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A cluster of meningococcal disease caused by rifampicin-resistant C meningococci in France, April 2012

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In April 2012, a cluster of two cases of meningococcal disease caused by rifampicin-resistant C meningococci was reported in the Champagne-Ardenne region, France. The two cases occurred in a student population living in the same town but studying at different schools. Bacteriological and epidemiological investigations of cases have shown that the isolates of both cases were non-differentiable.

Background

Neisseria meningitidis is a strictly human bacterium encountered in the pharynx in about 10% of the general population (asymptomatic carriage) [1]. This bacterium can also cause severe infections (mainly septicemia and meningitis) [2].

In France, the annual incidence of invasive meningococcal disease (IMD) varies between 0.9 and 1.5 cases per 100,000 population. Cases are mainly due to meningococci of serogroup B and C (65% and 27% respectively for the last 10 years) [3]. Chemoprophylactic treatment with rifampicin is particularly useful in preventing secondary cases among close contacts of a patient with IMD and in stopping the spread of pathogenic N. meningitidis. Rifampicin is recommended as first-line agent for chemoprophylaxis among contacts of patients with IMD in several European countries [4]. The efficacy of the chemoprophylaxis is usually estimated by the reduction of carriage rate of meningococci. This reduction has been reported to range between 82% and 98% at 7–14 days of follow-up [5–7]. Resistant meningococcal isolates may emerge among 10–27% of treated carriers [8, 9]. However, several studies have reported that rifampicin resistance is rare in invasive meningococcal isolates [10]. According to the annual report of the National Reference Center for Meningococci (NRCM) in Paris, the incidence of rifampicin-resistant meningococci isolated in France averages one per year with no expansion of these isolates and no secondary case [11]. We describe here the detection of a cluster of two cases of rifampicin-resistant C meningococci that were reported in the Champagne-Ardenne region, France in 2012.

Case reports

A student in his early twenties (Case one) presenting with signs of meningitis was admitted mid-April 2012 to a hospital, in the Ile-de-France region. The case who lived and studied in a town in the Champagne-Ardenne region, close to the Ile-de-France region, was immediately treated with cefotaxime and amoxicillin. Cultures of the patient's cerebrospinal fluid (CSF) and blood taken upon admission, yielded serogroup C meningococci. Following the French recommendations [12], rifampicin was recommended to the family and other close contacts three days hereafter, when the health agency in the Champagne-Ardenne region had received the notification. In addition to rifampicin, vaccination with meningococcal C conjugate vaccine was recommended for household contacts.

Eleven days after the notification of Case one, the health agency in the Champagne-Ardenne region received another notification of IMD. A student in his late teens (Case two) had been admitted the day before with signs of meningitis to a hospital, in the Champagne-Ardenne region and was immediately treated with cefotaxime and amoxicillin. Case two lived and studied in the same city as Case 1 but attended a different school, The CSF and blood cultures of Case two also yielded serogroup C meningococci.

Family and close contacts of Case two were given the same recommendations as those of Case one. On the second day after admission of Case two, antibiotic sensitivity testing results showed that the strain was rifampicin-resistant. As a result, chemoprophylaxis for contacts was recommended to be repeated with ciprofloxacin or ceftriaxone [12].

At the same time, the health agency in the Champagne-Ardenne region was informed that the strain of Case

one was also rifampicin-resistant. However, it was then too late (delay >10 days), according to the French recommendations [12], to repeat chemoprophylaxis with ciprofloxacin or ceftriaxone for the contacts of the Case one.

Epidemiological investigations found that Case two had attended a party organised by the schoolmates of Case one two days after admission of the first case.

Molecular typing

Strains of both cases were sent to the NRCM in Paris where phenotyping and genotyping was performed and rifampicin resistance confirmed. The characterisation by multilocus sequence typing, PorA variable regions, penA, FetA showed that the isolates were non-differentiable. The antigenic formula (serogroup: serotype: subtype) was C: NT: P1.7, 1. The genetic typing showed PorA VR1=7-1, VR2=1, FetA= F3-6 and *penA3*, and the strains were of the sequence type ST-11 (clonal complex ST-11). The resistance was due to the same mutation in the *rpoB* (D542V) that was previously reported to confer resitance to rifampicin [9]. A retrospective analysis revealed that in March 2012, a strain with identical markers had been isolated in a neighbouring region to the Champagne-Ardenne region. The patient was also a student, but we found no epidemiological link with the first and second cases described in this report.

