICD-10, excluding infections, which we separated from the organ-specific classification into a category of their own.

Data on Finnish travellers

Obtained from the database of OSF, the pre-existing traveller data contained annual numbers and median duration of at-least-overnight leisure and business visits abroad, and travellers' age groups by region and country. Country-specific data were available for those receiving more than 50,000 visitors per year. OSF data had initially been collected by monthly sample-based computer-assisted telephone interviews with Finnish residents aged 15 to 74 years; the upper age limit was extended to 84 years in 2012. Drawn systematically

Table 1

Characteristics of outpatient and inpatient cases[a] among travellers abroad and risk factors for hospitalisation, 2010–12 (n = 50,710)

Characteristic	Total	Outpatient cases	Inpatient cases	P value	Risk factors for hospitalisation	
					Univariable OR (95% CI)[b]	Multivariable OR (95% CI)[b]
Number of cases, n	50,710	42,371	8,339	NA	NA	NA
Sex, n (%)						
Male	22,849 (45.1)	18,500 (43.7)	4,349 (52.2)	<0.001	1.41 (1.34–1.47)	1.33 (1.26–1.40)
Female	27,861 (54.9)	23,871 (56.3)	3,990 (47.8)	<0.001	1.00	1.00
Age in years						
Median age (IQR)	45 (21–61)	44 (20–61)	48 (27–64)	<0.001	NA	NA
Age groups, n (%)						
0–14	9,752 (19.2)	8,687 (20.5)	1,065 (12.8)	<0.001	0.59 (0.56–0.62)	0.61 (0.57–0.65)
15–29	6,872 (13.6)	5,528 (13.0)	1,344 (16.1)	<0.001	1.17 (1.10–1.23)	1.08 (1.02–1.15)
30–44	8,373 (16.5)	6,978 (16.5)	1,395 (16.7)	0.132	0.96 (0.91–1.01)	0.85 (0.81–0.91)
45–59	11,135 (22.0)	9,373 (22.1)	1,762 (21.1)	<0.001	0.90 (0.86–0.96)	0.86 (0.82–0.91)
60–74	12,576 (24.8)	10,301 (24.3)	2,275 (27.3)	<0.001	1.06 (1.01–1.11)	1.13 (1.07–1.19)
75–100	2,002 (3.9)	1,504 (3.5)	498 (6.0)	<0.001	1.60 (1.46–1.73)	1.83 (1.66–2.02)
Region, n (%)						
Europe and eastern Mediterranean	**36,699 (72.4)**	**31,208 (73.7)**	**5,491 (65.8)**	**NA**	**NA**	**NA**
Southern Europe[c]	27,202 (53.6)	24,278 (57.3)	2,924 (35.1)	<0.001	0.17 (0.15–0.19)	0.16 (0.14–0.19)
Eastern Mediterranean[d]	7,539 (14.9)	5,684 (13.4)	1,855 (22.2)	<0.001	0.46 (0.40–0.52)	0.55 (0.48–0.64)
Rest of Europe[e]	1,958 (3.9)	1,246 (2.9)	712 (8.5)	0.004	0.80 (0.68–0.93)	0.73 (0.62–0.85)
Africa	**3,262 (6.4)**	**2,739 (6.5)**	**523 (6.3)**	**NA**	**NA**	**NA**
North Africa	3,121 (6.2)	2,721 (6.4)	400 (4.8)	<0.001	0.21 (0.18–0.24)	0.28 (0.24–0.33)
Sub-Saharan Africa[f]	141 (0.3)	18 (0.04)	123 (1.5)	<0.001	9.54 (5.96–15.25)	10.61 (6.54–17.22)
Asia	**10,119 (20.0)**	**8,019 (18.9)**	**2,100 (25.2)**	**NA**	**NA**	**NA**
South-east Asia	9,514 (18.8)	7,746 (18.3)	1,768 (21.2)	<0.001	0.32 (0.28–0.37)	0.37 (0.32–0.43)
South-central Asia[g]	361 (0.7)	167 (0.4)	194 (2.3)	<0.001	1.60 (1.29–2.04)	1.77 (1.40–2.25)
North-east Asia	194 (0.4)	90 (0.2)	104 (1.2)	0.001	1.60 (1.21–2.15)	1.49 (1.10–2.03)
Western Asia	50 (0.1)	16 (0.04)	34 (0.4)	<0.001	2.97 (1.70–5.18)	2.96 (1.63–5.37)
The Americas	**609 (1.2)**	**402 (0.9)**	**207 (2.5)**	**NA**	**NA**	**NA**
Central and South America and the Caribbean	366 (0.7)	214 (0.5)	152 (1.8)	0.940	0.99 (0.79–1.25)	1.13 (0.89–1.43)
North America	243 (0.5)	188 (0.4)	55 (0.7)	<0.001	0.41 (0.30–0.55)	0.31 (0.22–0.42)
Australia, New Zealand and Oceania	**21 (0.04)**	**3 (0.007)**	**18 (0.2)**	**<0.001**	**8.37 (2.72–25.74)**	**5.17 (1.64–16.27)**
Season, n (%)						
Winter[h]	30,032 (59.2)	25,054 (59.1)	4,978 (59.7)	NA	1.00	NA
Summer[i]	20,678 (40.8)	17,317 (40.9)	3,361 (40.3)	0.337	0.98 (0.93–1.03)	NA
Diagnostic category, n (%)						
Infections	30,386 (59.9)	26,324 (62.1)	4,062 (48.7)	NA	1.00	1.00
Injuries	7,095 (14.0)	5,592 (13.2)	1,503 (18.0)	<0.001	1.74 (1.63–1.86)	1.66 (1.55–1.78)
Skin diseases	2,639 (5.2)	2,615 (6.2)	24 (0.3)	<0.001	0.59 (0.04–0.09)	0.058 (0.04–0.09)
Musculoskeletal and connective tissue diseases	2,621 (5.2)	2,475 (5.8)	146 (1.8)	<0.001	0.38 (0.32–0.45)	0.38 (0.32–0.46)
Diseases of the digestive tract	1,292 (2.5)	836 (2.0)	456 (5.5)	<0.001	3.54 (3.14–3.98)	3.24 (2.86–3.67)
Vascular diseases	1,081 (2.1)	369 (0.9)	712 (8.5)	<0.001	12.50 (10.98–14.24)	12.40 (10.8–14.2)
Other	5,596 (11.0)	4,160 (9.8)	1,436 (17.2)	<0.001	2.40 (2.09–2.40)	2.30 (2.15–2.48)

CI: confidence interval; IQR: interquartile range; NA: not applicable; OR: odds ratio.
The values in bold indicate data for main geographical regions.

[a] A case was defined as a Finnish traveller abroad with one episode of illness or injury, handled by SOS International during 2010 to 2012. A person with several separate episodes was counted more than once.
[b] Deviation from average effect used as reference in variables region and age group.
[c] Balkan states, Cyprus, Greece, Italy, Malta, Portugal including Madeira, Spain including Canary Islands.
[d] Israel, Turkey.
[e] European countries not included in southern Europe.
[f] including South Africa.
[g] from Pakistan to Bangladesh.
[h] From October to March.
[i] From April to September.

Table 2

Characteristics of cases[a] among travellers abroad by diagnostic category, 2010–12 (n = 50,710)

Characteristic	Total	Infections	Injuries	Skin diseases	Musculoskeletal and connective tissue diseases	Diseases of the digestive tract[b]	Vascular diseases[c]	Other[d]	P value[e]
Total number, n (%)	50,710 (100)	30,386 (59.9)	7,095 (14.0)	2,639 (5.2)	2,621 (5.2)	1,292 (2.5)	1,081 (2.1)	5,596 (11.0)	<0.001
Inpatient cases, n (%)	8,339 (16.4)	4,062 (13.4)	1,503 (21.2)	24 (0.9)	146 (5.6)	456 (35.3)	712 (65.9)	1,436 (25.7)	<0.001
Case characteristics									
Male, n (%)	22,849 (45.1)	13,451 (44.3)	3,218 (45.4)	939 (35.6)	1,254 (47.8)	642 (49.7)	621 (57.4)	2,724 (48.7)	<0.001
Median age in years (IQR)	45 (21–61)	40 (15–59)	48 (27–62)	46 (23–59)	60 (47–67)	50 (30–63)	64 (56–70)	49 (26–64)	<0.001
Winter season[f], n (%)	30,032 (59.2)	18,380 (60.5)	3,694 (52.1)	1,485 (56.3)	1,638 (62.5)	768 (59.4)	730 (67.5)	3,337 (59.6)	<0.001
Region, n (%)[g]									
Southern Europe	27,202 (100)	15,406 (56.6)	4,005 (14.7)	1,263 (4.6)	1,806 (6.6)	601 (2.2)	647 (2.4)	3,474 (12.8)	<0.001
Eastern Mediterranean	7,539 (100)	4,858 (64.4)	1,008 (13.4)	377 (5.0)	309 (4.1)	204 (2.7)	137 (1.8)	646 (8.6)	<0.001
Rest of Europe	1,958 (100)	840 (42.9)	557 (28.4)	47 (2.4)	61 (3.1)	87 (4.4)	96 (4.9)	270 (13.8)	<0.001
North Africa	3,121 (100)	2,516 (80.6)	189 (6.0)	202 (6.5)	44 (1.4)	56 (1·8)	13 (0.4)	101 (3.2)	<0.001
Sub-Saharan Africa	141 (100)	70 (49.6)	28 (19.9)	1 (0.7)	3 (2.1)	5 (3.5)	4 (2.8)	30 (21.3)	<0.001
South-central Asia	361 (100)	257 (71.2)	45 (12.5)	5 (1.4)	5 (1.4)	12 (3.3)	12 (3.3)	25 (6.9)	<0.001
South-east Asia	9,514 (100)	6,081 (63.9)	1,113 (11.7)	711 (7.5)	354 (3.7)	269 (2.8)	141 (1.5)	845 (8.9)	<0.001
North America	243 (100)	60 (24.7)	46 (18.9)	7 (2.9)	18 (7.4)	27 (11.1)	8 (3.3)	77 (31.7)	<0.001
Central and South America and the Caribbean	366 (100)	220 (60.1)	53 (14.5)	18 (4.9)	9 (2.5)	10 (2.7)	9 (2.5)	47 (12.8)	0.351
Other[h]	265 (100)	78 (29.4)	51 (19.2)	8 (3.0)	12 (4.5)	21 (7.9)	14 (5.3)	81 (30.6)	<0.001

[a] A case was defined as a Finnish traveller abroad with one episode of illness or injury, handled by SOS International during 2010 to 2012. A person with several separate episodes was counted more than once.

[b] Other than acute gastroenteritis.

[c] Cardiovascular, cerebrovascular, other vascular diseases.

[d] Neoplasms; haematological diseases; endocrine, nutritional and metabolic diseases; mental and behavioural disorders; neurological diseases; eye diseases; ear diseases; respiratory diseases; genitourinary diseases; pregnancy, childbirth and perinatology; unclassified symptoms.

[e] Tested using chi-squared test, except for age, for which the Kruskal–Wallis test was used.

[f] From October to March.

[g] Proportion of diagnostic category according to region (percentages in rows).

[h] Western Asia, north-east Asia, Australia, New Zealand, Oceania.

from the central population register, the sample totalled 26,400 individuals annually in 2010 and 2011, and 28,200 in 2012 [22].

