

LONDON
SCHOOL of
HYGIENE
& TROPICAL
MEDICINE



Santos, AC; Roberts, JA; Cook, AJ; Simons, R; Sheehan, R; Lane, C; Adak, GK; Clifton-Hadley, FA; Rodrigues, LC (2011) Salmonella Typhimurium and Salmonella Enteritidis in England: costs to patients, their families, and primary and community health services of the NHS. *Epidemiology and infection*, 139 (5). pp. 742-53. ISSN 0950-2688 DOI: 10.1017/S0950268810001615

Downloaded from: <http://researchonline.lshtm.ac.uk/3355/>

DOI: [10.1017/S0950268810001615](https://doi.org/10.1017/S0950268810001615)

Usage Guidelines

Please refer to usage guidelines at <http://researchonline.lshtm.ac.uk/policies.html> or alternatively contact researchonline@lshtm.ac.uk.

Available under license: Copyright the publishers

***Salmonella* Typhimurium and *Salmonella* Enteritidis in England: costs to patients, their families, and primary and community health services of the NHS**

A. C. SANTOS^{1*}, J. A. ROBERTS¹, A. J. C. COOK², R. SIMONS², R. SHEEHAN²,
C. LANE³, G. K. ADAK³, F. A. CLIFTON-HADLEY² AND L. C. RODRIGUES¹

¹ London School of Hygiene and Tropical Medicine, London, UK

² Veterinary Laboratories Agency (VLA), Surrey, UK

³ Health Protection Agency (HPA), Centre for Infections, London, UK

(Accepted 7 June 2010; first published online 2 July 2010)

SUMMARY

This is the first study comparing societal costs of acute illness with *Salmonella* Typhimurium (ST) and *Salmonella* Enteritidis (SE) in the UK. It included the cost and severity of the illness and explored the impact of each *Salmonella* serovar on the patients, their families, the NHS, and the wider economy. The study ascertained confirmed cases of ST and SE between July and November 2008. The mean costs per case were £1282 (ST) and £993 (SE). The indirect costs associated with the work-time lost by the case, parents, or carers were £409 (ST) and £228 (SE); this difference was statistically significant. The aggregate cost of ST and SE identified using laboratory test results for the UK as a whole was estimated as £6.5 million. Work-time lost and caring activities are cost categories that are not frequently investigated within the infectious intestinal disease literature, although they represent an important societal cost.

Key words: Family costs, NHS costs, patient costs, *Salmonella*.

INTRODUCTION

Salmonella causes significant diarrhoea, vomiting, nausea, fever, and abdominal pain. It is one of the most important foodborne pathogens in the developed world. It levies a considerable burden in terms of morbidity and mortality [1, 2]. Outbreaks of human salmonellosis are common in many countries and infection has been linked to a range of food vehicles including eggs, chicken, beef, pork, salad vegetables and dairy products [3, 4]. Some cases are associated with travel [5].

Salmonella enterica is a zoonosis and different serovars can be carried by livestock raised for food

production. National surveillance shows that the number of cases of human salmonellosis has declined since 1997. This decline is mainly attributable to the reduction in the incidence of illness due to *Salmonella* Enteritidis (SE) phage type 4, following the introduction of vaccination against SE in the majority of flocks in the UK egg industry [6]. In 2008, there were about 9800 reported cases of human salmonellosis in the UK. Around 4200 were due to SE and 1800 were associated with *Salmonella* Typhimurium (ST) [7]. SE remains most strongly associated with poultry and poultry products. ST has a wide host range, including poultry, cattle, sheep and pigs [8–10]. In the UK, ST was found in about 14% of slaughter pigs in a European baseline abattoir survey [11].

Data from the first Infectious Intestinal Disease study in England (IID) [12], which was conducted in the early 1990s, estimated an annual incidence

* Author for correspondence: Dr A. C. Santos, Faculty of Public Health and Policy, Department of Health Services Research and Policy, London School of Hygiene and Tropical Medicine, 15–17 Tavistock Place, London WC1H 9SH, UK.
(Email: andreia.santos@lshtm.ac.uk)

of 3.2 cases/1000 population of *Salmonella* in the community and 2.3 cases/1000 persons-year to the cases that presented to General Practitioners (GPs). In a recent 10-year period study (1999–2008) in Cambridge, it was estimated that there was an annual incidence of 20.06 cases/100 000 persons, indicating that *Salmonella* infections are still causing considerable morbidity in England [13].

Salmonellosis has a significant socioeconomic impact on the daily activities of cases and carers. It produces considerable morbidity and although deaths are not common they do occur especially in vulnerable people. Families incur expenses and lose time off work because of the illness and their caring responsibilities. Society loses productivity and National Health Service (NHS) resources are used both in primary care and in hospital services [12, 14].

European Commission Regulations require member states to meet targets for reduction of *Salmonella* in different livestock sectors and each member state must present plans for approval in order to meet these reduction targets [15]. Preventive measures in egg production, for instance, have been shown to be successful in reducing morbidity and mortality for salmonellosis [7] and in Denmark, reduction in the prevalence of *Salmonella* infection in pigs was associated with a reduction in human cases [16]. Whether these measures are cost-effective requires investigation.

The research reported here is one component of a multidisciplinary project for *Salmonella* control in pigs. This paper reports on the costs of *Salmonella*, i.e. ST and SE. It includes the cost and severity of the illness and explores the impact of each type on the patients, their families, the NHS, primary and secondary services and the wider economy. This is the first study that compares societal costs of ST and SE in the UK. A subsequent paper will present the integration of these results to a quantitative microbial risk assessment and the cost-effectiveness of interventions to control *Salmonella* infection in pigs, examining the benefits of control represented as avoided cases of human salmonellosis.