Discussion and conclusion

In April 2012, at an approximate interval of 10 days, we observed two cases of IMD caused by rifampicin-resistant C meningococcus in students in the Champagne-Ardenne region. Failure of chemoprophylaxis, due to antibiotic resistance, could lead to the occurrence of secondary cases [13–15]. Therefore, the use of rifampicin in chemoprophylaxis against already resistant bacteria creates a positive selection for resistant strains that may then provoke secondary cases. The detection of the cluster of two cases with non-differentiable isolates of rifampicin-resistant C meningococci suggests the possible carriage and circulation of the ST-11 strain in the student population of the Champagne-Ardenne region.

We could assume that Case one could have transmitted *N. meningitidis* to one or more of his contacts before admission. Contacts of Case one could then have transmitted it to Case two during the party organised on 18 April.

Indeed, ST-11 serogroup C isolates (rifampicin susceptible) have been circulating in the northwestern part of France during the last two years in particular among student populations (unpublished data). This circulation and the repeated use of rifampicin in chemoprophylaxis may have accounted for the selection of rifampicin resistant ST-11 serogroup C isolates. Our detection of a case in a neighbouring region to the Champagne-Ardenne region in March 2012 (but unlinked to the reported cluster) due to rifampicin resistant ST-11 serogroup C isolates is in accordance with the hypothesis of the selection of rifampicin-resistant strain [10].

It is worth to note here that ST-11 isolates belonged to a hyperinvasive genotype that was one of the reasons to recommend systemic vaccination in France in 2009 among 1-24 year-olds, which has now been implemented [16, 17]. Our report underlines the need to monitor antibiotic resistance and both bacteriological and epidemiological investigations of cases even without obvious historical links in order to adapt chemoprophylaxis to the resistance profile of locally circulating strains.

To date, no new case of IMD had been notified in the local student population. Concerning this population, it is recommended to administer ciprofloxacin or ceftriaxone as chemoprophylaxis as soon as possible to protect contacts by reducing carriage of the strain if a new case of IMD occurs. This is recommended by the French High Council for Public Health on 16 April, 2012 [18]. The French recommendations insist on the importance of vaccination against C meningococcus using meningococcal C conjugate vaccine in 1-24 year-olds. The occurrence of IMD is an opportunity to remind the population and physicians of this recommendation [17, 19].

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Using an outbreak to study the sensitivity of the surveillance of enterohaemorrhagic Escherichia coli and other enteropathic Escherichia coli in Bavaria, Germany, January to October 2011

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Following an outbreak of enterohaemorrhagic *Escherichia coli* (EHEC) in Germany 2011, we observed increases in EHEC and non-EHEC E. coli cases in Bavaria. We compared the demographic, clinical and laboratory features of the cases reported during the outbreak period, but not related to the outbreak, to the cases reported before and after. The number of EHEC and non-EHEC E. coli cases notified per week during the outbreak was fivefold and twofold higher respectively, compared to previous years. EHEC cases notified during the outbreak were more often reported with bloody diarrhoea, and less often with unspecified diarrhoea, compared to the other periods. They were more often hospitalised during the outbreak and the following period compared to the period before. Their median age (26.5 years, range: 0–90) was higher compared to before (14.5 years, range: 0–94) and after (5 years, range: 0–81). The median age of non-EHEC E. coli cases notified during the outbreak period (18 years, range 0–88) was also higher than before and after (2 years, p<0.001). The surveillance system likely underestimates the incidence of both EHEC and non-EHEC E. coli cases, especially among adults, and overestimates the proportion of severe EHEC cases. Testing all stool samples from patients with diarrhoea for enteropathic E. coli should be considered.

Introduction

In Germany, the surveillance of intestinal pathogenic (enteropathic) *Escherichia coli* is laboratory based; laboratories are legally obliged to report all findings of enteropathic *E. coli* to the local health authority in the municipality where the infected person resides [1]. The local health authority gathers clinical and epidemiological information about the person and assesses if he or she fulfils national case definitions [2]. If so, the local health authority enters all the information into a notification software whereby each case is also assigned a notification week based on the calendar week (starting on a Monday). The case report is transmitted to the regional health authority that, in turn, forwards the case reports to the national health authority, the Robert Koch Institute.