Calculation of incidence

Proportionate morbidity figures were retrieved for all cases in the SOS database, whereas incidence calculation was restricted to adults for compatibility with the OSF population: only cases aged 15– 74 years in 2010–11 and 15–84 years in 2012 were included, and the geographical classification of OSF was applied (Nordic countries, Baltic states and Russia, eastern and western Europe; southern Europe and the eastern Mediterranean; Africa; Asia and Oceania; the Americas) [22].

Incidence figures were calculated as follows:

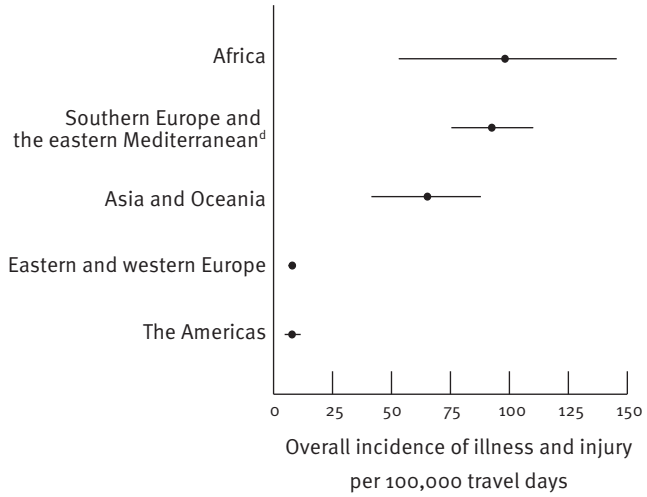
Total number of travel days = median duration of trip × estimated % of travellers with insurance × number of travellers

Incidence per 100,000 travel days = (number of cases/ total number of travel days) x 100,000.

Finns have access to state-provided healthcare in countries following European Union (EU) legislation; reimbursement for costs elsewhere can also be obtained by application to the Social Insurance Institution of Finland (Kela) [24]. As compared with the number of cases handled by SOS, the proportion Kela covers is 50% higher in countries following EU legislation than elsewhere. In the Nordic and Baltic countries, the proportion exceeds 50% (Timo Partio, Senior Statistical Analyst, Kela, personal communication, 7 October 2013) and, furthermore, Finns' visits to these countries and to Russia are

Figure 2

Overall incidence[a] of illness and injury among adult[b] Finnish travellers in various regions[c], 2010–12 (9,953,000 travellers)



The bars represent 95% Bayesian credible intervals.

[a] Incidence per 100,000 travel days = (number of cases divided by number of travel days) x 100,000.

[b] Travellers aged 15–74 years in 2010–11 and travellers aged 15–84 years in 2012 [22].

[c] Figures for Nordic and Baltic countries and Russia are not presented here; incidences for these countries are not comparable with those of other regions because proportionally more cases are covered by the Social Insurance Institution of Finland (Kela) [24] and trips are shorter than to other regions [22].

[d] Balkan states, Cyprus, Greece, Italy, Israel, Malta, Portugal including Madeira, Spain including the Canary Islands, Turkey.

Data source: Table 3.

shorter than elsewhere [22]. As such differences might hamper comparison with other regions, we chose not to present incidences for the Nordic or Baltic countries or Russia.

Statistical methods

Descriptive statistics were analysed with Microsoft Excel 2010 and IBM SPSS 19.0. Differences between groups were tested with chi-squared and Student's t-tests and the Kruskal–Wallis test, as appropriate. Risk factors of hospitalisation were analysed with logistic regression. Variables with $p < 0.2$ in univariable analysis were included in a multivariable model. For variables lacking a reference category, deviation from the average effect was used.

We estimated 95% Bayesian credible intervals (BCIs) for travel days of travellers with insurance, and thus 95% BCIs for incidences, using Bayesian modelling with Markov chain Monte Carlo (MCMC) Gibbs sampling with informative priors. The following assumptions were made: the proportion of travellers with insurance was lower (55–70%) for eastern and western Europe and higher (75–85%) for more distant destinations; trip durations were distributed similarly in all three years of the study (2010–12). In estimating the numbers of travellers to each destination, sampling variation in the numbers of those answering was taken into account.

Results

Study population in the SOS International database and case characteristics

The analysis included 50,710 cases; 83.6% were treated as outpatients, 16.4% as inpatients. The median age was 45 years (interquartile range (IQR): 21–61); 54.9% were women (Table 1). Most cases (n = 36,699; 72.4%) were reported to SOS in Europe plus the eastern Mediterranean. Spain had the highest number, 18,583 (36.6%), of whom 13,435 (72.3%) were in the Canary Islands.

Between regions, characteristics of cases differed significantly. Median ages ranged from 31 years (IQR: 22–45) for cases in north-east and western Asia, Australia, New Zealand and Oceania to 52 years (IQR: 23–65) in southern Europe ($p < 0.001$). The proportion of men ranged from 38.1% of cases in Australia, New Zealand, and Oceania to 54.5% of those in south-east Asia ($p < 0.001$). Most cases were reported during winter in all regions except in Europe plus the eastern Mediterranean ($p < 0.001$) (data not shown).

Diagnoses and repatriations

Infections (59.9%) and injuries (14.0%) constituted the largest diagnostic categories for outpatients and inpatients alike (Table 1, Table 2). The risk of hospitalisation proved greatest among cases with vascular diseases. Multivariable analyses showed other risk factors of hospitalisation to be male sex, aged 15–29 or ≥ 60 years, and travel to sub-Saharan Africa, Australia, New Zealand and Oceania, or to Asia (other than south-east Asia) (Table 1). Significant interactions were found between all these variables.

Acute gastroenteritis (11,543 cases) proved both the most common diagnosis (22.8% of all) and infection (38.0%). Respiratory tract infections (n = 10,475) were nearly as common (20.7% of all, 34.5% of infections). Injuries comprised 5,567 (78.5%) traumas and 1,528 (21.5%) others. Of the traumas, 4,270 (76.7%) were superficial, 952 (17.1%) fractures and 287 (5.2%) intracranial injuries.

Return travel itineraries remained unchanged for 48,842 cases (96.3%), an air ambulance was used for 113 (0.2%), and 1,556 (3.1%) had some other changed transport arrangement. Deaths totalled 199 (0.4%).

Incidence of illness or injury

Overall incidence of illness and injury was greatest in Africa and southern Europe plus the eastern Mediterranean, as well as Asia plus Oceania; incidences were lowest in the Americas and eastern plus western Europe (Table 3, Figure 2). Looking at individual countries' data available for comparison, incidence

Table 3a

Incidence of illness and injury among adult Finnish travellers[a], by geographical region[b] and selected countries[c], 2010–12 (9,953,000 travellers)*

Adult Finnish travellers 2010–12[a]				Number of travel days of travellers with travel insurance (95% BCI)[d,e]	Number of cases abroad handled by SOS International[f,g] 2010–12			Incidence of illness and injury among adult travellers per 100,000 travel days[h]		
Regions[b] and countries with more than 50,000 Finnish travellers/year[c]	Median age group in years	Number of travellers	Median duration of trip in days		Median age (IQR)	Outpatient cases	Inpatient cases	Outpatients (95% BCI)	Inpatients (95% BCI)	Total incidence (95% BCI)
Eastern and western Europe[i]	45–54	4,244,000	5.8	15,322,303 (12,630,000–18,670,000)	39 (25–55)	719	456	4.7 (3.8–5.8)	3.0 (2.4–3.7)	7.7 (6.3–9.4)
Germany	45–54	1,193,000	4.6	3,488,135 (2,967,000–4,117,000)	44 (30–56)	26	77	0.8 (0.5–1.1)	2.2 (1.7–2.9)	3.0 (2.3–3.8)
United Kingdom	35–44	798,000	7.4	3,717,048 (2,409,000–5,618,000)	38 (27–52)	9	21	0.3 (0.1–0.5)	0.6 (0.3–1.0)	0.9 (0.5–1.4)
France	35–44	596,000	5.3	1,998,866 (1,548,000–2,590,000)	41 (27–58)	15	91	0.8 (0.4–1.3)	4.6 (3.2–6.3)	5.4 (3.8–7.3)
The Netherlands	45–54	278,000	4.7	862,565 (577,100–1,271,975)	35 (19–53)	3	13	0.4 (0.1–0.9)	1.6 (0.7–2.8)	2.0 (1.0–3.4)
Poland	45–54	246,000	6.5	986,757 (453,100–1,929,000)	49 (41–55)	6	9	0.7 (0.2–1.7)	1.1 (0.3–2.4)	1.8 (0.6–3.8)
Austria	45–54	237,000	6.1	898,087 (703,300–1,147,000)	39 (29–53)	29	94	3.3 (2.0–4.9)	10.6 (7.6–14.3)	13.9 (10.1–18.5)
Switzerland	45–54	189,000	3.6	411,127 (326,900–517,900)	38 (30–46)	10	47	2.5 (1.1–4.4)	11.6 (7.8–16.4)	14.1(9.7–19.5)
Hungary	55–64	184,000	9.4	1,073,219 (717,700–1,578,000)	49 (29–63)	7	17	0.7 (0.3–1.4)	1.7 (0.8–2.9)	2.4 (1.3–3.9)
Belgium	35–44	159,000	1.8	177,066 (115,600–264,700)	39 (27–54)	4	16	2.4 (0.6–5.7)	9.5 (4.6–16.9)	11.9 (6.1–20.5)
Southern Europe and the eastern Mediterranean[j]	45–54	3,970,000	9.5	29,069,515 (24,130,000–35,220,000)	54 (39–64)	22,816	3,780	79.2 (64.7–94.5)	13.1 (10.7–15.5)	92.3 (75.4–110.1)
Spain including Canary Islands	45–54	1,703,000	11.5	15,229,947 (11,280,000–20,600,000)	60 (45–66)	12,801	1,815	86.0 (62.1–113.6)	12.3 (9.0–16.4)	98.3 (68.8–130.5)
Spain excluding Canary Islands	45–54	867,000	9.3	6,206,151 (4,753,000–8,096,000)	59 (38–67)	3,365	768	55.2 (41.5–70.9)	12.6 (9.3–16.6)	67.9 (50.9–91.3)
Canary Islands	55–64	836,000	14.0	9,662,893 (6,249,025–15,730,000)	60 (47–66)	9,436	1,047	102.8 (60.0–151.0)	12.6 (8.0–18.8)	115.4 (91.6–208.1)
Greece	45–54	688,000	9.7	5,120,660 (3,870,000–6,843,000)	50 (36–60)	5,206	267	103.8 (76.1–134.6)	5.3 (3.8–7.1)	109.1 (80.3–141.6)
Italy	35–44	546,000	5.9	2,524,458 (2,070,000–3,081,000)	42 (27–54)	93	53	3.7 (2.8–4.9)	2.1 (1.5–2.9)	5.9 (4.5–7.5)
Turkey	45–54	418,000	8.2	2,635,836 (2,076,000–3,351,000)	47 (33–69)	4,151	1,360	159.8 (123.7–200.2)	52.3 (40.2–66.0)	212.1 (162.4–264.6)
Portugal	45–54	238,000	10.3	1,884,158 (1,259,000–2,766,000)	57 (39–65)	34	44	1.9 (1.1–3.0)	2.4 (1.4–3.8)	4.3 (2.7–6.5)

BCI: Bayesian credible interval; IQR: interquartile range.

[a] Data from the Official Statistics of Finland (OSF): overnight leisure and business trips abroad; includes travellers aged 15–74 years in 2010–11 and travellers aged 15–84 years in 2012 [22].