METHODS

Study population, sample size and data collection

This economic study was conducted as part of a multidisciplinary project which addressed the epidemiology of *Salmonella* infection in pigs and the

risk of human *Salmonella* attributable to pig meat, through field-based studies. The study consisted of all laboratory-confirmed cases of human ST notified within 2–4 weeks of onset to the Health Protection Agency (HPA). Cases were identified through faecal and blood isolates referred to the HPA *Salmonella* Reference Unit (SRU) for serological and phage typing using the method described by Ward *et al.* [17]. To place ST in the broader context of the *Salmonella* group, we selected a comparable group (of equivalent age and gender) of SE cases, one for each ST case. The objective was to enable us to compare the relative burden of two different *Salmonella* serovars and, in addition, to provide information about SE that was not available from other sources. It was not a case-control study.

The inclusion criteria were as follows: all ages, both sexes, resident in the UK. Cases were included even if their 'stool' request form mentioned travel. Cases of ST and SE from persons in prisons or from those not able to give informed consent and who had no one to act on their behalf were not invited to participate. Cases arising from an outbreak which was known to be under investigation were not included, to avoid jeopardizing the outbreak investigation, but details of the investigation were requested from the investigating team.

It was not possible to determine, for an economic study, the dimensions needed for a statistically derived sample, as sparse information was available about the variation in parameters of notified cases. It was proposed that a replacement sample of 200 cases of ST and 200 age- and sex-matched cases of SE should be recruited into the study.

Ethical approval from the NHS Ethics Committee and the London School of Hygiene and Tropical Medicine was gained before the fieldwork took place. Cases of ST confirmed at the National SRU were randomly selected each week, which matched (age and gender) cases of SE. The addresses of all cases were obtained from the laboratory where the stool sample was initially tested. A consent letter, questionnaire, study information sheet describing the purpose of the study, and a letter from the HPA were sent by post. Those consenting were asked to complete a questionnaire and return it in the stamped addressed envelope provided. All responses were voluntary.

The data collected included: age, gender, household size, length of disease, severity, impact of the illness on the activities of daily living, the use of

healthcare resources, personal medical expenditure, time off work, lost income due to the illness, time off work and loss of income due to caring for the ill. The questionnaire also included a self-assessment on the cases' health status, using a standard methodology (SF-16 and Euroqol [18, 19]). Results of this assessment will be reported separately. Parents or carers of children and carers of infirm patients completed the questionnaire on their behalf. People with language difficulties were asked to use an interpreter who could record the patient's responses to the questionnaire on their behalf.

Cost methodology

This study presents the estimates of the direct costs incurred by parents, families and carers of cases and the direct costs for the use of the NHS by the patients. The costs of laboratory tests, sample collection and analysis were not included in the cost analysis. The frequency of patients' use of NHS resources was collected from the questionnaire. All costs were estimated using standard methodology, where the mean use of resource is multiplied by the unit cost of the referred resource to produce the estimated direct mean cost incurred by the families and the estimated direct mean cost of patients' use of the NHS resources [20, 21].

Direct costs incurred by parents, families and carers were estimated from information on out-of-pocket expenditures. Costs of drugs were assumed to be those informed by the case as direct expenditure for non-prescribed drugs. For prescribed drugs, we considered the prescription charge incurred by the patient, when the family was not eligible for free medicines. No case said they received free medicines. The NHS part of the cost of prescribed drugs was estimated as £18 per case charged, in accordance with 2008 NHS Department of Health figures [22]. This cost has been inputted to the NHS costs accordingly. That deals with the transfer payments.

Cases' cost per call to their GPs was estimated as the average duration of each call to GPs (estimated as 8 minutes and 48 seconds [23] multiplied by the cost per minute (£0.52 [24]). Thus the cost per call was estimated to be £0.44. Parental (and carer) costs of days/time of lost work and income were estimated using the Annual Survey of Hours and Earnings (ASHE) from the UK National Statistics [25] and the current occupation, as informed by the case. This

cost was assumed to be an indirect cost for society and corresponded to the social cost due to one case (parent or carer) being absent from work due to illness.

Costs of GP surgery and home visits, nurse visits, out-of-hours clinic, accident and emergency department (A&E) visits, in-patient infectious disease, intensive therapy unit (ITU), isolation ward (IW), and ambulance to the hospital were estimated based on NHS Reference Costs 2007/2008 data [26]. The unit cost of an in-patient infectious disease was assumed to be the average cost of the low-high infectious status, in accordance with the NHS definition [26]. ITU, IW and ambulance unit costs were also assumed to be an average cost from the general categories presented by the NHS study. Cost of GP phone call to patient was also assumed to be £0.44 per call (see above). NHS direct cost was assumed to be £25.53, based on 2007/2008 figures [23]. Estimation of the average cost for the nurse visits was only available for the period 2004/2005 [27]. Therefore, we have applied a consumer price index to this estimate to bring prices to 2008 levels and have a rough approximation for this cost, i.e. Retail Price Index for group 06 – Health (personal goods and services – health-related items) [28]. All costs are presented in 2007/2008 sterling (£) values.

Analysis

All analysis was undertaken using SPSS version 14.0 [29], where means and proportions were calculated. To test socioeconomic and demographic, and costs and use of resources, we used a Student's *t* test for independent-samples, which compares the means of a normally distributed random variable or the Mann-Whitney *U* test, if the distribution was non-normal. The χ^2 test was used to compare proportions. Only the *P* values of the tests are presented at a significance level of 95% (i.e. *P* = 0.05).

Because we have no statistical distribution of economic variables to test the robustness of estimates, we use sensitivity analysis, which indicates how the estimates would react to percentage changes in the value of the parameters of the model. The analysis was applied to the NHS cost categories. We assumed that the vectors were increased or decreased by 10%, 20% and 50% to indicate the likely boundaries of costs, provided by a 95% confidence interval [14].

RESULTS

Response rate

Between July and November 2008, 2869 reports of ST and SE were generated by the SRU. Of these reports 1254 were followed up to acquire postal address details, of which 724 had full study packs (consent letter, questionnaire, study information sheet and a letter from the HPA) posted. Consent was given by 353 (49%) and 296 (84%) returned the questionnaire. Reasons for non-consent were not provided. From the questionnaires returned, 35 (12%) were either incomplete, with no information at all, or with missing pages. The final useable response was 261 (36% of 724).

