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Epidemiology of infections with enteric salmonellae in Switzerland with particular consideration of travelling activities

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Summary

QUESTIONS UNDER STUDY: To describe the current epidemiological situation of enteric salmonellosis in Switzerland and its development in the last two decades, particularly by determining the ratio between domestic and travel-associated cases.

METHODS: Between 1 February 2011 and 31 January 2012, 14 medical laboratories continuously reported their isolations of enteric salmonellae to the Federal Office of Public Health (FOPH). Data on the travel history of salmonellosis patients was actively acquired from their treating physicians. These data were compared with the results of a case-control study on sporadic salmonellosis that was performed in 1993.

RESULTS: It could be shown that, concomitantly with the pronounced decline in incidence of reported laboratory notifications of enteric salmonellae since the early 1990s, the travel-associated portion of isolates belonging to the most frequently isolated serovar Enteritidis has increased significantly (more than doubled). The three serovars that followed *S.* Enteritidis in frequency of isolation (Typhimurium, Bardo, monophasic 4,12:i:-) are predominantly of domestic origin.

CONCLUSIONS: The significant increase in the percentage of travel-related *S.* Enteritidis infection, demonstrated by the comparison between the data from 2012 and 1993, might be a consequence of the reduction in domestic infections during this period. The fact that infections due to this serovar are now significantly more often travel-related than domestic clearly illustrates the success of the preventive measures taken. These consist of legal measures that were necessary to reduce the transmission of the pathogen in raw eggs, and sanitation measures taken by the producers that aimed to contain the chicken meat reservoir.

Abbreviations

FOPH	Federal Office of Public Health
FVO	Federal Veterinary Office
NENT	National Reference Centre for enteropathogenic Bacteria and Listeria
PFGE	pulsed field gel electrophoresis

Key words: *enteric salmonellae; travel-related salmonellosis; foodborne salmonellosis*

Introduction

In the European countries, salmonellosis is the second most frequently reported zoonotic infection [1]. Currently, over 2,500 serovars of *Salmonella enterica* subsp. *enterica* are known. The animal reservoir of this pathogen is broad and transmission to humans happens almost exclusively via ingestion of contaminated foods. Contrary to *Campylobacter*, which is mostly found in foods of animal origin for example poultry meat or raw milk, *S. enterica* was demonstrated to be present in a large variety of foods. Enteric salmonellae differ from *Campylobacter* in two other important aspects: *Campylobacte*r has a rather low resistance to environmental influences such as oxygen and cannot grow in foods. Salmonellae behave differently, under ideal conditions, they multiply rapidly in many foods and are able to persist in the environment rather a long time [2].

Salmonellosis belongs to the infectious disease group which has to be reported mandatorily in Switzerland. Since 1992, the number of reported cases is declining, a phenomenon which is also observed within the European Union. An improvement of the epidemiological situation is also reflected by the decreasing annual number of outbreaks [3].

In the present article, the current epidemiological status of salmonellosis in Switzerland is shown and a glance is thrown at the situation of the past twenty years. The main objective of this work was to find out and discuss possible explanations for the continuous decrease of human cases. On the one hand, salmonellosis is a foodborne disease, and reasons for its decrease are probably related to improvements of the food legislation (hygiene, transport and storage of foods, sampling and screening), as well as improvements of quality systems in the food industry, in gastronomy and catering businesses. On the other hand, it is also well known that salmonellosis is to a certain degree a travel-related disease. For that reason, information on travel activities of patients is crucial. Without such data, the impact of measures in the food industry to control *Salmon-*

ella cannot be estimated. Unfortunately, the official reporting system does not request information on the travel history of salmonellosis patients. Therefore, the information that was needed was generated in a one-year inquiry. The study which was performed permitted discovery of the current ratio between domestic and travel-associated cases of enteric salmonellosis and frequencies of different serovars. Furthermore, information on travel destinations linked with a risk for *Salmonella* infections was collected. The data obtained allowed, to a certain degree, the explanation of the decline of salmonellosis in the past two decades and to identify problems that have to be solved in the context of this foodborne disease.