[b] The geographical classification used by OSF was applied for the calculation of incidence.

[c] Country-specific data from OSF were only available for countries receiving more than 50,000 Finnish visitors per year.

[d] Estimated proportion of travellers with travel insurance was 70%; source: [30]. An assumption was made that the proportion of travellers with insurance was lower (55–70%) for eastern and western Europe and higher (75–85%) for more distant destinations.

[e] Number of travel days calculated as follows: median duration of leisure and business trips multiplied by number of travellers with travel insurance.

[f] Includes cases aged 15–74 years in 2010–11 and those aged 15–84 years in 2012. A case was defined as a Finnish traveller abroad with one episode of illness or injury, handled by SOS International during 2010 to 2012. A person with several separate episodes was counted more than once.

[g] Data of SOS International cover about 95% of Finnish cases handled by assistance organisations of insurance companies.

[h] Incidence per 100,000 travel days = (number of cases divided by number of travel days) x 100,000.

[i] Figures for Nordic and Baltic countries and Russia are not presented here; incidences for these countries are not comparable with those of other regions because proportionally more cases are covered by the Social Insurance Institution of Finland (Kela) [24] and trips are shorter than to other regions [22].

[j] Balkan states, Cyprus, Greece, Israel, Italy, Malta, Portugal including Madeira, Spain including Canary Islands, Turkey.

Table 3b

Incidence of illness and injury among adult Finnish travellers[a], by geographical region[b] and selected countries[c], 2010–12 (9,953,000 travellers)

Adult Finnish travellers 2010–12[a]				Number of travel days of travellers with travel insurance (95% BCI)[d,e]	Number of cases abroad handled by SOS International[f,g] 2010–12			Incidence of illness and injury among adult travellers per 100,000 travel days[h]		
Regions[b] and countries with more than 50,000 Finnish travellers/year[c]	Median age group in years	Number of travellers	Median duration of trip in days		Median age (IQR)	Outpatient cases	Inpatient cases	Outpatients (95% BCI)	Inpatients (95% BCI)	Total incidence (95% BCI)
Asia and Oceania	45–54	955,000	18.6	13,270,311 (8,932,000–20,680,000)	47 (39–64)	6,429	1,887	50.6 (31.0–72.1)	14.4 (9.3–20.7)	65.0 (41.5–87.9)
Thailand	45–54	365,000	14.9	4,049,129 (2,534,000–6,278,000)	48 (34–59)	6,047	1,351	157.6 (96.2–238.6)	34.0 (20.7–52.3)	191.6 (109.4–286.0)
China	45–54	180,000	13.8	1,915,398 (1,452,000–2,525,000)	35 (28–48)	58	77	3.1 (2.1–4.4)	4.1 (2.8–5.7)	7.2 (5.1–9.7)
The Americas	35–44	511,000	18.5	7,218,042 (4,574,000–10,950,000)	39 (29–55)	333	191	4.9 (3.0–7.4)	2.8 (1.6–4.3)	7.6 (4.7–11.5)
United States	35–54	319,000	17.1	4,194,332 (2,302,000–7,272,000)	38 (28–51)	137	44	3.6 (1.8–6.1)	1.1 (0.6–2.0)	4.7 (2.4–8.3)
Africa	35–54	273,000	13.6	2,743,830 (1,661,000–4,266,000)	41 (31–53)	2,087	460	80.8 (49.0–125.9)	17.2 (10.2–27.2)	97.9 (53.1–145.5)
Egypt	35–44	132,000	9.7	1,016,085 (605,300–1,547,000)	41 (31–53)	2,068	316	215.2 (133.1–342.3)	33.9 (20.1–53.1)	249.1 (158.2–393.7)

BCI: Bayesian credible interval; IQR: interquartile range.

[a] Data from the Official Statistics of Finland (OSF): overnight leisure and business trips abroad; includes travellers aged 15–74 years in 2010–11 and travellers aged 15–84 years in 2012 [22].

[b] The geographical classification used by OSF was applied for the calculation of incidence.

[c] Country-specific data from OSF were only available for countries receiving more than 50,000 Finnish visitors per year.

[d] Estimated proportion of travellers with travel insurance was 70%; source: [30]. An assumption was made that the proportion of travellers with insurance was lower (55–70%) for eastern and western Europe and higher (75–85%) for more distant destinations.

[e] Number of travel days calculated as follows: median duration of leisure and business trips multiplied by number of travellers with travel insurance.

[f] Includes cases aged 15–74 years in 2010–11 and those aged 15–84 years in 2012. A case was defined as a Finnish traveller abroad with one episode of illness or injury, handled by SOS International during 2010 to 2012. A person with several separate episodes was counted more than once.

[g] Data of SOS International cover about 95% of Finnish cases handled by assistance organisations of insurance companies.

[h] Incidence per 100,000 travel days = (number of cases divided by number of travel days) x 100,000.

Table 4

Incidence of injuries and infections among adult Finnish travellers[a] in various geographical regions[b] and selected countries[c], 2010–12 (9,953,000 travellers)

Regions and countries visited[b,c]	Number of cases[d,e] and incidence (per 100,000 travel days)[f] of injuries and infections among adult travellers							
	Largest diagnostic main categories				Largest infection subcategories			
	Injuries total		Infections total		Acute gastroenteritis		Acute respiratory infections	
Regions and countries with more than 50,000 Finnish travellers/year	Number	Incidence (95% BCI)	Number	Incidence (95% BCI)	Number	Incidence (95% BCI)	Number	Incidence (95% BCI)
Eastern and western Europe[g]	401	2.6 (2.1–3.2)	461	3.0 (2.4–3.7)	191	1.3 (1.0–1.6)	140	0.9 (0.7–1.2)
Germany	26	0.8 (0.5–1.1)	20	0.6 (0.3–0.9)	7	0.2 (0.1–0.4)	6	0.2 (0.1–0.3)
United Kingdom	13	0.4 (0.2–0.7)	7	0.2 (0.1–0.4)	0	0.0 (0–0)	5	0.1 (0–0.3)
France	50	2.6 (1.7–3.6)	16	0.8 (0.4–1.3)	9	0.5 (0.2–0.8)	2	0.1 (0–0.3)
The Netherlands	10	1.2 (0.5–2.3)	1	0.1 (0–0.5)	1	0.1 (0–0.5)	0	0.0 (0–0)
Poland	4	0.5 (0.1–1.3)	4	0.5 (0.1–1.2)	0	0.0 (0–0)	2	0.2 (0–0.8)
Austria	103	11.7 (8.3–15.7)	8	0.9 (0.4–1.7)	5	0.6 (0.2–1.2)	2	0.2 (0–0.7)
Switzerland	39	9.6 (6.3–13.9)	8	2.0 (0.8–3.7)	1	0.3 (0–1.0)	3	0.8 (0.2–1.8)
Hungary	6	0.6 (0.2–1.3)	6	0.6 (0.2–1.3)	2	0.2 (0–0.6)	2	0.2 (0–0.6)
Belgium	7	4.2 (1.5–8.6)	3	1.8 (0.4–4.7)	1	0.6 (0–2.4)	1	0.6 (0–2.4)
Southern Europe and the eastern Mediterranean[h]	4,034	14.0 (11.4–16.7)	14,607	50.6 (40.7–60.4)	4,655	16.2 (13.4–19.2)	6,199	21.4 (17.4–25.4)
Spain including Canary Islands	1,863	12.7 (9.2–17.0)	8,128	55.0 (39.7–74.7)	2,201	15.1 (10.9–20.1)	4,140	27.6 (20.1–35.5)
Spain excluding Canary Islands	631	10.3 (7.6–13.5)	1,945	31.7 (23.2–42.0)	439	7.2 (5.3–9.6)	976	16.1 (11.8–21.3)
Canary Islands	1,232	14.6 (8.9–22.9)	6,183	72.3 (47.8–107.6)	1,762	21.4 (13.2–32.8)	3,164	36.7 (23.1–56.6)
Greece	1,137	22.5 (16.2–29.8)	2,682	52.8 (37.7–70.6)	598	11.9 (8.6–15.7)	1,107	21.9 (15.9–29.0)
Italy	53	2.1 (1.5–2.9)	53	2.1 (1.5–2.9)	7	0.3 (0.1–0.5)	26	1.0 (0.6–1.6)
Turkey	775	29.7 (22.7–37.7)	3,353	127.4 (97.9–161.4)	1,766	67.9 (52.5–85.3)	786	30.2 (22.9–38.3)
Portugal	26	1.4 (0.8–2.4)	16	0.9 (0.4–1.6)	6	0.3 (0.1–0.7)	7	0.4 (0.1–0.8)
Asia and Oceania	1,089	8.2 (5.4–11.8)	5,042	37.4 (23.8–53.5)	2,663	20.6 (14.2–29.5)	1,170	8.9 (5.9–13.0)
Thailand	946	23.7 (14.6–36.4)	4,538	112.0 (66.0–165.3)	2,341	59.0 (37.5–90.8)	1,088	27.8 (17.5–41.4)
China	27	1.4 (0.9–2.2)	37	2.0 (1.2–2.9)	14	0.8 (0.4–1.3)	13	0.7 (0.3–1.2)
The Americas	89	1.3 (0.8–2.0)	244	3.5 (2.1–5.3)	120	1.8 (1.1–2.7)	67	1.0 (0.6–1.5)
United States	34	0.9 (0.4–1.6)	45	1.2 (0.6–2.1)	7	0.2 (0.1–0.4)	17	0.4 (0.2–0.9)
Africa	181	6.7 (3.8–10.5)	1,977	77.0 (48.3–119.5)	1,684	63.0 (38.0–100.3)	179	6.6 (3.9–10.5)
Egypt	144	15.6 (9.0–25.2)	1,904	197.9 (114.7–308.1)	1,631	184.6 (110.6–290.5)	173	18.6 (10.7–29.8)

BCI = Bayesian credible interval.

[a] Data from the Official Statistics of Finland (OSF): overnight leisure and business trips abroad; includes travellers aged 15–74 years in 2010–11 and travellers aged 15–84 years in 2012 [22].

[b] The geographical classification used by OSF was used for the calculation of incidence.

[c] Country-specific data from OSF were only available for countries receiving more than 50,000 Finnish visitors per year.

[d] Includes cases aged 15–74 years in 2010–11 and 15–84 years in 2012, who sought medical care abroad during 2010 to 2012, handled by SOS International. A case was defined as a Finnish traveller abroad with one episode of illness or injury, handled by SOS International during 2010 to 2012. A person with several separate episodes was counted more than once.

[e] The data of SOS International cover about 95% of Finnish cases handled by assistance organisations of insurance companies.