Characteristics of the cases

In the ST group, 59% were women (mean age 38 years), and about 41% of the cases were employed; whereas in the SE group 47% were female (mean age 35 years), and 37% were working. For both groups, there was an average of three people living in the household.

Considering these general characteristics, the groups did not significantly differ from each other. However, when we stratified by age group, costs and health outcome in children aged <5 years were significantly different between ST and SE.

Characteristics of the illness and impact on activities of daily living

Diarrhoea, abdominal pain, fever, and headache were the most frequent symptoms associated with ST and SE, although the frequency of vomiting and joint pain was also relatively high. The mean number of days with each symptom was, for ST and SE, respectively: diarrhoea, 8.5 and 9 days; abdominal pain, 6.5 and 7 days; fever, 4 days for both and headache 3 days for both.

The severity of the disease was mostly measured by the ability of the cases to re-start their normal activities. In this study, in spite of diarrhoea symptoms having a mean duration of 8.5 and 9 days for ST and SE, respectively, the reported length of illness from the beginning until the individual was able to carry out daily activities was, on average, 13.5 days and 12 days, respectively. Cases were away from paid work for 5 days and 3 days, from nursery, school or college for 1 and 1.5 day, and from planned leisure and/or social activities for 4 days and 3 days for ST

and SE, respectively. About 21% of ST cases and 22% of SE cases were still suffering from the symptoms at the time of the survey (average of 48 and 49 days for ST and SE, respectively).

Caring activities were observed in different contexts. Cases needed 'someone else to take their place as a carer' (14% and 13%); 'someone to take care of them' (69% and 59%); someone 'to visit the GP surgery' (51% and 15%); help to visit 'out-of-hours clinic' (12% and 10%); help with 'A&E visits' (22% and 10%); someone to 'accompany them to hospital' (13% and 9.5%); and someone to 'stay with them in hospital' (9%), for both ST and SE, respectively. Carers were mostly relatives and friends. For the group who needed someone to take care of them (the major carer group), 10.5% and 15% of the carers took time off work, with an average time of 1.1 and 1.3 days off work. We did not find a statistically significant difference between the ST and SE groups.

Direct out-of-pocket expenses to cases

Costs reflected the severity of the disease. The mean direct out-of-pocket cost (for all age groups) was £55 for ST and £58 for SE, where transport and other costs had a higher proportion of the total (Table 1). Only the 'replacement of clothing cost' was significantly different between the two groups. However, when we stratified by age group, the ST and SE groups presented differences of costs: for children aged <5 years, transport cost ($P=0.006$), extra laundry ($P=0.019$), special food ($P=0.035$), prescribed medicines ($P=0.033$), and toys/books ($P=0.026$) were statistically significant. The average direct costs within these groups were £78 for ST and £40 for SE ($P=0.017$); for adults aged >20 years, the only significant cost that accounted for the difference between ST and SE groups was the special foods cost ($P=0.046$) which was higher for ST adults aged >20 years (£64). The overall *Salmonella* direct cost for the cases was £56 (ST and SE).

The societal indirect cost associated with the loss of work-time by the case, parents of ill children, or carer was £409 for ST and £228 for SE, and this difference was statistically significant between the groups (Table 2). This reflected the distribution of cases and employment status of the cases, parents and carers.

Use and costs of resources to the NHS

The estimated average NHS cost per patient, was £818 and £707, for ST and SE, respectively, where the

Table 1. Direct out-of-pocket expenses to cases by age group (£ sterling, 2008 prices)

	ST (N=124)	SE (N=137)	P value
Children <5 years: mean (range; s.d.)	n=12	n=25	
Transport (including parking)	38.28 (0-400; 114.23)	3.28 (0-20; 6.41)	0.006
Extra laundry	2.5 (0-15; 5.00)	1.12 (0-10; 2.52)	0.019
Replacement of clothing	3.75 (0-20; 7.72)	2.80 (0-20; 5.60)	0.344
Nappies	10.25 (0-40; 12.56)	9.95 (0.35; 9.97)	0.496
Special foods	0.58 (0-7; 2.02)	2.80 (0-30; 6.93)	0.035
Medicines (bought)	2.58 (0-20; 5.76)	2.56 (0-20; 4.80)	0.963
Prescribed medicines (charges)	0	3.60 (0.10-45; 11.77)	0.033
Toys/books, etc.	3.58 (0-43; 12.41)	0.92 (0-10; 2.64)	0.026
Other (disinfectants, phone calls, etc.)	16.67 (0-200; 57.73)	13.12 (0-150; 34.76)	0.490
Average direct cost (children <5 years)*	78.20 (0-440; 129.84)	40.15 (0-180; 44.77)	0.017
Adults >20 years: mean (range; s.d.)	n=84	n=84	
Transport (including parking)	7.31 (0-104; 17.22)	5.73 (0-210; 25.35)	0.759
Extra laundry	2.33 (0-40; 6.80)	1.94 (0-20; 4.63)	0.444
Replacement of clothing	1.68 (0-75; 9.30)	3.75 (0-200; 22.21)	0.144
Nappies	1.18 (0-40; 5.64)	0.81 (0-40; 4.87)	0.370
Special foods	4.57 (0-60; 11.37)	2.20 (0-60; 8.86)	0.046
Medicines (bought)	4.81 (0-50; 9.20)	3.64 (0-30; 6.39)	0.077
Prescribed medicines (charges)	3.06 (1.0-40; 6.97)	2.62 (0.10-25; 5.80)	0.431
Toys/books, etc.	0.30 (0-10; 1.62)	0.31 (0-10; 1.46)	0.944
Other (disinfectants, phone calls, etc.)	38.72 (0-1000; 169.34)	33.01 (0-1600; 184.02)	0.729
Average direct cost (adults >20 years)*	63.94 (0-1000; 198.14)	53.94 (0-1600; 191.80)	0.775
All age groups: mean (range; s.d.)	n=124	n=137	
Transport (including parking)	10.04 (0-400; 39.25)	7.50 (0-300; 33.21)	0.634
Extra laundry	2.47 (0-40; 6.85)	1.86 (0-20; 4.46)	0.204
Replacement of clothing	1.68 (0-75; 8.14)	3.85 (0-200; 19.48)	0.039
Nappies	1.99 (0-40; 6.71)	2.49 (0-40; 6.83)	0.329
Special foods	3.79 (0-60; 9.96)	2.26 (0-60; 8.03)	0.057
Medicines (bought)	3.94 (0-50; 8.12)	3.23 (0-30; 5.92)	0.118
Prescribed medicines (charges)	2.09 (1.0-40; 5.90)	2.35 (0.10-45; 6.86)	0.350
Toys/books, etc.	0.83 (0-43; 4.43)	1.12 (0-50; 5.23)	0.379
Other (disinfectants, phone calls, etc.)	28.08 (0-1000; 141.11)	32.86 (0-1600; 168.59)	0.672
Average family direct costs*	54.93 (0-1350; 169.40)	57.52 (0-1644; 197.33)	0.782
Overall <i>Salmonella</i> cost (ST + SE = 261 cases)	56.43 (0-1644; 183.53)		