Methods

The present study was conducted between 1 February 2011 and 31 January 2012, in collaboration with 14 medical laboratories in Switzerland. They continously reported their isolations of enteric salmonellae to the FOPH, Microbiological and Biotechnological Risks Section. According to the mandatory reporting system, the laboratory reports concerning enteric salmonellae comprise the following data: date of sampling, method and material used for identification, serovar of isolated *Salmonella* sp., date of birth of patient, and gender of patient. In the context of the present study, the participating laboratories complemented this information by actively acquiring data on travel from the treating physicians: travel abroad within 3 days before onset of illness, and travel destination.

Salmonella serovars other than Enteritidis and Typhimurium were identified by the National Centre for Enteropathogenic Bacteria and Listeria (NENT), University of Zurich.

The results of the present study are put into a context with an earlier study and with the insights gained from outbreak investigations, allowing the illustration of the development and trends of human salmonellosis in Switzerland.

Results

Data from the mandatory reporting system and outbreak investigations, 1988–2011

Within the scope of the Swiss mandatory reporting system, the medical laboratories report isolations of enteric salmonellae to the cantonal health authority and the FOPH. In addition to this case-oriented reporting, the physicians communicate observations of unusual frequencies of diseases which points to probable outbreaks.

Table 1: Incriminated foods in outbreaks with enteric salmonellae (Total: 148), Switzerland, 1992–2011.

Food	Number of outbreaks
Egg dishes	92
Meat and meat products	8
Raw milk	3
Cheese	3
Precooked dishes / sauces	2
Salads	1
Unknown source	39

Electronic data acquisition at the FOPH started in 1988. A maximum of laboratory notifications was recorded in 1992 (7,886 detections, 133.6 per 100,000 residents) and since then an almost continuous decline has been observed. In the time period covered here, *S.* Enteritidis has always been the most frequently observed serovar, but its share in the total number of *Salmonella* isolates has dropped as well (fig. 1). Concomitantly, the number of outbreaks (more than one diseased person traced back to the same source) due to salmonellae decreased, from 31 in 1993 to only one each in the years 2009-2011. Among 148 *Salmonella* outbreaks investigated, the large majority of those with successful identification of the source (84.4%) were found to be related to dishes involving raw or inadequately cooked eggs (table 1). In addition, some of these outbreaks could even be traced back to flocks of laying hens. The settings for infection were sites of collective catering, in the first place restaurants, hotels and canteens, followed by institutions of medical and/or social care like hospitals, psychiatric clinics, nursing homes and residential establishments (table 2). In the setting "Household", the illnesses often originated from commercially available products. In five of these events, the outbreak affected several cantons, and in four of them, the source could be determined: The foods concerned in outbreaks of *S.* Braenderup, *S.* Typhimurium and *S.* Virchow were meat products [4–6], and a soft cheese product was identified as the source of the *S.* Stanley outbreak of 2006/07 [7]. Factors contributing to outbreaks of salmonellosis were lack of hygiene, technically

Table 2: Setting for outbreaks with enteric salmonellae (total = 148), Switzerland, 1992–2011.

Infection setting	Number of Outbreaks
Restaurant/hotel/ canteen	56
Hospital/institution	34
Household	16
Celebration/party	10
School/nursery	7
Army	6
Youth camp / holiday camp	4
Foreign travel	3
Street vendor / kiosk / fast-food stand	1
No data	11

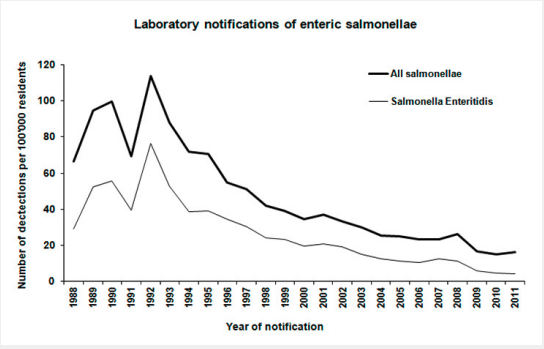

Figure 1

Notifications by medical laboratories recorded through the mandatory reporting system of the FOPH (reproduced from [3]).

wrong handling or storage of foods, or faulty preparation of dishes including cross-contamination.