The *E. coli* pathovar associated with the most severe illness is the Shiga toxin-positive enterohaemorrhagic *E. coli* (EHEC). The most commonly reported pathovar in Germany and Bavaria, the enteropathogenic *E. coli* (EPEC), is Shiga toxin-negative but carries the gene eae and can express the attachment-protein intimin [3]. Some EHEC strains also carry the eae gene. Within the German Communicable Diseases Law Reform Act, the Protection against Infection Act divides EHEC and the other *E. coli* pathovars into two separate notification categories [1].

The electronic case reports for EHEC and non-EHEC *E. coli* cases include information about age, sex, symptoms, hospitalisation, toxins (for EHEC), pathovars (for non-EHEC E. coli) and laboratory diagnostic methods used. Cases of EHEC can be reported with one or more of the following symptoms 'bloody diarrhoea', 'diarrhoea (unspecified)', 'stomach cramps' and 'vomiting'. The corresponding options for non-EHEC cases are 'diarrhoea (unspecified)' and 'stomach cramps'. Several laboratory diagnostic methods can be reported per case. EHEC cases can furthermore be reported with 'Shiga toxin 1', 'Shiga toxin 2', 'Shiga toxin (undifferentiated)', and/or 'intimin', whereas no information regarding virulence factors for non-EHEC *E. coli* cases is reported. Negative results are not reported.

In the years 2006–2010, an average of three symptomatic EHEC cases and 18 symptomatic non-EHEC *E. coli* cases were reported to the Bavarian Health and Food Safety authority (Bayerisches Landesamt für Gesundheit und Lebensmittelsicherheit, LGL) per week; this corresponds to incidences in Bavaria of 1.4 EHEC and 7.6 non-EHEC *E. coli* cases per 100,000 inhabitants. The notification rates however show seasonal

differences, with fewer cases being reported early in the year and more cases between May and November [4].

In mid-May 2011 (week 21), an increase in cases of haemolytic-uraemic syndrome (HUS) in Germany unveiled a HUS/EHEC outbreak caused by an enteroaggregative Shiga toxin-producing *E. coli* O104:H4, which was Shiga toxin 2-positive, Shiga toxin 1-negative and intimin-negative [5]. From week 21 an increase in the number of notified EHEC cases was seen in Bavaria, well above the typical level associated with the season. However, an analysis of the case reports showed that only a minority of the notified EHEC cases could be connected to the HUS/EHEC-outbreak. Furthermore, an increase in non-EHEC *E. coli* cases, such as EPEC, could also be seen.

Our hypothesis was that this increase in enteropathic *E. coli* cases was not a true increase in incidence, but rather an effect of the media attention associated with the HUS/EHEC-outbreak leading to increased testing of patients with EHEC-compatible symptoms. The objective of this study was to describe the *E. coli* cases (both EHEC and non-EHEC) notified when the notification rate peaked and compare them to the cases notified before and after the HUS/EHEC-outbreak to assess the sensitivity of the surveillance system in order to guide interventions for improvements.

Methods

Information about all EHEC and non-EHEC *E. coli* cases notified in Bavaria and reported to the LGL between 3 January and 30 October 2011 were extracted from the LGL notification software SurvNet@RKI [6]. The number of cases reported to the LGL in 2006–2010 was also extracted.

The cases from 2011 were divided into three periods based on their notification weeks: the pre-outbreak period (weeks 1–20), the outbreak period (weeks 21–29) and the post-outbreak period (weeks 30–42). The period intervals chosen were based on the notification rates. The mean number of EHEC and non-EHEC *E. coli* cases, respectively, reported in the corresponding weeks 2006–2010 was calculated for comparison.

We classified the EHEC cases reported with serotype O104 and only Shiga toxin 2 as outbreak cases. Cases of EHEC notified during the outbreak period with undifferentiated Shiga toxin (stx1/2) or Shiga toxin 2, but without a serogroup, were defined as possible outbreak cases. Outbreak cases and possible outbreak cases were excluded from the analysis. Cases notified as EHEC without information about any toxin were also excluded. We considered the remaining EHEC cases and all non-EHEC *E. coli* cases to be unrelated to the HUS/EHEC-outbreak (sporadic cases).