* This is the sum of all direct cost items.

P value (0.05) of the *t* test for the difference in means for independent-samples or the Mann-Whitney *U* test if the distribution was non-normal.

main expenditures were for hospitalization (£449 and £319), ITU (£116 and £217), and isolation ward care (£118 and £74). Patients who were admitted to hospital had spent, on average, 1.2 days (those with ST) and 1 day (those with SE) there; there were 20 (16%) and 24 (17%) patients hospitalized, for ST and SE, respectively. Three patients in the ST group and one patient in the SE group were admitted to the ITU; whereas 15 and 13 patients with ST and SE were admitted to the IW (Table 3).

Visits to the GP were common in cases: 97 patients were seen by a GP in the ST group and 115 in the SE group, with an average of 1.5 and 1.8 days of visits,

respectively. The mean cost of a GP surgery visit was £32 and £37 for ST and SE, respectively.

In general, patients in each group were similar to each other, except for GP home visits ($P=0.035$), out-of-hours clinics ($P=0.004$), A&E visits ($P=0.000$) and IW care ($P=0.045$).

When stratified by age we observed that, in our sample, the use of ITU and ambulance were not reported by children aged <5 years. The main costs for this group were for hospitalization (62% and 52%), IW (17% and 13.5%), and GP surgery visits (7% and 14%) for ST and SE, respectively. ST and SE groups were statistically different in this age category for

Table 2. Work time lost, total mean cost (£ sterling, 2008 prices)

Value of work time lost (categories)	Unit cost*	ST (N=124)		SE (N=137)		P value
		Time lost (days) n (mean; s.d.)	Total mean cost (£ 2008)	Time lost (days) n (mean; s.d.)	Total mean cost (£ 2008)	
I	141.84	0	0	5 (1.60; 2.30)	226.94	
II	154.24	17 (10.29; 14.68)	1587.13	12 (4.92; 6.93)	758.86	
III	110.72	6 (8.17; 3.60)	904.58	6 (5.00; 8.15)	553.60	
IV	73.20	7 (9.86; 9.19)	721.75	10 (6.20; 6.14)	453.84	
V	82.08	0	0	1 (28.00; 0)	2298.24	
VI	62.80	8 (7.5; 7.27)	471.00	5 (7.00; 5.83)	439.60	
VII	51.12	11 (11.18; 11.09)	571.52	6 (0.17; 0.41)	8.69	
VIII	70.88	0	0	1 (3.00; 0)	212.64	
IX	52.72	2 (11.50; 19.09)	606.28	6 (15.17; 12.80)	799.76	
Overall	84.24	124 (4.86; 9.43)	409.41	137 (2.71; 6.31)	228.29	0.003

The Annual Survey of Hours and Earnings (ASHE), United Kingdom National Statistics (<http://www.statistics.gov.uk/StatBase/Product.asp?vlnk=15187>).

n, Number of respondents; mean: all respondents including zeros.

Categories: I, Managers and senior; II, professional occupations; III, associate professional and technical occupations; IV, administrative and secretarial occupations; V, skilled trades occupation; VI, personal services; VII, sales and customer services occupation; VIII, process, plant and machine operations; IX, elementary occupations.

* Unit cost per day by work category; calculated as median hourly paid (excluding overtime) multiplied by 8 hours.

P value (0.05) of the *t* test for the difference in means for independent-samples or the Mann-Whitney *U* test if the distribution was non-normal.

A&E visits, hospitalizations, IW costs, and prescribed medicine costs.

For the >20 years group, hospitalization (53% and 40.5%), ITU (19% and 40.5%) and IW (13% and 7%) accounted for the main NHS costs for ST and SE, respectively. A&E visits and IW explained the differences between the ST and SE groups.

Sensitivity analysis

Table 4 shows the sensitivity analysis. NHS costs were robust estimates lying within the 10% sensitivity band, which means that variations of 10% (to more or less) of the best estimated values were still lying within the confidence interval. The limits for the 95% confidence interval were large for most of the estimated costs, especially for hospitalization, ITU and IW (categories that contribute most to the NHS total mean cost), GP home visit, out-of-hours clinic, and ambulance, and it reflected the skewed distribution of illness.

Mean and total costs to society

Costs of use of NHS resources were proportionally the highest social cost related to ST and SE: 64% and

71%, respectively. Families faced 4% and 6% of the total social cost; and the proportions of the indirect cost with work-time lost were 32% and 23% for ST and SE, respectively. The mean social costs per case of salmonellosis were £1282 (ST) and £993 (SE). Considering 1829 ST cases and 4190 SE cases were reported in 2008 that shared the same case definition as the cases reported [30], the total cost for the UK economy for these two bacteria was more than £6.5 million. Of this, the NHS cost would have approximated to £4.5 million (68.5% of the total). The share of the burden to cases and carers was estimated as £2 million (31.5%) (Table 5).

DISCUSSION

This is the first study where the societal costs were compared for two different *Salmonella* serovars, showing how this illness can affect the families and the NHS.