Inquiry on foreign travel, 2011/12

Between 1 February 2011 and 31 January 2012, a total of 499 human isolates of enteric salmonellae were identified by the participating laboratories (table 3). All but three isolates belonged to *Salmonella enterica* subspecies *Enterica*. Among the great number of different serovars belonging to *Enterica*, Enteritidis is, as usual, on top of the list, followed by Typhimurium. The otherwise rare serovar Bardo is next due to an outbreak affecting several cantons and lasting almost a year. In total, it affected about 90 persons, and these cases were more or less evenly distributed over the period. However, the source of this event could not be determined (unpublished data). The monophasic variant 4,12:i:- of *S.* Typhimurium is of growing significance for several years. Moreover, many other monophasic serovars and strains were found. Further 54 different serovars could be identified, each represented by one to eight isolates. Finally, three cases were rare infections with serovars belonging to the subspecies *arizonae* and *houtenae*.

The sex ratio among the cases is balanced and included 50.7% of female and 49.3% of male patients. The distribution by age group (table 4) exhibits a maximum of cases in infants and a smaller peak in young adults. This is a pattern that has proven to remain very stable since 1988 (e.g. [8] for the year 1992). Almost one third (30.7%) of the patients had to be hospitalised.

In table 5, the collected data on foreign travel is shown and compared to the respective results of a case-control study which was carried out in 1993 to determine the risk factors for sporadic cases of salmonellosis in Switzerland [9]. In total, about a third (35.7%) of case persons who responded to the respective question reported having been abroad in the relevant time segment before falling ill. This is a slight but not statistically significant (overlapping confidence intervals) increase with respect to the 28.7% that were found 18 years before. However, when only cases with isolates belonging to the serovar Enteritidis are taken into consideration, the travel-associated portion more than doubled (45.4% compared to 20.4%), resulting in a significant increase. On the other hand, when regarding only isolates belonging to serovars other than Enteritidis, a sig-

Table 3: *Salmonella* subspecies and serovars isolated from 499 patients included in the study, Switzerland, February 2011 to January 2012.

Serovar	Number of isolates	Percent
Salmonella enterica ssp. *enterica*		
– Enteritidis	144	28.8
– Typhimurium	93	18.6
– Bardo	47	9.4
– 4,12:i:- (monophasic variants of S. Typhimurium-like strains)	43	8.6
– Other monophasic serovars: - 11:i:- - 4,12:b:- - 4,12:d:- - 9,12:l,v:- - 41:z4,z24:- - monophasic strains, undifferentiated	26 2 2 1 1 1 19	5.0
– Newport	8	1.6
– Infantis, Kentucky	7 each	1.4 each
– Corvallis, Hadar, Napoli, Panama, Virchow	5 each	1.0 each
– Brandenburg, Senftenburg	4 each	0.8 each
– Agona, Anatum, Derby, Java, Veneziana, Weltevreden	3 each	0.6 each
– Agbeni, Bareilly, Bovismorbificans, Braenderup, Kottbus, Montevideo, Muenchen, Oranienburg, Reading, Tennessee*, Thompson	2 each	0.4 each
– Belem, Blockley, Brancaster, Colindale, Decatur, Doncaster, Ealing, Eboko, Give, Goldcoast, Haifa, Hessarek, Indis, London, Matopeni, Minnesota, Monschaui, Obogu, Oslo, Saintpaul, Schwarzengrund, Stanley, Stourbridge, Telekebir	1 each	0.2 each
– 8,20:-:- (O-Form)	1	0.2
– rauh:e,h:e,n,z15 (O-Rauhform)	1	0.2
– rauh:i:1,2 (O-Rauhform)	1	0.2
– Serogroup B	5	1.0
– Serogroup C	7	1.4
– Serogroup D	3	0.6
– Serogroup E	2	0.4
– Enterica, undifferentiated	5	1.0
Salmonella enterica ssp. *arizonae*		
– 41:z4,z23:-	1	0.2
Salmonella enterica ssp. *houtenae*		
– 44:z4,z23:- *	1	0.2
– 38:z4,z23:-	1	0.2
Total	500*	100.0