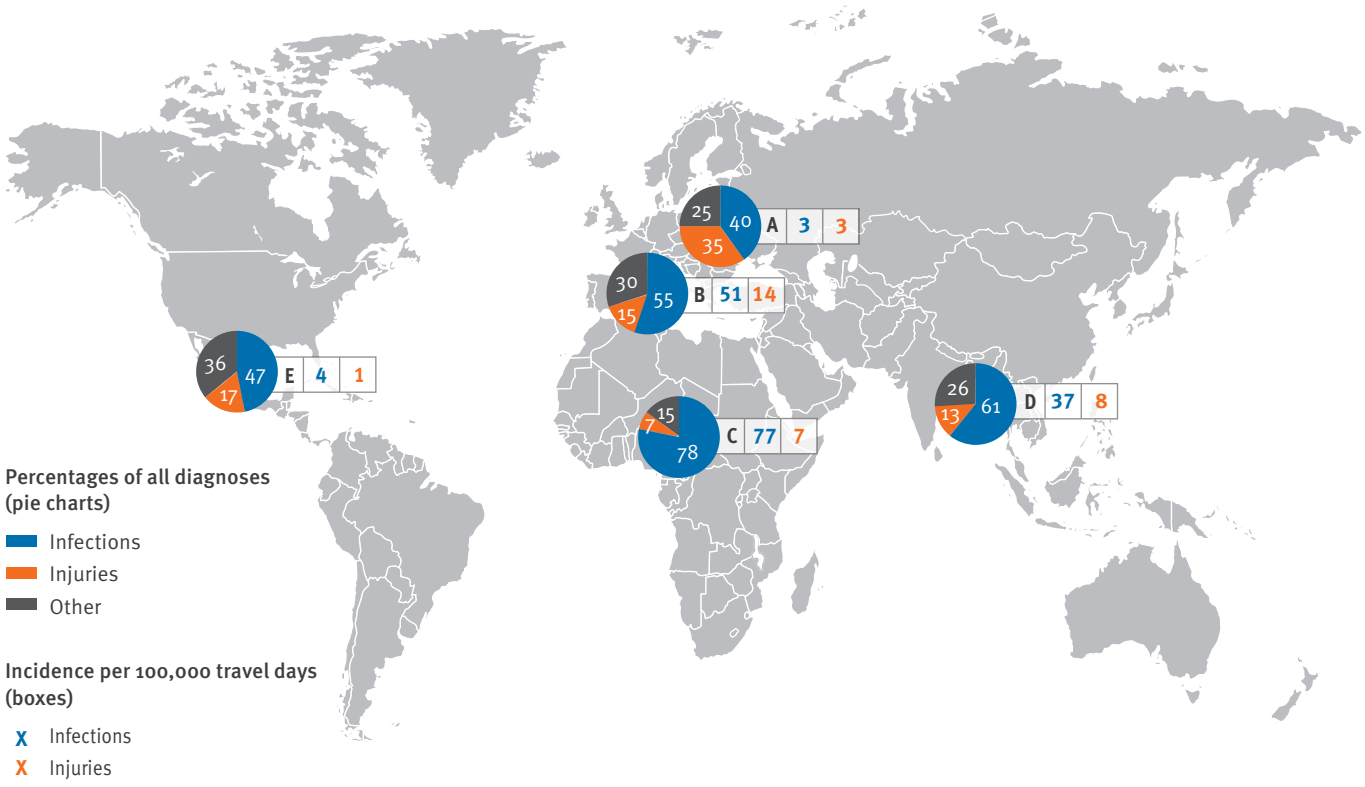
[f] Incidence per 100,000 travel days = (number of cases divided by number of travel days) x 100,000.

[g] Figures for Nordic and Baltic countries and Russia are not presented here; incidences for these countries are not comparable with those of other regions because proportionally more cases are covered by the Social Insurance Institution of Finland (Kela) [24] and trips are shorter than to other regions [22].

[h] Balkan states, Cyprus, Greece, Israel, Italy, Malta, Portugal including Madeira, Spain including Canary Islands, Turkey.

Figure 3

Infections and injuries of Finnish travellers[a] by geographical regions[b], 2010–2012 (9,953,000 travellers)



A: eastern and western Europe; B: southern Europe and the eastern Mediterranean; C: Africa; D: Asia and Oceania; E: the Americas.

'Other' refers to diagnoses other than infections or injuries (skin diseases; musculoskeletal and connective tissue diseases; diseases of the digestive tract; vascular diseases; neoplasms; haematological diseases; endocrine, nutritional and metabolic diseases; mental and behavioural disorders; neurological diseases; eye diseases; ear diseases; respiratory diseases; genitourinary diseases; pregnancy, childbirth and perinatology; unclassified symptoms).

[a] Includes cases aged 15–74 years in 2010–11, and those aged 15–84 years in 2012. A case was defined as a Finnish traveller abroad with one episode of illness or injury, handled by SOS International during 2010 to 2012. A person with several separate episodes was counted more than once.

[b] Figures for Nordic and Baltic countries and Russia are not presented here; incidences for these countries are not comparable with those of other regions because proportionally more cases are covered by the Social Insurance Institution of Finland (Kela) [24] and trips are shorter than to other regions [22].

Data source: Table 4.

proved highest in Egypt, Turkey, and Thailand, and varied between countries within southern Europe.

Infection incidence was greatest in Africa, followed by southern Europe plus the eastern Mediterranean, and Asia plus Oceania. As for injuries, incidence proved highest in southern Europe plus the eastern Mediterranean (Table 4, Figure 3).

Discussion

Principal findings

For decades, travel medicine research has striven to outline the risks of health problems at various destinations. As data have been unrelated to numbers of travellers per site, the main point of criticism has been that proportions of health problems easily suffer distortion [20]. Some reports have described single imported diseases in relation to national travel statistics [25] or World Tourism Organization data [26,27], but a thorough overview of travellers' health risks has been lacking.

Our investigation draws on the exceptional situation in Finland, with two large databases available: one maintained by a single travellers' assistance organisation, covering about 95% of Finnish cases, and the other by OSF, providing numerical data on Finnish travellers to various destinations. Combining these enabled not only a virtually comprehensive nationwide analysis of proportionate morbidity for various diagnoses, but also incidence calculation of health problems abroad. These data reveal the great incidence of infections and the significant difference in incidence of illness and injury between the various regions.

Strengths and weaknesses

The major novelty of our work lies in presenting incidences of illnesses and injuries in various geographical regions. Even though the proportionate morbidity data presented in this and previous [2-19] studies are very informative, the incidence figures are of special value, as they describe more accurately the risks for travellers and, as illustrated in Figure 3, allow comparisons between various regions. Our study sample represents the most severe cases, yet the actual incidence of health problems among travellers needing medical care abroad may in reality be sixfold higher than that presented here (Figure 1). While this study is, to the best of our knowledge, the largest to date reporting health problems of travellers while abroad, the data do not cover travellers who did not contact insurance companies/assistance organisations, nor those without insurance, or those making a claim afterwards directly to the insurance company. According to Finland's largest travel insurance company, the last group mentioned comprise mostly uncomplicated outpatient cases, while nearly all inpatients abroad are cared for by assistance organisations (Ilkka Valanne, Claims Specialist, Eurooppalainen, personal communication, 2 October 2013). As our study material covers 95% of all Finnish cases handled by assistance organisations, the data represent quite comprehensively the most serious health problems faced by Finnish travellers.

The SOS database lacked information on duration of and reason for travel, and itinerary of individual cases, and no evaluations could be made in relation to these factors. Studies relying on questionnaires and telephone interviews [2,7-14] represent travellers' own reports, not evaluations made by healthcare professionals; those based on travel insurance claims [15,16] are a mixture of both. One of the strengths of our study is data collection directly from clinicians treating the patient abroad.

Results in relation to findings in other studies

Findings on proportionate morbidity

In our study, infections clearly outnumbered all other health problems during travel. The proportion of infections proved higher than in studies from Switzerland, Australia and Norway, also using data of assistance organisations (60% vs 20–40%) [17-19], possibly because, instead of organ-specific categories, we grouped all infections together, in a category of their own.

The most common single diagnosis was acute gastroenteritis (23%), consistent with previous findings on illness abroad [2,8-14,28], accounting for one third of inpatient cases. Respiratory infections proved nearly as common (21%), yet with less frequent hospitalisation than for gastroenteritis. In prospective studies, respiratory infections have been reported in 2–26% of travellers [2,7-14].

Findings on incidence of illness and injury

The overall incidence proved highest in Africa, southern Europe plus the eastern Mediterranean, and Asia plus Oceania. One remarkable finding was that in southern Europe plus the eastern Mediterranean, figures for injuries and infections proved higher than those for eastern plus western Europe. The infection profile differed from that in Africa and Asia: instead of acute gastroenteritis, incidence in southern Europe plus the eastern Mediterranean was highest for respiratory tract infections, except for Turkey, which showed the opposite.

Comparisons of incidence figures were possible between countries with more than 50,000 annual visitors. Some caution should, however, be used when making comparisons, since differences between healthcare services may influence the figures in Europe: in countries with large numbers of tourists, such as Spain, there are private clinics directly contacting assistance organisations, whereas for countries with fewer private hospitals, the proportion of cases reported to SOS may remain smaller.

In eastern plus western Europe, where data could be compared between several countries, there was on the whole a minor incidence of health problems. The incidence of injuries was high in Austria and Switzerland, probably mostly accounted for by skiing accidents (Mikael Fotopoulos, SOS International, personal communication, 14 July 2014). In southern Europe plus the eastern Mediterranean, comparisons could be made between Greece, Italy, Portugal, Spain, and Turkey. In Italy and Portugal, overall incidence of illness and injury proved similar to that in eastern plus western Europe. The high overall incidence in Turkey was attributed to gastroenteritis, whereas the next highest figures in Greece and Spain were mainly due to respiratory tract infections. Greenwood et al. described a low risk of gastroenteritis for southern Europe [27], yet we found an elevated incidence in Greece and Spain.

The incidence figures reflect not only health hazards, but also the characteristics of travellers: in the multivariable analysis, vascular diseases, male sex and age ≥ 60 years, for example, were risk factors for hospitalisation.

Likelihood of illness increases with duration of travel [2,29]. In the OSF data, the farther the destination, the longer was the stay (Table 3). For travellers to southern Europe plus the eastern Mediterranean, the median duration was longest for the Canary Islands; intermediate for mainland Spain, Greece and Portugal; and shortest for Turkey and Italy. The overall incidence of illness and injury proved, however, highest in Turkey and the Canary Islands, followed by Greece and mainland Spain. Thus, length of stay alone does not account for these differences. Within this same region, travellers to the Canary Islands were older, and to Italy younger than those to other destinations, consistent with the

age distribution of our cases. Travellers' age and travel duration may thus partly explain the high incidence in the Canary Islands and the low in Italy. Nevertheless, it appears that the overall incidence in southern Europe plus the eastern Mediterranean exceeded that elsewhere in Europe.

Conclusions

This study shows a clear predominance of infections among Finnish travellers' health problems. This investigation is the first to present such comprehensive data on incidence of illnesses and injuries during travel. It thus provides tools for risk assessment, destination-specific travel counselling and post-travel evaluation. As the types of exposure in a given destination are alike for all travellers, regardless of the country of origin, the results of this study should be applicable to any country with a similar travel pattern.

A noteworthy conclusion is that travel within Europe is not without risk. Pre-travel advice may also be needed also for visitors to southern Europe.

*Erratum

In Table 3, the number of travellers in eastern and western Europe were incorrect. Also the median age group for Spain excluding the Canary Islands was incorrect. These errors were corrected on 25 May 2015, at the request of the authors.

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Conflict of interest

None declared.

Authors' contributions

Study concept and design: HS, AK; acquisition of data HS, MF; analysis and interpretation of data HS, PK, AK; statistical analysis HS, PK, JO; drafting of the manuscript HS, AK; critical comments on the manuscript PK, MF, JO; final approval of the version published HS, PK, MF, JO, AK.