Salmonellosis due to ST and SE had a substantial social cost: an average of £1282 and £993 per case, respectively, and a total cost for the UK wider economy of more than £6.5 million. This estimate does not include the community cases that either did not see

a GP or saw a GP but were not asked to bring a stool sample for examination. As demonstrated in the IID study, the average cost per case is lower if the community cases who did not seek medical advice are included. The difference of the estimated costs between the two serovars is explained largely by the absence of NHS cost in the community group and by the reduced severity of illness and less time off work. Cases with ST would spend more time away from paid work and would need more time from someone else to take care of them, to accompany them to visit the doctors and/or to be with them at the hospital. Cases with ST would also spend more NHS resources compared to the SE group. However, these results should be interpreted with caution due to many inherent biases that might influence the estimated average costs and the difference between them.

The study may have lacked power to detect differences in some categories due to the limited sample size, which was composed of cases identified in the laboratory that returned the questionnaire, not from a required sample size for hypothesis tests. This procedure can lead to bias of selection where only individuals from a better economic standard and educational level may have been included, affecting the estimated costs and the differences between them [31]. This may have been reflected in the work categories used as the basis to calculate the work-time lost by cases, on the selection of patients with underlying medical conditions associated with ST and SE, which may have affected their hospitalization time and time at the ITUs or IWs. The selection bias may also have been associated with the many unique genotypes represented in both the ST and SE categories. No further investigations were conducted to overcome these possible sources of bias.

Whereas the difference between the estimated work-time lost by cases may have been affected by selection bias, our results clearly suggest that the health burden of salmonellosis in terms of absence from work is considerable: ST cases lost, on average, 4.86 days and SE cases 2.71 days.

Work-time lost by cases, parents or carers and caring activities are cost categories that are not frequently investigated within the infectious intestinal disease literature, although they represent an important societal cost, as demonstrated in this study. In most previous studies attention has been concentrated on hospitalization and ambulatory costs. In the first IID study conducted in England [12], the overall mean loss of days of paid employment of salmonellosis

cases, parents or carers was 4.83 days. Specifically for SE, this was 3.48 days, with an overall mean cost of £370 to the case and £71 to the carer (total case and carer £440); whereas in our study, cases with SE spent, on average, 2.71 days away from paid work, costing £228 to society. No societal specific cost per ST case was reported by the IID study, probably due to the small sample size.

There were very large differences in the NHS costs estimated by the IID study and our study: the ST mean cost was estimated as £133 (excluding laboratory costs) in the IID study and £818 in our study; for SE it was £48 and £707, respectively. These differences can be explained by the hospitalization costs. In the IID study, no cases reported admission to the ITU or IW, while in our study, four cases (three ST and one SE) said they used ITU resources and 28 cases (15 ST and 13 SE) used IW resources. These costs represented 29% and 41% of our total NHS estimated direct costs. Another substantial cost was for hospital admission: ST cases reported about 0.36 days spent at hospital in the IID study, while in our study the average was 1.24 days; for SE, no cases said they had spent time at the hospital in the IID investigation, but in our study cases stated they spent, on average, 0.88 days in hospital. The hospital costs represented 55% and 45% of the total NHS direct cost per patient with ST and SE, respectively [12].

The fact that the first IID study did not report on admission to ITUs and IWs might be related to the small sample size that was available for analysis during that period and, hence, has made it difficult to capture information from the more serious cases. It is also possible that some of the seriously ill cases who were admitted to hospital were lost to the study sample (J. A. Roberts, personal communication). On the other hand, the 261 cases investigated by our study could represent a more severely ill group of people, for whom laboratory specimens were available. We did not conduct any medical record investigations to dissociate *Salmonella* from any other medical condition, and then estimate the costs accordingly. Moreover, this study did not include cases that were not tested, i.e. those in the community and those presenting to a GP who were not asked for a stool examination. Consequently, these findings may not be representative of the whole population.

The difference in NHS costs for the two groups was statistically significant only for GP home visits ($P=0.035$), out-of-hours clinics ($P=0.004$), A&E visits ($P=0.000$) and IW care ($P=0.045$). This suggests

Table 3. Breakdown of NHS costs per case (£ sterling, 2007/2008 prices)