* One double infection with *S. tennessee* and *S. houtenae* 44:z4,z23:-.

nificantly smaller portion of travel-association than in 1993 was found (31.8% compared to 55.6%). However, this portion increased to 37.7% (and the difference compared to 1993 becomes insignificant) if the two serovars Bardo and monophasic 4,12:i:- are removed from the non-Enteritidis group. These two serovars were not present in 1993, and as already mentioned, the appearance of *S.* Bardo was outbreak-related, and the occurrence of the monophasic serovar 4,12:i:- can also be regarded as an epidemic problem. In a recent molecular-genetic analysis of serovar 4,12:i:- clones isolated from human sources between 2007 and 2011, Gallati et al. found that as many as 42% of them belonged to the same pulsotype. At the same time, this pulsotype was also the most prevalent among the monophasic pork isolates [10].

The three serovars that followed *S.* Enteritidis in frequency of isolation (table 3) are for the most part of domestic origin. If the non-Enteritidis group is analysed without these three, its travel-associated portion is 43% and therefore very similar to the corresponding portion in patients infected with *S.* Enteritidis (table 5).

Almost half of the travel destinations (48.6%) were situated in Europe, predominantly in countries of Southern Europe and the Balkans. Asia is represented by almost a quarter of the cases (table 6). This pattern differs considerably from the one that is produced by infections with *Salmonella* Typhi, causative agent of the typhoid fever. In Switzerland, this disease is almost exclusively travel-associated, the majority of cases being imported from Asia, predominantly from the Indian subcontinent [11].

Discussion

Salmonellosis and travelling

Apart from salmonellosis being a foodborne infection, it remains to a greater extent a travel-related illness. The significant increase in the percentage of travel-related *S.* Enteritidis infections that is demonstrated by the comparison between the data from 2012 and 1993 might be a consequence of the reduction of domestic infections in this time period. In 2010, official surveillance programmes in Switzerland found 2 of 376 (0.53%) flocks of layer hens to be positive for *S.* Enteritidis [12]. In the same period of observation, the average flock prevalence in the EU countries was about four times higher (1.6%) than in Switzerland, and in a few countries, the prevalence was still >5% [1]. It is fair to assume that on trips to certain European countries, the probability of getting an egg-related salmonellosis is higher than in Switzerland.

Table 4: Isolation rate of *Salmonella* sp. by age group in 499 patients included in the study (number of isolations per 100,000 residents), Switzerland, February 2011 – January 2012.

Age group (years)	No.	No./100'000
0–4	67	16.8
5–9	38	9.8
10–19	61	7.1
20–29	82	8.0
30–39	48	4.4
40–49	57	4.4
50–59	62	5.7
60–69	45	5.2
70+	39	4.1

Table 5: Travel abroad in the 3 days preceding onset of illness, based on the number of patients from whom information about travel activity could be recovered. Switzerland, February 2011 to January 2012.

Travel abroad (yes / no)	Number of isolates	Percent (95% CI)	CC-Study 1993* Percent (95% CI)
All serovars (total: 415):			
Yes	148	35.7 (31.2–40.4)	28.7 (23.1–34.9)
No	267	64.3	71.3
Serovar Enteritidis (total: 119):			
Yes	54	45.4 (36.6–54.4)	20.4 (14.8–27.0)
No	65	54.6	79.6
All serovars non-Enteritidis (total: 296):			
Yes	94	31.8 (26.6–37.2)	55.6 (42.2–68.4)
No	202	68.2	44.4
Serovar Typhimurium (total: 74):			-
Yes	20	27.0	
No	54	73.0	
Serovar Bardo (total: 41):			-
Yes	6	14.6	
No	35	85.4	
Serovar 4,12:i:- (monophasic) (total: 32):			-
Yes	4	12.5	
No	28	87.5	
Serovars non-Enteritidis, without Bardo and 4,12:i:- (monophasic) total: 223):			-
Yes	84	37.7 (31.5–44.2)	
No	139	62.3	
Serovars non-Enteritidis, without Typhimurium, Bardo and 4,12:i:- (monophasic) (total: 149):			
Yes	64	43.0 (35.2–51.0)	
No	85	57.0	