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Seroprevalence in blood donors reveals widespread, multi-source exposure to hepatitis E virus, southern France, October 2011

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The apparent seroprevalence of hepatitis E Virus (HEV) varies greatly among developed countries depending on the geographical area and the sensitivity of immunoassays. We used a validated assay to determine the prevalence of HEV IgG and IgM antibodies among 3,353 blood donors living in southern France, who gave blood during the two first weeks of October 2011 and participated in the study. Demographic and epidemiological information was collected using a specific questionnaire. We also screened 591 samples for HEV RNA. Overall IgG seroprevalence was 39.1% and varied from 20% to 71.3% depending on the geographical area ($p<0.001$) while IgM seroprevalence was 3.31%. Anti-HEV IgG was significantly correlated with increasing age ($p<0.001$), eating uncooked pork liver sausages ($p<0.001$), offal ($p=0.003$), or mussels ($p=0.02$). Anti-HEV IgM was associated with being male ($p=0.01$) and eating uncooked pork liver sausages ($p=0.02$). HEV RNA was detected in one of the 99 anti-HEV IgM-positive samples, but in none of the 492 anti-HEV IgM-negative samples. HEV is hyperendemic in southern France. Dietary and culinary habits alone cannot explain the epidemiology of HEV in this region, indicating that other modes of contamination should be investigated.

Introduction

Hepatitis E virus (HEV) is a non-enveloped single-stranded, positive-sense RNA virus, a member of the Hepeviridae family, genus Hepevirus [1]. At least four genotypes of HEV are recognised. Genotypes 1 and 2 are restricted to humans and are prevalent in developing countries in Asia and Africa, where hepatitis E is a waterborne disease associated with sporadic infections and large epidemics linked to drinking water contaminated with faeces. Genotypes 3 and 4 are transmitted zoonotically and are prevalent in many industrialised countries in Asia, Europe and North America. HEV has been detected in a range of animals including pigs, wild boar, deer and rabbits and the concept of zoonosis is supported by the similarities of the sequences of human HEV strains and HEV from animals [2].

About half of HEV-infected patients in developing countries show symptoms of acute hepatitis. The patients most at risk of death are pregnant women (third trimester) and those with chronic liver disease [2]. Most HEV infections occurring in developed countries are asymptomatic. Only patients with chronic liver diseases are at great risk of fulminant hepatitis. An HEV infection can also lead to chronic hepatitis in 60% of immunosuppressed patients, which can rapidly progress to cirrhosis [2,3].

Reports of autochthonous infections in areas with good sanitation, particularly in France are becoming more frequent [4], while imported cases among travellers returning from developing countries are less frequent. These autochthonous infections are most often of genotype 3 and involve transmission through contaminated food. However transmission through occupational exposure to animals, particularly pigs [5] and through infected blood products has been reported [6]. The HEV seroprevalence among blood donors or the general population in high income countries varies widely, from 1.9% [7] to 52.5% [8]. This is partly due to variations in the sensitivity of the assays used for detection [9].

Several lines of evidence suggest that HEV transmission is frequent in southern France where locally acquired HEV infections have been documented [4] and chronic hepatitis E described in immunosuppressed

Table 1

Prevalence of hepatitis E virus antibodies depending on regions and respective administrative areas, southern France, October 2011

Administrative regions and areas (ID number)	Population density (inhabitants per km²)	Anti-HEV (n)			Seroprevalence	
		IgG positive	IgM positive	Tested	IgG % (95% CI)	IgM % (95% CI)
Midi-Pyrénées	64.3	787	71	1,897	41.5 (39.9–43.1)	3.7 (2.9–4.6)
Ariège (09)	30.9	67	3	94	71.3 (62.1–80.5)	3.2 (0–6.7)
Aveyron & Lot (12 & 46)	32.3	40	6	172	23.2 (16.9–29.5)	3.5 (0.7–6.2)
Gers (30)	29.9	64	9	171	37.4 (30.1–44.6)	5.3 (1.9–8.6)
Haute Garonne (31)	195.1	360	33	777	46.3 (42.8–49.8)	4.3 (2.2–6.3)
Hautes Pyrénées (65)	51.4	77	5	234	32.9 (26.9–38.9)	2.1 (0.3–4.0)
Tarn (81)	65.0	96	9	263	36.5 (30.7–42.3)	3.4 (1.2–5.6)
Tarn et Garonne (82)	64.4	83	6	186	44.6 (37.5–51.7)	3.2 (0.7–5.8)
Languedoc-Roussillon	97.2	523	40	1,456	35.9 (33.4–38.4)	2.7 (1.9–3.5)
Aude (11)	57.7	124	8	191	64.9 (58.1–71.7)	4.2 (1.3–7.0)
Gard & Lozère (30 & 48)	71.8	54	5	246	21.9 (16.7–27.1)	2.0 (0.2–3.7)
Hérault (34)	169.1	212	18	656	32.3 (28.7–25.9)	2.7 (1.5–4.0)
Pyrénées Orientales (66)	108.3	133	8	363	36.6 (31.6–41.6)	2.2 (0.7–3.7)

CI: confidence interval; HEV: hepatitis E virus: ID: identity.

patients [3]. The incidence of HEV in transplant recipients reached 3.2/100 person-years in south-western France between 2004 and 2009 [10]. Previous serological studies on blood donors living in the same area found a high seroprevalence (52.5%), particularly in rural areas [8].

We therefore determined the prevalence of anti-HEV IgG and IgM among 3,353 blood donors from two administrative regions of southern France and studied potential contributing factors such as age, sex, as well as eating habits, hobbies, place of residence, profession, travel history, and type of dwelling. We also looked for HEV RNA in IgM-positive samples and in donors randomly selected from among those that were anti-HEV IgM-negative.

Methods

Ethics statement

All the blood donors had completed the national medical questionnaire and had been interviewed before blood collection to ensure that they fulfilled the criteria for blood donation and to eliminate anyone with temporary or permanent contra-indications. The donors gave their informed consent for the study. Information and approval documents were printed in duplicate and signed by both the donor and medical staff. One copy was given to the donor, the other is kept by the staff for 10 years.

The study was approved by the Toulouse University Hospital Research Ethics Committee.

Setting

The two administrative regions of this study are located in the south of France and represent 13.4% of the French metropolitan area. The Midi-Pyrénées region (MP) is the largest region in metropolitan France (45,348 km²), while Languedoc-Roussillon (LR) is the eighth largest (27,376 km²). Their combined population is 5,615,339 inhabitants (8.4% of the French population). LR's eastern border is the Mediterranean coast. The population density in MP (64.3 per km²) is lower than in LR (97.2 per km²). Both these densities are lower than the mean (114 inhabitants/km²) in metropolitan France.

The three main rivers that flow through the two regions arise in the Pyrenees and are the Garonne, the Aude and the Ariège.

Both regions are divided into administrative areas: Eight areas in MP and five in LR. All the areas in LR are close to four MP areas.

Population

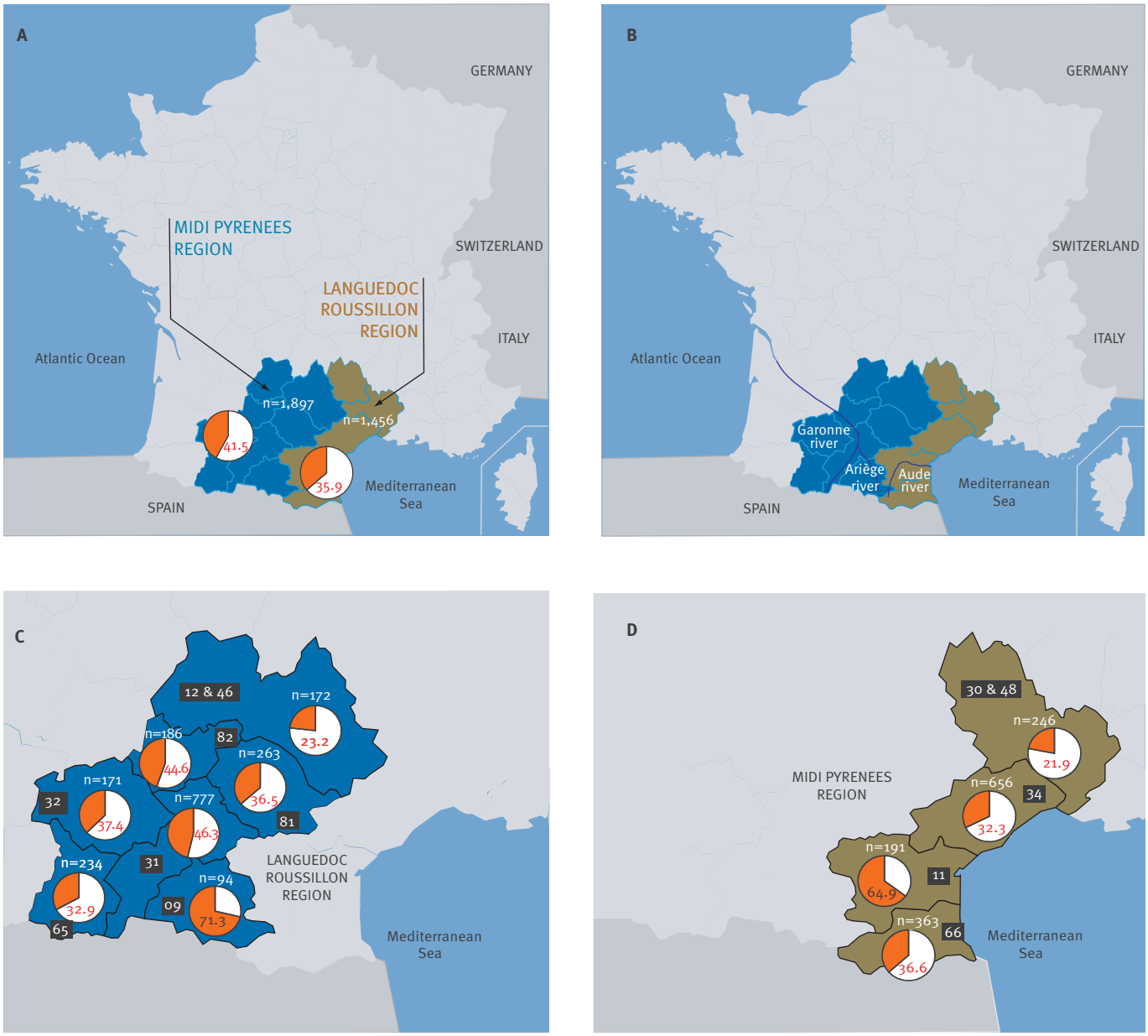
The study was carried out on blood samples from 3,353 unpaid donors, 1,897 from MP and 1,456 from LR. As stipulated by French law, they were all aged between 18 and 70 years.

Blood samples

Blood samples were randomly collected in all the administrative areas of the LR and MP regions during the two first weeks of October 2011 to determine anti-HEV IgG and IgM seroprevalences. The blood from groups of donors such as students and the military were discarded to avoid donors having the same risks of exposure.

Figure 1

Location of the Midi-Pyrénées and Languedoc-Roussillon regions, as well as main rivers, and anti-hepatitis E IgG prevalences in the regions, France, October 2011 (n = 3,353 blood donor samples)



HEV: hepatitis E virus.

White numbers on a black background identify administrative areas. Midi-Pyrénées region: 9, Ariège; 12 and 46, Aveyron and Lot; 31, Haute Garonne; 32, Gers; 46, Lot; 65, Hautes Pyrénées; 81, Tarn; 82, Tarn et Garonne. Languedoc-Roussillon region: 11, Aude; 30 and 48, Gard and Lozère; 34, Hérault; 66, Pyrénées Orientales.