NHS cost category	NHS reference price (£)	ST (N=124)		SE (N=137)		P value
		n (mean; s.d.)	Cost per case (£)	n (mean; s.d.)	Cost per case (£)	
Children <5 years, n (mean; s.d.)		n=12		n=25		
GP surgery visit	21.40	11 (1.92 t; 1.16)	41.09 (7.4%)	23 (2.04 t; 1.48)	43.66 (14.2%)	0.594
GP home visit out of hours	93.73	0	0	1 (0.04 t; 0.20)	3.75 (1.2%)	0.160
Nurse home visit*	56.00	2 (0.25 t; 0.62)	14.00 (2.5%)	6 (0.40 t; 0.82)	22.40 (7.3%)	0.288
GP phone call: NHS	0.44	10 (1.92 t; 1.44)	0.85 (0.2%)	20 (1.96 t; 1.64)	0.86 (0.3%)	0.850
GP phone call: patient	0.44	4 (0.42 t; 0.67)	0.18 (0.0%)	15 (1.12 t; 1.27)	0.49 (0.2%)	0.101
NHS direct	22.50	5 (0.56 t; 0.53)	12.60 (2.3%)	10 (0.40 t; 0.50)	9.00 (2.9%)	0.063
Out-of-hours clinic	75.00	1 (0.08 t; 0.29)	6.00 (1.0%)	2 (0.16 t; 0.62)	12.00 (3.9%)	0.400
A&E visit	79.00	4 (0.50 t; 0.90)	39.50 (7.1%)	3 (0.12 t; 0.33)	9.48 (3.1%)	0.002
In-patient: infectious disease	362.00	4 (0.96 d; 1.74)	347.52 (62.1%)	6 (0.44 d; 0.92)	159.28 (51.7%)	0.038
Intensive therapy unit	1447.00	0	0	0	0	—
Isolation ward	130.00	2 (0.75 d; 1.76)	97.50 (17.4%)	3 (0.32 d; 0.90)	41.60 (13.5%)	0.033
Ambulance (to the hospital)	212.00	0	0	0	0	0.918
Prescribed medicine (charges)†	18.00	0	0	3 (0.52 m; 1.66)	5.76 (1.9%)	0.028
NHS cost children <5 years			559.24 (100%)		308.28 (100%)	
Adults >20 years, n (mean; s.d.)		n=84		n=84		
GP surgery visit	21.4	66 (1.49 t; 1.33)	31.89 (3.5%)	69 (1.75 t; 1.63)	37.45 (4.2%)	0.724
GP home visit out of hours	0	11 (0.15 t; 0.42)	14.06 (1.6%)	10 (0.15 t; 0.45)	14.06 (1.6%)	0.945
Nurse home visit*	93.73	24 (0.40 t; 0.89)	22.40 (2.5%)	18 (0.27 t; 0.87)	15.12 (1.7%)	0.175
GP phone call: NHS	56.00	56 (1.57 t; 1.75)	0.69 (0.1%)	52 (1.55 t; 1.59)	0.68 (0.1%)	0.945
GP phone call: patient	0.44	51 (0.87 t; 0.89)	0.38 (0.0%)	51 (0.95 t; 1.07)	0.42 (0.0%)	0.529
NHS direct	0.44	23 (0.29 t; 0.46)	6.52 (0.7%)	11 (0.15 t; 0.37)	3.37 (0.4%)	0.025
Out-of-hours clinic	22.50	6 (0.14 t; 0.64)	10.50 (1.2%)	3 (0.07 t; 0.37)	5.25 (0.6%)	0.087
A&E visit	75.00	20 (0.26 t; 0.49)	20.54 (2.3%)	7 (0.08 t; 0.28)	6.32 (0.7%)	0.000
In-patient: infectious disease	79.00	13 (1.32 d; 4.01)	477.84 (52.9%)	14 (1.00 d; 3.25)	362.00 (40.5%)	0.233
Intensive therapy unit	362.00	3 (0.12 d; 0.65)	173.64 (19.2%)	2 (0.25 d; 2.30)	361.75 (40.5%)	0.289
Isolation ward	1447.00	11 (0.93 d; 3.06)	120.90 (13.4%)	8 (0.51 d; 2.09)	66.30 (7.4%)	0.050
Ambulance (to the hospital)	130.00	7 (0.09 t; 0.29)	19.08 (2.1%)	6 (0.08 t; 0.27)	16.96 (1.9%)	0.186
Prescribed medicine (charge)†	212.00	18 (0.43 m; 1.01)	4.68 (0.5%)	16 (0.34 m; 0.78)	3.50 (0.4%)	0.259
NHS cost >20 years	18.00		903.12 (100%)		893.18 (100%)	

Table 3 (cont.)

NHS cost category	NHS reference price (£)	ST (N = 124)		SE (N = 137)		P value
		n (mean; s.d.)	Cost per case (£)	n (mean; s.d.)	Cost per case (£)	
All age groups, n (mean; s.d.)		n = 124		n = 137		
GP surgery visit	21.40	97 (1.48 t; 1.28)	31.67 (3.9%)	115 (1.75 t; 1.52)	37.45 (5.3%)	0.557
GP home visit out of hours	93.73	13 (0.22 t; 1.02)	20.62 (2.5%)	12 (0.12 t; 0.38)	11.25 (1.6%)	0.035
Nurse home visit*	56.00	31 (0.36 t; 0.88)	20.16 (2.5%)	30 (0.30 t; 0.82)	16.80 (2.4%)	0.343
GP phone call: NHS	0.44	82 (1.48 t; 1.60)	0.65 (0.1%)	91 (1.55 t; 1.51)	0.68 (0.1%)	0.971
GP phone call: patient	0.44	68 (0.77 t; 0.85)	0.34 (0.0%)	85 (0.96 t; 1.04)	0.42 (0.1%)	0.714
NHS direct	22.50	35 (0.31 t; 0.46)	6.97 (0.9%)	26 (0.20 t; 0.40)	4.50 (0.6%)	0.147
Out-of-hours clinic	75.00	12 (0.19 t; 0.83)	14.25 (1.7%)	4 (0.07 t; 0.39)	5.25 (0.7%)	0.004
A&E visit	79.00	25 (0.25 t; 0.56)	19.75 (2.4%)	12 (0.09 t; 0.29)	7.11 (1.0%)	0.000
In patient: infectious disease	362.00	20 (1.24 d; 3.85)	448.88 (54.9%)	24 (0.88 d; 2.97)	318.56 (45.0%)	0.083
Intensive therapy unit	1447.00	3 (0.08 d; 0.53)	115.76 (14.2%)	1 (0.15 d; 1.79)	217.05 (30.7%)	0.373
Isolation ward	130.00	15 (0.91 d; 3.19)	118.30 (14.5%)	13 (0.57 d; 2.17)	74.01 (10.5%)	0.045
Ambulance (to the hospital)	212.00	9 (0.08 t; 0.27)	16.96 (2.1%)	7 (0.05 t; 0.23)	10.60 (1.5%)	0.762
Prescribed medicine (charge)†	18.00	19 (0.30 m; 0.85)	3.31 (0.4%)	20 (0.33 m; 0.96)	3.59 (0.5%)	0.511
NHS cost per case			817.62 (100%)		707.27 (100%)	
Overall <i>Salmonella</i> NHS cost/case (ST + SE = 261 cases)	762.44					

n, Number of respondents; mean, all respondents including zeros; d, days; t, times; m, medicines.

* 2004/2005 price.

† We have reduced the charges paid by cases to account for transferences.

P value (0.05) of the *t* test for the difference in means for independent-samples or the Mann–Whitney *U* test if the distribution was non-normal.