* Case-control study on sporadic cases of salmonellosis, carried out in 1993. This study included 223 case-control pairs [9].
CI = confidence interval

A contrasting development could be observed regarding human *Campylobacter* infections. *Campylobacter* is the most frequently notified infectious pathogen in Switzerland, since it exceeded the number of *Salmonella* infections in 1995, and the long term trend is upwards [3]. In 1991, a case-control study to determine the risk factors for sporadic cases of *Campylobacter* enteritis in Switzerland identified the consumption of poultry and poultry liver within 5 days prior to the outbreak of the illness as the risk factors among foods. It was also found that a large part of the infections were acquired through catering on foreign travel (46.1% of the cases against 9.2% for the controls) [13]. However, campylobacteriosis due to foreign travel has markedly decreased in the meantime: a study carried out in 2009 reported that 82% of isolates were obtained from domestic cases [14]. It seems evident that for *Campylobacter*, the cause for the rising trend in infections is mainly domestic and is related to the unsolved problems concerning *Campylobacter* presence in poultry flocks and chicken meat [15].

Studies in other European countries also came to the conclusion that salmonellosis is partly travel-related. The results of a recent case-control study in Lower Saxony, Germany [16], indicated a portion of 10.4% of case persons being abroad within 3 days before onset of illness, but in the multiple logistic regression analysis, this was only of borderline significance. In an earlier Danish study (1997–1999), foreign travel was found to be a major risk factor for sporadic *S.* Enteritidis infection, as 25% of cases were attributed to travel outside of Denmark in the week before onset of symptoms [17]. In the Netherlands (2002/03), travelling abroad was reported by 31% of S. Enteritidis and 15% of S. Typhimurium cases, resulting in a strong association in the single-variable analysis [18].

The highest degree of travel association was found in the Scandinavian countries Sweden and Norway. In a Swedish study (1997–2003), 78% of cases were associated with travel to 151 different countries of which the ten most often stated were, in descending order: Spain, Thailand, Greece, Turkey, Tunisia, Poland, Morocco, Portugal, Cyprus and Indonesia [19]. The same database was used to calculate the risk of being notified with a *Salmonella* infection after return from each European country. The highest risk for acquiring salmonellosis was estimated for Bulgaria, followed by Turkey and Malta [20]. The reduction of domestic cases in Sweden was achieved by a stringent *Salmonella* surveillance and control programme. It started already 1970 by voluntary (and since 1984 mandatory) bacteriological testing of broiler flocks before slaughter. This was followed in 1990 by voluntary (and since 1994 mandatory) bacteriological examination of pooled fecal samples of layer flocks with subsequent culling of positive flocks [21]. In Norway (1975–1996), it was found that 90% of the cases from whom a travel history is available have acquired their infection abroad. The only factor among foods which remained independently associated with an increased risk in conditional logistic regression analysis was consumption of chicken meat purchased abroad during holiday visits to neighbouring countries [22].

Reasons for the decrease of salmonellosis cases in Switzerland

From the mid-1980s to 1992, the incidence for salmonellosis was increasing, and infections with *Salmonella* Enteritidis were epidemic, in Switzerland [3] as well as in many other industrialised countries [23]. Many studies demonstrated the ability of *S.* Enteritidis to cause a mostly symptomless, invasive infection in laying hens, leading to colonisation of their ovaries, followed by transmission of the bacteria to the contents of the eggs [24, 25]. Case-control studies performed in several countries yielded the result that raw or undercooked eggs were the most important risk factors among foods for the acquisition of an *S.* Enteritidis infection (e.g. [9, 17, 18, 26, 27]). According to the most recent scientific report of the European Food Safety Authority (EFSA) and the European Centre for Disease Prevention and Control (ECDC) on trends and sources of zoonoses, zoonotic agents and food-borne outbreaks, *S.* Enteritidis and *S.* Typhimurium are the serovars most frequently associated with human illness in the EU. Human *S.* Enteritidis cases are most commonly associated with the consumption of contaminated eggs and poultry meat, while *S.* Typhimurium cases are mostly associated with the consumption of contaminated pig, poultry and bovine meat [1]. From 1992 on, the number of cases of salmonellosis began to drop steadily. A key factor which initiated this trend was the development of an ELISA to test shell eggs for antibodies against *S.* Enteritidis making a rapid and simple screening of flocks of layer hens possible [28]. This test was com-