We limited the analysis to symptomatic cases. These were described by age, sex, symptoms, hospitalisation status, and reported laboratory methods and toxins, and compared by time period of notification using Stata/IC 10.1 (StataCorp LP, College Station, TX, USA). Some variables were additionally analysed by age-groups. To this end, the cases were divided into adults (≥18 years-old) and children (<18 years-old). The variable 'any diarrhoea' was created and included cases reported with either bloody diarrhoea or unspecified diarrhoea, or both. Medians were compared by Wilcoxon rank-sum test and equal proportions within a group using the two-sided binomial probability test. Correlations between categorical variables were estimated using Pearson's chi-square test. The alpha error was set at 0.05. Odds ratios (OR) were calculated when relevant.

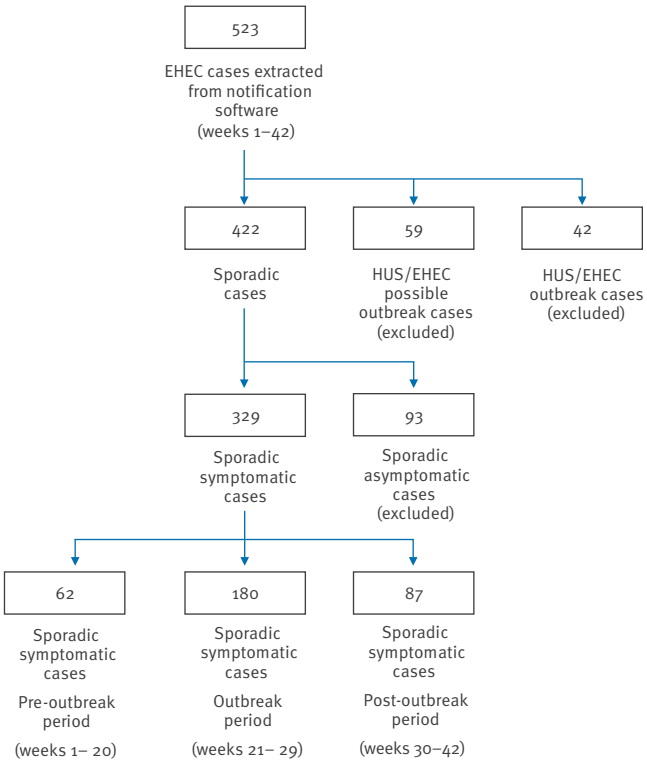
Results

Enterohaemorrhagic Escherichia coli

A total of 523 EHEC cases were notified during weeks 1–42 2011, of which 42 (8%) were classified as outbreak cases and 59 (11%) as possible outbreak cases and therefore excluded. Ninety-three asymptomatic cases, corresponding to 20/82 (24%) reported in the

Figure 1

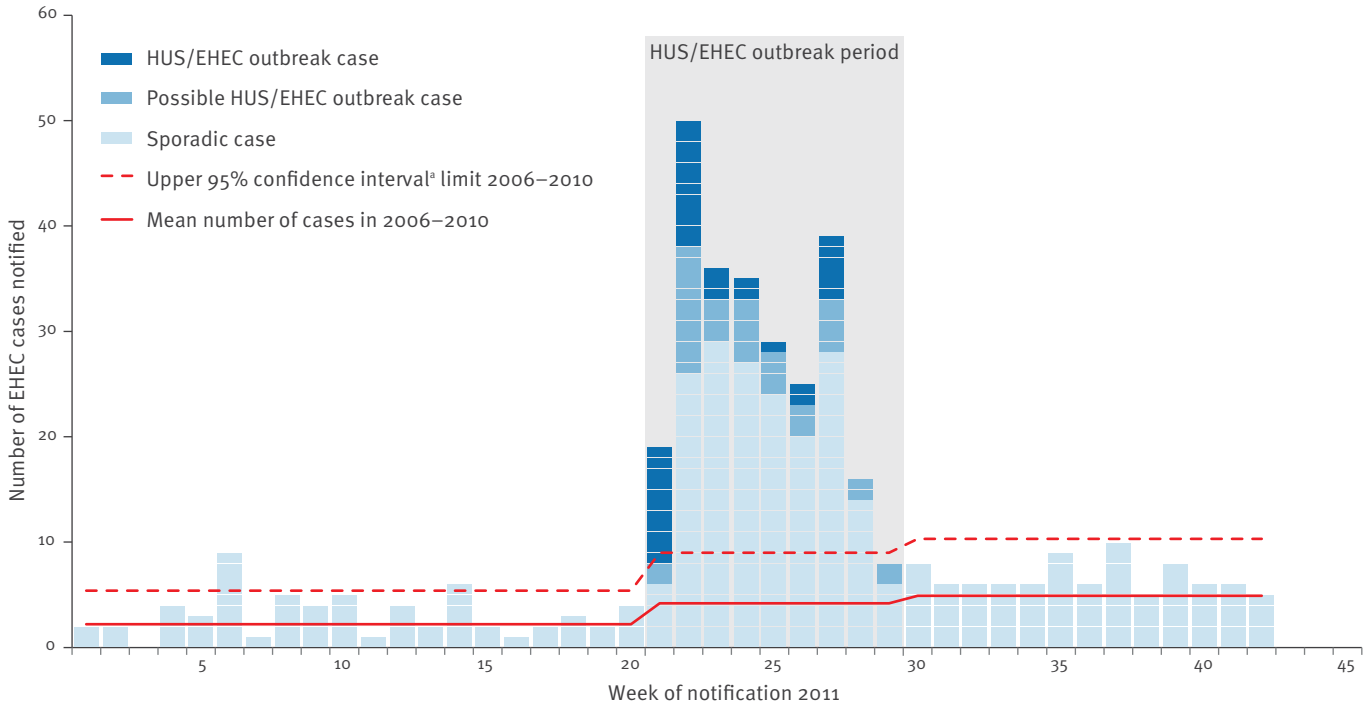
Flowchart of exclusion of particular EHEC cases among those reported between notification weeks 1 and 42 and assignment of remaining cases (n=329) into study periods, Bavaria, Germany, 2011