Table 4. *Sensitivity analysis*

NHS cost category	-50%	-20%	-10%	Best estimate	95% CI	+10%	+20%	+50%
ST NHS cost per case								
GP surgery visit	15.84	25.34	28.50	31.67	26.75-36.38	34.84	38.00	47.51
GP home visit out of hours	10.31	16.50	18.56	20.62	3.75-37.49	22.68	24.74	30.93
Nurse home visit	10.08	16.13	18.14	20.16	11.76-29.12	22.18	24.19	30.24
GP phone call: NHS	0.33	0.52	0.59	0.65	0.52-0.77	0.72	0.78	0.98
GP phone call: patient	0.17	0.27	0.31	0.34	0.27-0.40	0.37	0.41	0.51
NHS direct	3.49	5.58	6.27	6.97	4.95-9.00	7.67	8.36	10.46
Out-of-hours clinic	7.13	11.40	12.83	14.25	3.75-25.50	15.68	17.10	21.38
A&E visit	9.88	15.80	17.78	19.75	11.85-27.65	21.73	23.70	29.63
In patient: infectious disease	224.44	359.10	403.99	448.88	199.10-695.04	493.77	538.66	673.32
Intensive therapy unit	57.88	92.61	104.18	115.76	101.29-260.46	127.34	138.91	173.64
Isolation ward	59.15	94.64	106.47	118.30	44.20-192.40	130.13	141.96	177.45
Ambulance (to the hospital)	8.48	13.57	15.26	16.96	6.36-27.56	18.66	20.35	25.44
Prescribed medicine (charges)	1.66	2.65	2.98	3.31	1.10-66.00	3.64	3.97	4.97
Total	408.81	654.10	735.86	817.62	—	899.38	981.14	1226.43
SE NHS cost per case								
GP surgery visit	18.73	29.96	33.71	37.45	31.89-42.80	41.20	44.94	56.18
GP home visit out of hours	5.63	9.00	10.13	11.25	4.69-16.87	12.38	13.50	16.88
Nurse home visit	8.40	13.44	15.12	16.80	9.52-24.64	18.48	20.16	25.20
GP phone call: NHS	0.34	0.54	0.61	0.68	0.57-0.80	0.75	0.82	1.02
GP phone call: patient	0.21	0.34	0.38	0.42	0.34-0.50	0.46	0.50	0.63
NHS direct	2.25	3.60	4.05	4.50	3.15-6.30	4.95	5.40	6.75
Out-of-hours clinic	2.63	4.20	4.73	5.25	0.75-10.50	5.78	6.30	7.88
A&E visit	3.56	5.69	6.40	7.11	3.16-11.06	7.82	8.53	10.67
In patient: infectious disease	159.28	254.85	286.70	318.56	130.32-492.32	350.42	382.27	477.84
Intensive therapy unit	108.53	173.64	195.35	217.05	0-665.62	238.76	260.46	325.58
Isolation ward	37.01	59.21	66.61	74.01	26.00-120.90	81.41	88.81	111.02
Ambulance (to the hospital)	5.30	8.48	9.54	10.60	2.12-19.08	11.66	12.72	15.90
Prescribed medicine (charge)	1.80	2.87	3.23	3.59	1.10-66.00	3.95	4.31	5.39
Total	353.64	565.82	636.54	707.27	—	778.00	848.72	1060.91

Table 5. *Total and mean societal cost for ST and SE (£ sterling, 2007/2008 prices)*

	ST (N=124)	SE (N=137)
Cases and families direct costs	54.93 (4%)	57.52 (6%)
Indirect costs	409.41 (32%)	228.29 (23%)
NHS direct costs	817.62 (64%)	707.27 (71%)
Mean societal costs (per case)	1281.96 (100%)	993.08 (100%)
Number of cases notified in 2008*	1829	4190
Total family costs (per group)	100 466.97 (A)	241 008.80 (B)
Total indirect costs (per group)	748 810.89 (C)	956 535.10 (D)
Total NHS direct costs (per group)	1 495 426.98 (E)	2 963 461.30 (F)
Total societal costs (A + B + C + D + E + F)		6 505 710.04

Source: HPA, 2009 [30].

* Provisional data.

that ST might be more expensive to treat than SE. These findings are similar to those found in the IID study, although no test to detect differences between

groups was conducted by that investigation. However, our limited sample size precluded a fully reliable estimate of the costs.

Comparing our findings with the international estimates, we can find some similarities. In a 2009 study in Spain, the cost of a non-specific *Salmonella* infection was estimated to be €2411 (£2150; 2009 mean exchange rate). However, this investigation included patients with human immunodeficiency virus – acquired immune deficiency syndrome (HIV-AIDS), neoplasias or immunological cases. No specific cost was estimated for ST or SE [32]. Another study in Spain estimated an overall health system cost of €710 (£633; 2009 mean exchange rate) for gastrointestinal diseases, including *Salmonella*. This estimated cost included hospital admission, visits to A&E, visits to the GP, and laboratory investigations but no costs to patients [33].

The estimated overall direct out-of-pocket expenses of *Salmonella* cases were relatively stable. For the IID study, an overall mean cost of £32 was estimated. The IID study was about 26% higher than our estimates. Nappies, bleach and washing powder represented a large element of costs for cases in 1994. In 2007/2008 respondents expended more on transport, nappies and other items.

The estimated costs in our study are likely to be underestimated, as we have not included the costs of cases that were treated at home, investigation costs and laboratory costs. We did not estimate the cost for the time lost from education or leisure or the extended time suffering from *Salmonella*, in spite of the high estimated number (and proportion) of days when activities of daily living were affected.

The sensitivity analysis showed that our estimates were robust and the high variation of the confidence limits reflected the severity of the disease and the small number of cases in some categories.

This study shows the important impact that *Salmonella* infections have on public health costs and family costs and draws attention to the need to develop actions aimed at controlling this disease. Our results will help policy-makers in determining cost-effective interventions on farms or in abattoirs and ensure that these costs are commensurate with the public health impact of salmonellosis.

ACKNOWLEDGEMENTS

This study would not have been possible without the kind cooperation of the participating patients. This work was funded by the UK Department for Environment, Food and Rural Affairs as part of Project OZ0323. We also thank Paula Francis, Zoe

Chapman, Alexander ‘Sandy’ Miller, the EuroQol Group, and other colleagues throughout LSHTM, VLA and HPA for their assistance, and two anonymous referees for their valuable comments for the improvement of this paper.