Table 6: Destinations of patients who had travelled abroad in the 3 days preceding illness, Switzerland, February 2011 to January 2012.

Continent and country	No.	Percent
Europe		
Southern Europe (Greece, Italy, Portugal, Spain, Turkey)	29	19.8
Balkan States (Albania, Bosnia-Herzegovina, Kosovo, Croatia, Macedonia, Romania, Serbia)	18	12.3
Other Eastern European countries (Poland, Czech Republic, Russia)	3	2.8
Western Europe (Austria, Belgium, France, Germany, United Kingdom)	18	12.3
Northern Europe (Norway, Sweden)	2	1.4
Asia		
China, Dubai, India, Indonesia, Israel, Malaysia, Maldives, Nepal, Singapur, Sri Lanka, Thailand, Vietnam	35	23.9
Africa		
Egypt, Ghana, Kenya, Morocco, Mauritius, Namibia, Senegal, Seychelles, Tansania, Tunisia	20	15.6
The Americas		
Argentina, Bahamas, Brazil, Costa Rica, Dominican Republic, Ecuador, Cuba, Mexico, USA	13	9.7
Australia and Oceania		
Australia	1	0.7
Unknown	5	3.4

mercialised and shortly after declared mandatory by the Ordinance on Epizootic Diseases [29] for the surveillance of layer flocks. The implementation of this legal measure and the consequent culling of positive flocks played an important role in the control of the *S.* Enteritidis epidemic in Switzerland, as they allowed the extent of the transmission of the pathogen by raw eggs to be limited. Other measures concerned the transport and storage of the eggs and the imports of chicks. Furthermore, quality systems in gastronomy and catering businesses addressed the safe handling of dishes containing raw eggs. Subsequently, the number of laboratory notifications for S. Enteritidis declined and outbreaks became significantly rarer. The remaining few outbreaks occurred mainly in private households where the recommendations on safe handling and use of raw eggs were less well known than in the retail business and in gastronomy.

A second reason for the significant decrease of cases of salmonellosis might be chicken meat which is known to be a relevant source for salmonellae of various serovars. In 1990 and 1991, a study of the FOPH revealed 130 of 945 (13.8%) samples of neck skin lobs from slaughtered broilers to be positive for *Salmonella* [30]. In 2010, about 20 years later, only 38 of 1,363 (2.8%) samples of fresh chicken meat were shown to be positive in test programmes of the poultry industry [12]. This is a dramatic decrease demonstrating the effect of sanitation measures taken by the producers of chicken meat. There is no doubt that the containment of the chicken meat reservoir had an impact on the number of clinical cases.

In the European Union, monophasic *S.* Typhimurium 4, [5],12:i:- has entered the top 10 group as the fourth most commonly reported serovar (1.5 % of reported cases) [1]. A similar situation is true for Switzerland where cases with this serovar were steadily increasing in the past few years. Pigs seem to be the most relevant reservoir, and in Germany, 4, [5],12:i:- strains from pigs and humans were shown to be highly related [31]. Some recent outbreaks could be traced back to pork sausages [32, 33]. The presence of monophasic *S.* Typhimurium 4, [5],12:i:- in pig fattening farms is only a part of the problem. It could also be shown that slaughtering, dressing, cutting and deboning operations contribute to the spread of salmonellae [34]. The Swiss Ordinance on Hygiene, which is congruent with the regulations on food hygiene of the European Community, decrees a microbiological criteria for *Salmonella* spp. in minced meat and meat preparations from all types of meat except chicken meat [35]. This criterion should be consequently enforced by the authorities of food control in order to direct pork producers to a more efficient containment of *Salmonella* spp. in the primary production, in the slaughterhouse and in meat processing.