Global anti-HEV IgG prevalences in the regions (panel A) and the administrative areas (panel C and D). The totals of donors tested and the anti-HEV IgG prevalence are shown for the regions and areas.

Pie charts: red parts are the proportion of anti-HEV IgG positive donors; prevalences (percentages) are indicated in the charts.

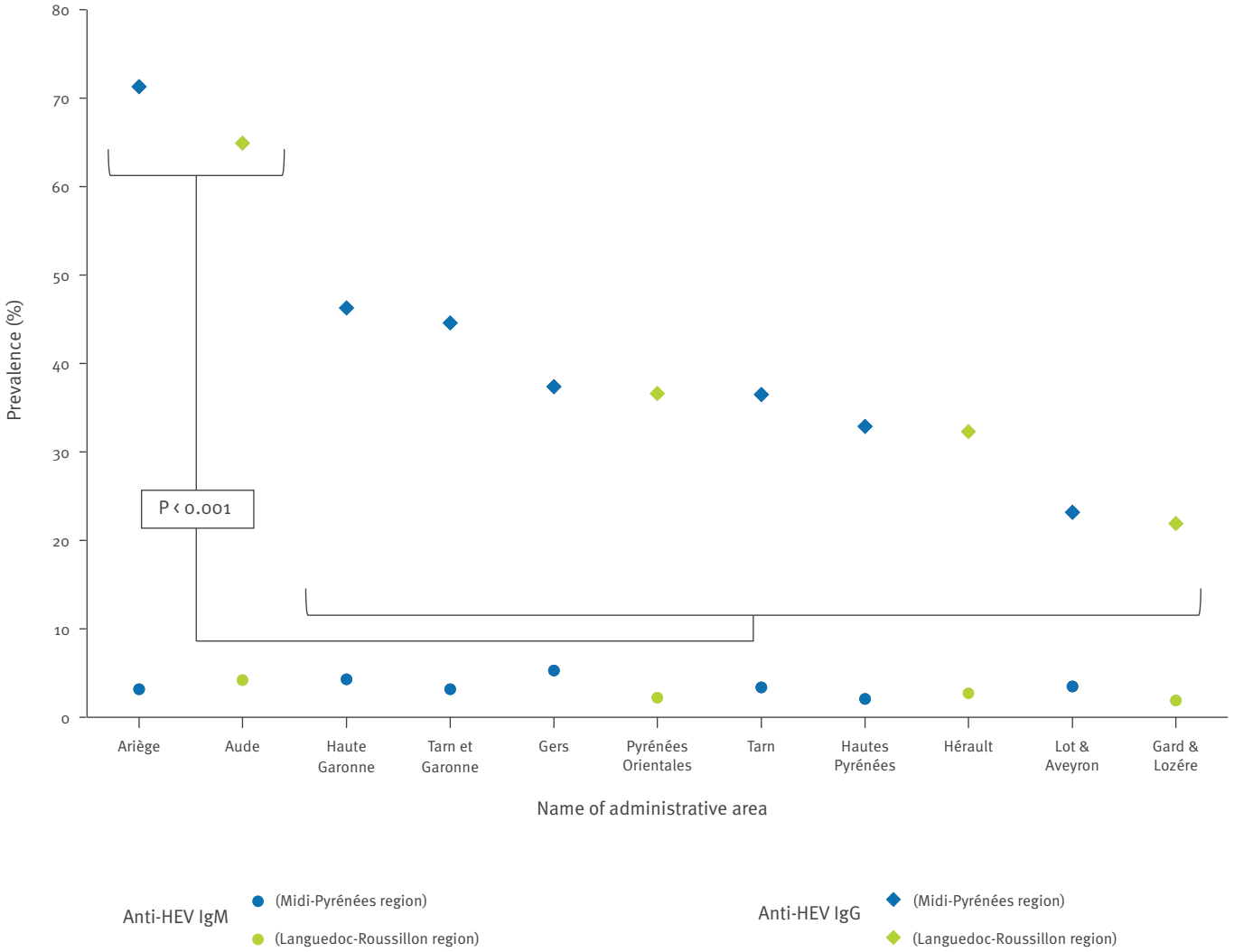
All anti-HEV IgM-positive sera except those that were too small (<100 µL) were tested for HEV RNA. A group of 492 randomly selected sera from MP donors who tested negative for anti-HEV IgM were also tested for HEV RNA.

Laboratory methods

Sera were tested for anti-HEV IgG and IgM using two commercial enzyme immunoassays (Wantai Pharmaceutical Enterprise, Beijing, PRC). These assays use antigens encoded by a structural region of open reading frame (ORF)-2 from a Chinese isolate of genotype 1 HEV and were performed according to the manufacturer's instructions. Serum samples that gave an absorbance value greater than the cutoff value were

Figure 2

Anti-hepatitis E virus IgG and IgM seroprevalences in each administrative area of the Languedoc-Roussillon and Midi-Pyrénées regions, France, October 2011 (n = 3,353 blood donor samples)



HEV: hepatitis E virus.

The prevalences of anti-HEV IgG significantly differed between Ariège and Aude taken together, and all the other administrative areas considered ($p < 0.001$).

considered to be positive for HEV antibodies. These enzyme-linked immunosorbent assays (ELISAs) have been previously evaluated; their analytical and clinical performances were excellent [11,12]. The limit of detection of the IgG assay was as high as 0.25 World Health Organization (WHO) units/mL [11].

Nucleic acids were extracted using Cobas AmpliPrep-Total Isolation kits on a Cobas Ampliprep sSystem instrument (Roche Molecular Systems, Inc, Branchburg NJ US). HEV RNA was detected by amplifying a 70-base fragment from ORF3 [13] using a Light Cycler 480 instrument (Roche Molecular Systems). The limit of detection was 60 international units (IU)/mL.

Questionnaire

Each donor completed a structured, specific questionnaire to document demographic data and putative risk factors. It covered demographics, type of dwelling (apartment, house, farm, institution) and its waste water system (main sewer, septic tank), professional and recreational activities and travel history. Information about frequent contact with pets and/or domestic farm animals was also recorded, as were the donor's eating habits, including if garden fruit and vegetables were consumed. The questions concerned how frequently meat and other products were consumed; the products comprised ham, sausages, pâté, shellfish and fish, uncooked and unpeeled vegetables. The way in which meat or meat-based products were cooked as well as which of such items were eaten uncooked were also recorded. Last, we recorded the source of drinking water (bottled mineral water, tap water, untreated private well).

Table 2

Identifying factors associated with anti-hepatitis E virus IgG and IgM seropositivity, Languedoc-Roussillon and Midi-Pyrénées regions, France, October 2011 (n = 3,353 blood donors)

Factors	Anti-HEV IgG				Anti-HEV IgM			
	Univariate analysis		Multivariate analysis		Univariate analysis		Multivariate analysis	
	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value
Age >45 years (median age)	1.59 (1.31–1.92)	<0.001	1.46 (1.16–1.82)	<0.001	0.49 (0.28–0.86)	0.04	0.52 (0.29–0.92)	0.02
Male sex	1.32 (1.15–1.52)	<0.001	1.19 (0.96–1.47)	0.12	1.37 (0.94–2.02)	0.1	1.69 (1.1–2.6)	0.01
Region MP or LR[a]	1.27 (1.10–1.46)	<0.001	1.59 (1.26–2.00)	<0.001	1.41 (0.95–2.01)	0.09	1.32 (0.79–2.21)	0.29
Administrative area	1.16 (1.13–1.19)	<0.001	1.16 (1.12–1.19)	<0.001	0.91 (0.60–1.40)	0.6	–[a]	–
Eating uncooked pork liver sausage	2.44 (2.09–2.86)	<0.001	2.17 (1.73–2.72)	<0.001	1.71 (1.13–2.59)	0.01	1.88 (1.10–3.23)	0.02
Offal consumption	1.99 (1.69–2.35)	<0.001	1.45 (1.14–1.85)	0.003	1.60 (0.99–2.58)	0.05	1.54 (0.85–2.79)	0.16
Rabbit meat consumption	1.40 (1.16–1.68)	<0.001	1.27 (0.95–1.66)	0.1	1.22 (0.72–2.08)	0.4	–[a]	–
Game meat consumption	1.36 (1.17–1.59)	<0.001	1.12 (0.89–1.40)	0.35	0.95 (0.63–1.44)	0.82	–[a]	–
Oyster consumption	1.80 (1.48–2.17)	<0.001	1.16 (0.80–1.67)	0.44	0.85 (0.56–1.30)	0.46	–[a]	–
Mussel consumption	1.45 (1.14–1.83)	0.002	1.38 (1.07–1.79)	0.02	1.24 (0.64–2.41)	0.5	–[a]	–
Drinking untreated water	1.35 (1.13–1.63)	<0.01	1.27 (0.99–1.63)	0.052	1.34 (0.80–2.25)	0.27	–[a]	–
Consuming items grown in garden	1.10 (1.04–1.17)	<0.01	1.09 (0.99–1.18)	0.053	1.03 (0.87–1.23)	0.7	–[a]	–

CI: confidence interval; HEV: hepatitis E virus; LR: Languedoc-Roussillon; MP: Midi-Pyrénées; OR: odds ratio.

Each variable statistically significant at p ≤ 0.1 in univariate analysis was included into the logistic regression model.
[a] The variables of p >0.1 were excluded from the multivariate analysis.

Statistical analysis

Data collected by the questionnaires were verified and digitised. They were analysed using Stata version 9.2 (StataCorp LP, College Station, TX, US). Demographic and life style factors associated with HEV antibodies were evaluated using univariate analyses. Chi-squared and Fisher's exact tests were used to analyse categorical variables when appropriate. Quantitative variables are expressed as means (± standard deviation (SD)) and compared using Student's *t*-test or the Mann–Whitney U test; others are given as medians (25th–75th percentile). Variables with a p value ≤ 0.10 by univariate analysis were entered into a multivariate, backwards, stepwise logistic regression analysis to identify variables independently associated with HEV seroprevalence. The odds ratios (OR) for all variables were calculated by univariate and multivariate logistic regression. Statistical significance was set at p < 0.05.

Results

Samples from 3,353 blood donors (1,897 from MP and 1,456 from LR) were analysed for HEV antibodies. There were 1,744 (52%) males and the median age was 42.9 ± 13.8 years.

Anti-hepatitis E virus IgG and IgM seroprevalences in Languedoc-Roussillon and Midi-Pyrénées

A total of 1,311 blood donors were IgG-positive, corresponding to an overall seroprevalence of 39.1%. (95% confidence interval (CI): 37.4–40.7). Seroprevalence varied from one administrative area to another: it was highest in in Ariège with 71.3% (95% CI: 62.1–81.5) and lowest in Gard and Lozère with 21.9% (95% CI: 16.7–27.1). Population densities and seroprevalences by regions and areas which were not statistically associated are shown in Table 1.

The locations of the administrative regions and respective areas within France, the courses of the main rivers, and the anti-HEV IgG seroprevalences are shown in Figure 1.