DECLARATION OF INTEREST

None.

REFERENCES

1. Mead PS, *et al.* Food-related illness and death in the United States. *Emerging Infectious Diseases* 1999; **5**: 607–625.
2. Adak GK, Long SM, O’Brien SJ. Trends in indigenous foodborne disease and deaths, England and Wales: 1992 to 2000. *Gut* 2002; **51**: 832–841.
3. Adak GK, *et al.* Disease risks from foods, England and Wales, 1996–2000. *Emerging Infectious Diseases* 2005; **11**: 365–372.
4. Irvine RM, *et al.* Outbreak of Newcastle disease due to pigeon paramyxovirus type 1 in grey partridges (*Perdix perdix*) in Scotland in October 2006. *Veterinary Record* 2009; **165**: 531–535.
5. Smith-Palmer A, Cowden JM. Overseas outbreaks of infectious intestinal disease identified in Scotland, 2003 to 2007. *Journal of Travel Medicine* 2009; **16**: 322–327.
6. Cogan TA, Humphrey TJ. The rise and fall of *Salmonella* Enteritidis in the UK. *Journal of Applied Microbiology* 2003; **94**: 114S–119S.
7. Defra. Zoonoses Report United Kingdom, 2008. England: Department for Environment, Food & Rural Affairs, 2010.
8. Snow LC, *et al.* Survey of the prevalence of *Salmonella* species on commercial laying farms in the United Kingdom. *Veterinary Record* 2007; **161**: 417–476.
9. Snow LC, *et al.* Survey of *Salmonella* prevalence on commercial broiler farms in the United Kingdom, 2005/2006. *Veterinary Record* 2008; **163**: 649–654.
10. Milnes A, *et al.* Intestinal carriage of verocytotoxigenic *Escherichia coli* O157, *Salmonella*, thermophilic *Campylobacter* and *Yersinia enterocolitica*, in cattle, sheep and pigs at slaughter in Great Britain during 2003. *Epidemiology and Infection* 2008; **136**: 739–751.
11. Anon. Report of the Task Force on Zoonoses Data Collection on the analysis of the baseline survey on the prevalence of *Salmonella* in slaughter pigs, Part A. *EFSA Journal* 2008; **135**: 1–111.
12. FSA. A report of the study of infectious intestinal disease in England. England: Food Standards Agency, 2000.
13. Matheson N, *et al.* Ten years experience of *Salmonella* infections in Cambridge, UK. *Journal of Infection* 2010; **60**: 21–25.
14. Roberts JA, *et al.* The study of infectious intestinal disease in England: socio-economic impact. *Epidemiology and Infection* 2003; **130**: 1–11.

15. **Anon.** Regulation (EC) No. 2160/2003 of the European Parliament and the Council of 17 November 2003 on the control of salmonella and other specified food-borne zoonotic agents. *Official Journal of the European Union* 2003; **L325**: 1–15 (<http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2003:325:0001:0015:EN:PDF>).
16. **Nielsen B, et al.** A new Salmonella surveillance and control programme in Danish pig herds and slaughterhouses. *Berliner und Münchener Tierärztliche Wochenschrift* 2001; **114**: 323–326.
17. **Ward LR, De Sa JDH, Rowe B.** A phage typing scheme for *Salmonella enteritidis*. *Epidemiology and Infection* 1987; **99**: 291–294.
18. **EuroQol Group.** EQ-5D measure of health outcome. Rotterdam, The Netherlands: The EuroQol Group (<http://www.euroqol.org/eq-5d/what-is-eq-5d.html>). Accessed 7 January 2008.
19. **Ware JE, et al.** How to score version 2 of the SF-12 Health Survey. Lincoln, RI, USA: QualityMetric, 2002.
20. **Rice DP, Hodgson TA, Kopstein AN.** The economic costs of illness: a replication and update. *Health Care Financing Review* 1985; **7**: 61–80.
21. **Akobundu E, et al.** Cost-of-illness studies: a review of current methods. *Pharmacoeconomics* 2006; **24**: 869–890.
22. **BBC.** Call to curb rising NHS drug bill. BBC News 2008 (<http://news.bbc.co.uk/1/hi/health/7190267.stm>).
23. **Hansard.** Health: NHS Direct. England: Hansard (House of Commons Daily Debates) 2009, column 1105W.
24. **BT.** BT price list database (<http://bt.com/pricing/zdocs/index.htm>). Accessed 7 September 2009.
25. **ONS.** 2008 Annual survey of hours and earnings, first release. Newport, United Kingdom: Office for National Statistics, 2009.
26. **Department of Health.** NHS reference costs 2007–08. United Kingdom: Department of Health database (http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_098945). Accessed 3 May 2009.
27. **Healthcare Commission.** Are NHS Services delivered efficiently and effectively? London: Healthcare Commission, 2006.
28. **ONS.** Retail Price Index for group 06 – Health 2009. United Kingdom: Office for National Statistics, 2009.
29. **SPSS Inc.** SPSS version 14.0. Chicago: SPSS Inc., 2005.
30. **HPA.** Salmonella in humans (excluding *S. typhi*; *S. Paratyphi*). Faecal and lower gastrointestinal tract isolates reported to the Health Protection Agency Centre for Infections. England and Wales, 1990–2008. England: Health Protection Agency. Epidemiological database (http://www.hpa.org.uk/webw/HPAweb&HPAwebStandard/HPAweb_C/1195733760280?p=1191942172078). Accessed 3 May 2009.
31. **Heckman J.** Sample selection bias as a specification error. *Econometrica* 1979; **47**: 153–161.
32. **Gil Prieto R, et al.** Epidemiology of hospital-treated Salmonella infection; data from a national cohort over a ten-year period. *Journal of Infection* 2009; **58**: 175–181.
33. **Parada Ricart E, Inoriza Belurze JM, Plaja Roman P.** Severe gastroenteritis: costs of a potentially avoidable cause. *Anales de Pediatría* 2007; **67**: 368–373.