In the present survey of 2011/12, *S.* Bardo belonged to the four most frequent serovars. PFGE-typing carried out by the NENT showed all *S.* Bardo isolates belonging to the same pulsotype. This finding was evidence for an outbreak. Unfortunately, subsequent interviews with patients did not allow to identify the food-stuff responsible for the infections [36]. *S.* Bardo is a rare serovar which was demonstrated on chicken carcasses, in bovines and in pet reptiles [37–39]. To our knowledge, the cluster of clinical cases due to *S.* Bardo in Switzerland is the first outbreak with this serovar.

Finally, it can be concluded that measures to reduce the prevalence of enteric salmonellae in livestock taken in the industrialised countries achieved a significant drop of human infections in the past two decades. Switzerland belonged to those countries which controlled the epidemic by specifically screening shell eggs for contamination with *S.* Enteritidis already in the early 1990s. The fact that infections due to this serovar are now significantly more often travel-related than domestic clearly illustrates the success of the measures taken.

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Figures (large format)

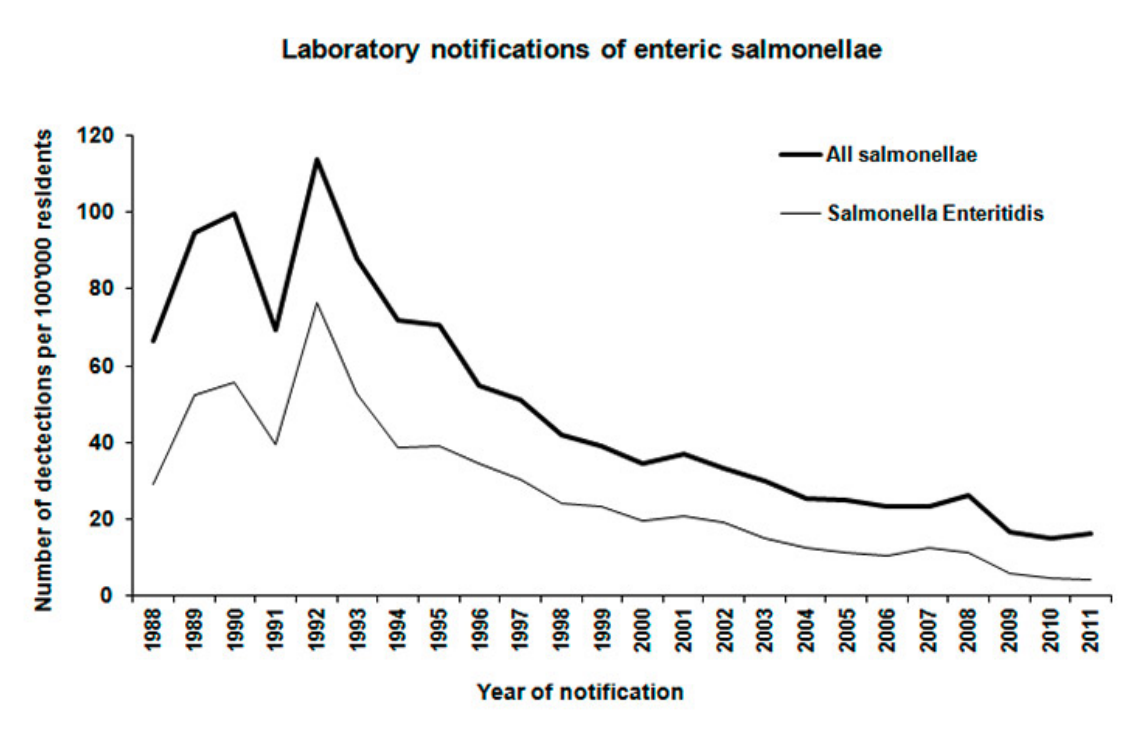

Figure 1

Notifications by medical laboratories recorded through the mandatory reporting system of the FOPH (reproduced from [3]).