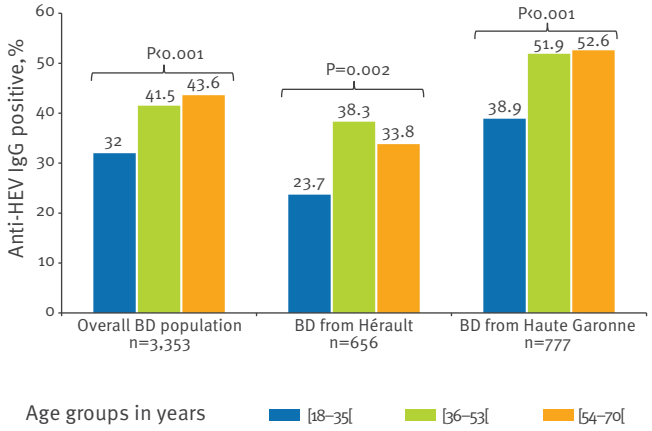
We identified four categories of areas according to the seroprevalence of anti-HEV IgG. The anti-HEV IgG prevalences were significantly different from each other. The first includes areas in which the seroprevalence was over 50% (Ariège and Aude); the prevalences in the other areas were 40 to 50% (Haute Garonne and Tarn et Garonne), 30 to 40% (Gers, Pyrénées Orientales, Tarn, Hautes Pyrénées), and below 30% (Lot and Aveyron and Gard and Lozère) (Figure 2).

Factors associated with anti-hepatitis E virus IgG or IgM seroprevalence

Several characteristics were associated with the presence of anti-HEV IgG (Table 2). Multivariate analysis identified five independent factors associated with the presence of anti-HEV IgG. These included eating uncooked pork liver sausages, offal and mussels. It is noteworthy however, that the prevalence of anti-HEV IgG among donors who declared that they had never

Figure 3

Prevalence of anti-hepatitis E virus IgG in donors by age group, among all blood donors in the study and among donors from the most populated areas (Haute Garonne and Hérault), southern France, October 2011



BD: blood donor; HEV: hepatitis E virus.

eaten uncooked pork liver sausage, offal or mussels was 18.1% (95% CI: 12.3–23.9). The other factors linked to the presence of IgG were the region of residence (MP or LR), as well as increasing age (Figure 3).

We found 111 (3.3%; 95% CI: 2.7–3.9) sera that were anti-HEV IgM-positive. The IgM seroprevalence in MP was 3.7% (95% CI: 2.9–4.6), whereas it was 2.7% (95% CI: 1.9–3.6) in LR (Table 1). Multivariate analysis (Table 2) showed that being male was associated with a higher seroprevalence (adjusted OR: 1.69; 95% CI: 1.10–2.60), as was eating uncooked pork liver sausage (adjusted OR: 1.87; 95% CI: 1.22–2.86). The prevalence of anti-HEV IgM among donors who declared that they had never eaten uncooked pork liver sausage was 2.4% (95% CI: 1.6–3).

Hepatitis E virus RNA detection

We tested for the presence of HEV RNA in two groups of sera including (i) 99 IgM-positive samples (the 12 remaining positive samples were too small) and (ii) 492 randomly selected from all IgM-negative specimens, independent of IgG status. HEV RNA was detected in only one IgM-positive sample (virus load: 630 copies/mL). Genotyping was unsuccessful due to low viraemia.

Discussion

The assay used gave an overall prevalence of HEV IgG antibodies as high as 39.1%, quite similar to those observed in China using the same assay [14]. Exposure seemed to vary from one area to another: from 20 to 71.3%. Associated factors were the consumption of uncooked pork liver sausages, offal and mussels.

There have been few serological studies using this type of sensitive assay on blood donors in Europe; those that have been done found that seroprevalence varied widely from one country to another. The lowest prevalence was in Scotland (4.7%) in sera collected between 2004 and 2008 [15] and the highest reported was in MP in France (52.5%), where we had collected and tested 512 blood donors samples between 2003 and 2004 [8]. The figures reported for the Netherlands (27%) in 2011 and 2012, and Germany (29%) in 2010 were intermediate [9,16].

Our previous serological study among blood donors demonstrated that HEV infection is endemic in south-western France [8]. The present study was done to complete the earlier data [8], it involved a 6.5-times larger blood donor population living in a 6.4-times larger area, covering two administrative regions in the south of France. This enabled us to demonstrate that prevalence varied from 20% to 71.3%, depending on the geographic area.

The wide range of prevalence observed clearly implies that there is more than one main risk factor for HEV contamination. Previous studies have shown that age [8], occupation [17], food consumed [18] and even hobbies [8] are linked to a high seroprevalence. We also found that the seroprevalence increased with age, in line with a cumulative lifetime exposure to the virus whatever the mode of contamination. The regional variation in HEV seroprevalence was not linked to differences in the age profile of our subjects.

The consumption of uncooked pork liver sausages is one of the modes by which people living in southern France become infected with HEV. We previously reported finding HEV-RNA in eight of 18 uncooked pork liver sausages bought in MP [8]. Eating pork liver sausage had already been implicated in autochthonous cases of hepatitis E in the south-eastern part of France [18]. This convinced the French Health Authorities to compel, in May 2009, the manufacturers of uncooked pork liver sausages to include recommendations for cooking their product to consumers. We also found that the consumption of offal was linked to hepatitis E. This correlates well with the findings of a German case–control study, that eating offal was a risk factor for Hepatitis E infection [19].

A case–control study among transplant recipients in MP found a significant association between HEV infection and the consumption of game meat [20]. The virus was detected in the livers of wild boar from the forests of the Ariège and Aude; these virus strains were very similar, genomically, to those isolated from patients suffering from hepatitis E (data not shown). It was demonstrated recently that wild boar from southern France are almost four times more likely to test positive for anti-HEV IgG than similar animals from northern France [21]. However, the present study does not associate the consumption of game meat with HEV seroprevalence after multivariate analysis.

The fourth dietary factor that we found to be linked to the presence of IgG is the consumption of mussels. This was described in a previous study on solid organ transplant recipients who developed autochthonous hepatitis E in south-western France [20]. Eating mussels was also responsible for a hepatitis E outbreak on a cruise ship [22]. The consumption of shellfish is a known risk factor for many viral infections, particularly for viral hepatitis as the shellfish act as a reservoir of HEV.

Shellfish are cultivated in estuarine waters into which may flow human or animal effluent, sewage or contaminated rivers. Bivalves filter and concentrate virus particles. As they are frequently eaten raw or lightly cooked they can pass on these particles, which explains their role in human hepatitis E epidemiology. Multivariate analysis indicated that eating oysters was not linked to the presence of anti-HEV IgG (Table 2). This could be due to differences in the way the oysters are cultivated. Further studies are needed to test this hypothesis.

The dietary and culinary habits of people living in southern France do not completely account for the epidemiology of HEV. The dietary habits of about one fifth of the blood donors who were positive for anti-HEV IgG did not appear to include any risk factors, such as uncooked pork liver sausage, offal or mussels. In the same way some donors who had never eaten pork liver sausage were positive for HEV IgM antibodies. The main parameters of the multivariate analysis explain only 10% of variability. There are probably other silent modes of contamination, probably linked to the environment, that explain the high seroprevalences in these subjects.

The epidemiology of HEV in southern France may share some characteristics with that of developing countries where HEV is responsible for frequent outbreaks linked to contaminated drinking water [2]. Autochthonous cases of hepatitis E associated with drinking water from a private source have been previously described in France [23]. In the present study, seroprevalence among blood donors living in the Ariège and Aude was found particularly high. This did not appear to be related to older age of donors in these areas, as the mean age of the donors from Ariège, where the highest IgG seroprevalence occurred, and the mean age of the donors from the other areas in the two regions considered were not different (data not shown).

Ariège and Aude have similar geological and ecological characteristics, and host the main rivers in MP and LR respectively. Water, including river water, can act as vehicles for HEV. For example, HEV has been detected in surface water in the Netherlands [24] and in Slovenia, where over 3% of the samples tested were positive [25]. Of the urban sewage samples taken in Spain, which neighbours the areas in this study, 30% were positive for HEV RNA [26].

Factories producing cold meats whose main ingredient is uncooked pork liver are located in Ariège and Aude as well as a number of pig farms. The prevalence of HEV antibodies can reach 88% in pig farms in France [27], and HEV RNA is frequently detected in porcine stool samples at all times of the breeding cycle [25]. Hence, sewage from pig farms, slaughterhouses and cold meat factories, as well as humans, can pollute the environment and potentiate virus dissemination. Wild boars, which are abundant in both areas, probably also excrete HEV for months or years, which can contaminate the areas where they live and pollute the river catchments. In this way Ariège and Aude could be considered the 'epidemiological epicentre' of the hepatitis E in the south of France because the prevalence decreased from these areas in concentric circles. River water samples should be tested for HEV RNA to confirm this hypothesis.

Of note, no association has been found between the density of the pig population and HEV antibodies in humans in north European countries as Denmark [28]. But the ecological and environmental characteristics of these pig farms are different, which probably explains why these data differ from those for our areas.

The great prevalence of anti-HEV IgM reported here (3.3%) agrees well with the prevalence of anti-HEV IgG and the incidence of hepatitis E (3.2/100 person-years) among solid organ transplant recipients from the same area [10]. This suggests that these people had asymptomatic hepatitis E in the recent past. Moreover the detection of HEV RNA in only 1% of IgM positive sera could be in line with the prolonged persistence of IgM described with the same assay [12]. As observed for IgG antibodies, anti-HEV IgM were more prevalent among consumers of uncooked pork liver sausage.

The rate at which donated blood tests positive for HEV RNA depends on the country. Figures obtained from mini-pools can vary throughout Europe: from 1:1,240 in Germany [29] to 1:7,986 in Sweden [30]. Even if the blood donor population is small, analysis of our data suggests that the incidence of silent hepatitis E among blood donors from the two south of France regions can reach or even exceed that described in Germany by Vollmer [29]. A 1:1,240 incidence adjusted to the 184,000 annual blood donations in the two regions could lead to 148 RNA-positive donations per year. But the risk of transfusion-transmitted hepatitis E infections by contaminated blood products remains unknown and transfusion-related hepatitis E seems to be rare in our area, even in multi-organ-transplanted recipients [2].

In conclusion, HEV is endemic in southern France and hyper-endemic in some areas. There appears to be a correlation between the presence of HEV antibodies and eating pork, offal and mussels. We need to look for infectious HEV particles in water from rivers and

initiate studies to determine the risk of HEV transmission through HEV-contaminated blood products.

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Conflict of interest

None declared.

Authors' contributions

Jean-Michel Mansuy: drafting the manuscript; Karine Sauné: statistical analysis; Henri Rech: blood collection; Florence Abravanel: National HEV reference centre, laboratory analyses; Catherine Mengelle: specimen and information collection; Sébastien L Homme: National HEV reference centre, laboratory analyses; François Destruel: blood collection; Nassim Kamar: supervision of the study; Jacques Izopet: National HEV reference centre; supervisor of the study.

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Ten years experience of syndromic surveillance for civil and military public health, France, 2004-2014

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Difficulties by France to identify and properly estimate the impact and consequences of the intensive 2003 heatwave, and the identification of a need for an interoperable real time medical surveillance system in the French military deployed forces, has prompted France to establish two syndromic surveillance systems. These systems, a civil syndromic surveillance system 'Surveillance sanitaire des urgences et des décès' (SurSaUD) [1] and a military syndromic surveillance system, 'Le Système d'Alerte et de Surveillance en Temps Réel' (ASTER) [2] were set up in 2004. The aim of these systems is to reinforce the early warning capacity of public health events. Syndromic surveillance, defined as the (near) real time collection, analysis, interpretation and dissemination of health-related data aims at detecting, monitoring and evaluating unexpected, emerging or expected public health threats and contributes to the monitoring and assessment of the impact of these [3].

After a 10-year existence, the two systems SurSaUD and ASTER are pillars of the national and international public health surveillance. In November 2014, a joint meeting was organised in Paris by the French Institute for Public Health Surveillance (InVS) and the French Center for Epidemiology and Public Health for the French Armed Forces (Centre d'Epidémiologie et de Santé Publique des Armées, CESPA), including all stakeholders of the two systems. This meeting aimed at sharing the experiences and keys to success of the two systems and to promote the exchange and discussion between the different actors towards a collaborative future. All the presentations are available on the InVS website [4].

This meeting report summarises the key points of the 10-year experience, the feedback and expectations of the different stakeholders, in particular data providers and decision makers, and presents the outlook and future collaborations at a national and international level for the two systems.

Ten years of experience

Céline Caserio-Schönemann (InVS, Saint-Maurice) presented the civil syndromic surveillance system, SurSaUD. The SurSaUD system collects morbidity data from the emergency department network 'Organisation de la surveillance coordonnée des urgences' (OSCOUR) and from the emergency association of general practitioners, SOS Médecins, whose members perform home visits. The system also collects mortality data from the civil status offices and from electronic certificates. All information is transmitted automatically on a daily basis and analysed by the InVS. This system captures information about the general population in France.

The design of the military system ASTER, as presented by Jean-Baptiste Meynard (CESPA, Marseille) is quite different from SurSaUD as patient information is collected by military physicians in all areas where forces are deployed. Mobility and adaptability to several operational contexts constitute major issues for ASTER. The system requires that all data providers are still computerised for collecting data without supplementary overload.

During the meeting, three sessions illustrated how the systems have been used for each syndromic surveillance objective. Early detection was the initial objective of these systems, however syndromic surveillance has also proven useful to identify and follow trends in seasonal epidemics or for early health impact assessment of several environmental situations (extreme weather conditions, disasters, industrial accidents) or planned events (mass gatherings, exceptional events). Early detection was illustrated by Pascal Vilain (InVS, La Reunion Island Regional Office) and Gabriel Bédubourg (CESPA, Marseille) with examples of spatio-temporal analysis of several epidemics in La Reunion Island and the detection of dengue fever in French Guyana. Situational awareness with examples based on winter seasonal epidemics (influenza, bronchiolitis, gastroenteritis), asthma and the recent chikungunya fever outbreak in the Caribbean [5] was presented by Marc Ruello

and Vanina Bousquet (InVS, Saint-Maurice), Vincent Pommier de Santi ((Direction Interarmées du Service de santé (DIASS), French Guyana Armed Forces)) and Elise Daudens (InVS, Caribbean Regional Office). Pascal Vilain, Arnaud Mathieu (InVS, Normandy Regional Office) and Vincent Pommier de Santi presented feedback from the surveillance of several exceptional events such as natural disasters, mass gatherings or industrial accidents to illustrate the objective of health risk assessment in real time.

All the presentations concluded that a key for success of these surveillance systems is the close collaboration with all the stakeholders. Continuous communication between data providers, epidemiologists, and decision makers is required to ensure efficient public health surveillance for reactive alert and action. Two open sessions of the meeting were dedicated to exchange about the feedback and expectations of data providers and decision makers.

Lessons learned from data providers and decision makers

In both the SurSaUD and ASTER surveillance systems, computerisation is a necessary prerequisite. For robust and pertinent analyses, good quality data must be collected and there must be strong adherence by healthcare professionals to the system. In order to optimise adherence, the system must limit the increased workload for data providers who must provide coding information, particularly for medical diagnoses. Data comparability requires a common definition and homogeneous thesaurus by all data providers. Development and dissemination of these tools have been facilitated by regional partners, the academic community, and national federations of health professionals. Ensuring good quality data required time for networking and frequent exchanges with all data providers as showed by Leslie Banzet (InVS, Languedoc-Roussillon Regional Office) and Olivier Onde (Observatoire regional des urgences du Languedoc-Roussillon, Montpellier). Sharing expertise between health professionals and epidemiologists at a regional level but also through steering committees at a national level has been another way to improve the knowledge of strengths and weaknesses of the system and to reinforce the confidence in collected datasets and in analyses produced by epidemiologists.

Though both systems are based on voluntary participation they cover a large area. One lesson learned is the importance to know and to deal with daily challenges of the data providers. Involvement in a syndromic surveillance network imposes some new constraints for health professionals in their activity (to adapt to technical tools or to mobility conditions but also to code medical information). An added value has to be found to maintain long-term participation and motivation of data providers as reported by Christophe Leroy from Louis Mourier Hospital Emergency Department, Colombes / La Société Française de Médecine d'Urgence (French Society of Emergency Medicine) and Pascal Chansard from SOS Médecins France, Paris. Direct or indirect benefits for health professionals encourages adherence to a heath surveillance system. Targeting professional needs and expectations is a challenge as they may differ widely among and within the different networks (private or hospital physician, junior physician or head of department, mobile or in-hospital service, civilian or military context).

An added value is the health professional network that can be activated. This human dimension of the network is as important as the data transmission and analysis. Early detection is dependent on health professionals reporting unusual events.

The last main lesson learned from decision makers was the evidence of the usefulness and relevance of both systems. Communication and discussions underline the leading position of SurSaUD and ASTER as references respectively for public health surveillance and for military health surveillance at an international level.

Expectations of data providers and decision makers

Data providers primarily expect appropriate and useful feedback from epidemiologists, enabling better anticipation for healthcare organisation and a better knowledge of profiles of patients who may require emergency facilities. Data providers underline the usefulness of feedback to administrative staff in order to adapt hospital organisation to various epidemiological situations, specifically when there is a risk of overcrowding.

Alain Cadou (Champagne-Ardennes Health Regional Agency) and Catherine Guichard (Ministry of Health, Paris) recalled that communication is a crucial issue from the decision maker point of view. Epidemiological data analysis should provide clear messages that should be transmitted to the appropriate contact person for timely decision making. The information needed by health authorities should be easily understandable and should be transmitted using the most appropriate means of communication. The baseline, i.e. what is expected in normal situation, has to be specified as well as temporal elements concerning when the situation will recover, underlined Emmanuel Angot from the Military Health Service (Service de santé des armées), Paris. Because syndromic surveillance provides time-sensitive data, it is important to ensure consistency between the request of decision makers for the most up to date information and the epidemiologist's capacity to effectively assess the information. This is particularly pertinent in situations with intensive media coverage. Time for decision making is different from time for epidemiological analysis and output. A balance has to be struck between both the needs to select what is relevant to communicate, to ensure a minimum of data reliability and not to burn out forces. Health authorities can explore two approaches. One approach is to develop 'positive' communication targeted to

media out of any heath event that aims to educate and to limit media pressure on health authorities in case of a public health event. Gilles Viudes from the Federation of Regional Observatories for Emergency Activities (Fédération des Observatoires régionaux des urgences) suggested that another approach for decision makers is to improve anticipation and preparedness with tools such as management protocols for different geographical scales using information accrued from the ten years of experience with the syndromic surveillance systems. For example, adapting regional control measures to anticipate seasonal influenza, gastroenteritis or bronchiolitis epidemics that occur every year at about the same period could be strongly relevant to reduce hospital overcrowding. These protocols would have to be widely disseminated to allow for a proper understanding of what is to be done, who needs to act and when. Health authorities should consider syndromic surveillance as a timely, sound scientific basis to better support preparedness and decision making.

All data providers and decision makers agreed that IT aspects, particularly business software solutions, are a major issue for these systems. Even if syndromic surveillance systems have been probable levers for accelerating health professional computerisation in the past, a real challenge and a recurrent request from data providers is to make software tools (especially coding tools) and applications more user-friendly and better suited to clinical practice. This is essential in order to maintain the participation of data providers and encourage the practice of coding medical information. Collaboration with software developers would be useful in order to develop effective and interoperable electronic information systems including tools to streamline procedure and to enable exchange of high quality datasets.

Prospects

Prospects for both systems deal with mutual concerns but also specific issues.

Both systems aim to increase methodological developments to enhance data analysis. Both syndromic surveillance systems now are based on huge databases with ten years worth of historical data. The implementation of robust and performant statistical methods is required in order to meet the objective of detection of the systems. From a technical point of view, additional tools have to be developed in order to adapt systems to the rapid evolution of IT technology and in order to deal with the concern of the increase in data volume and the need to develop new tools to analyse this vast amount of data. Céline Caserio-Schönemann suggested that new technological strategies can be explored such as developing free text analysis and data mining, and promoting training with the use of simulation platform as underlined by Hervé Chaudet (CESPA, Marseille).

Common goals are also geared towards long-standing international collaborations. European collaborations have been strengthened by the Triple S project from 2010 to 2013 [6] led by the InVS and involving CESPA as reported by Anne Fouillet (InVS, Saint-Maurice), Hervé Chaudet (CESPA, Marseille) and Anne Bronner of the French Agency for Food, Environmental and Occupational Health and Safety, Lyon (Agence nationale de sécurité sanitaire de l'alimentation, de l'environnement et du travail). The Triple S project made it possible to build a European syndromic surveillance network and to share expertise. It resulted in the publication of deliverables such as the European definition of syndromic surveillance [3], guidelines for designing and implementing a syndromic surveillance system [7], and the proposal for a European strategy for syndromic surveillance [8]. At an international level, collaborations should also be reinforced through the International Society for Disease Surveillance [9]. For the ASTER system one crucial issue is to enter fully into a process of industrialisation and deployment at an international level in order to build the model for the future North Atlantic Treaty Organization syndromic surveillance system as explained by Benjamin Queyriaux (Deployment Health Surveillance Capability, Munich).

Some issues are specific to the SurSaUD system. The first is the strengthening of existing data sources. If efforts have to be done to maintain the emergency department network OSCOUR as an exhaustive network without compromising quality, special attention has to be paid to develop the use of electronic death certificates. Grégoire Rey from the French Epidemiological Center for Medical Causes of Death (Centre d'épidémiologie sur les causes médicales de décès, Le Kremlin Bicêtre), expressed his regret at the fact that at the end of 2014 only 6% of deaths were certified online. This level is insufficient to allow proper analysis for timely health surveillance and alert. Regional Health Agencies should examine this issue and promote the use of electronic death certificates in healthcare facilities. In parallel, a specific methodological issue for the syndromic surveillance team concerns building pertinent and efficient indicators based on free text analysis of the medical causes of death.

The introduction of new data sources in the surveillance system in order to have a better overview of health population is also being explored. Developing collaboration with the Emergency Medical Services (Service d'Aide Médicale Urgente) to gain in complementary and earlier information is in progress as presented by Florian Franke (InVS, South Regional Office).

Conclusions

After ten years of existence both civilian and military French syndromic surveillance systems are mature systems with fruitful experiences demonstrating the efficiency and complementarity with traditional surveillance systems. The future of syndromic surveillance is open to innovation, sharing of expertise and development of scientific synergies with data providers, syndromic surveillance partners (in human

and veterinarian fields) and the scientific community emphasised Anne Gallay (InVS, Saint-Maurice) and Rémy Michel (CESPA, Marseille). Scientific promotion of French syndromic surveillance results will certainly help to meet the goals.

Designing and implementing a communication strategy towards stakeholders is crucial. In particular, attempts should be made to simplify information content, improve user awareness and tailor information and feedback to the needs of users in order to ensure that syndromic surveillance proves helpful for decision making in public health.

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Conflict of interest

None declared.

Authors' contributions

Both authors contributed to the writing of the meeting report.

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