EHEC: enterohaemorrhagic *Escherichia coli*; HUS: haemolytic-uraemic syndrome.

Figure 2

Symptomatic EHEC cases (n=406) by week of notification and HUS/EHEC outbreak connection, Bavaria, Germany, 2011, and mean number of cases reported weekly in Bavaria in 2006–2010



EHEC: enterohaemorrhagic *Escherichia coli*; HUS: haemolytic-uraemic syndrome.

[a] The lower limit of the 95% confidence interval (not shown) is zero.

Table 1

Demographic and clinical features of sporadic symptomatic EHEC cases notified during the HUS/EHEC outbreak period, compared to the preceding and following periods, Bavaria, Germany, 2011 (n=329)

Characteristics of cases	Pre-outbreak period (weeks 1–20) n=62		Outbreak period (weeks 21–29) n=180	Post-outbreak period (weeks 30–42) n=87	
	n/N(%)[a]	p	n/N(%)[a]	n/N(%)[a]	p
Median age in years (range)	14.5 (0–94)	0.111	26.5 (0–90)	5 (0–81)	0.003
Children <18 years-old	34/62 (55)	0.029	70/180 (39)	49/87 (56)	0.007
Adults ≥18 years-old	28/62 (45)	0.029	110/180 (61)	38/87 (44)	0.007
Females	37/60 (62)[b]	0.180	92/178 (52)[b]	49/86 (57)[b]	0.419
Among children <18 years-old	21/33 (64)[b]	0.197	34/68 (50)[b]	20/48 (42)[b]	0.376
Among adults ≥18 years-old	16/27 (59)[b]	0.542	58/110 (53)	29/38 (76)[c]	0.011
Diarrhoea, any[d]	55/62 (89)	0.054	172/180 (96)	82/87 (94)	0.643
Diarrhoea, bloody	6/62 (10)	0.001	58/180 (32)	17/87 (20)	0.031
Diarrhoea, unspecified	50/62 (81)	0.022	117/180 (65)	66/87 (76)	0.073
Stomach cramps	28/62 (45)	0.236	97/180 (54)	38/87 (44)	0.118
Vomiting	18/62 (29)	0.115	35/180 (19)	10/87 (11)	0.104
Hospitalisation	15/62 (24)	0.021	73/180 (41)	29/87 (33)	0.255
Among children <18 years-old	11/34 (32)	0.384	17/70 (24)	13/49 (27)	0.781
Among adults ≥18 years-old	4/28 (14)	<0.001	56/110 (51)	16/38 (42)	0.349
Median duration of hospitalisation in days (range)	4.5 (1–10)	0.417	4 (1–20)	5 (2–22)	0.055

EHEC: enterohaemorrhagic *Escherichia coli*; HUS: haemolytic-uraemic syndrome.

[a] Unless otherwise specified.

[b] For cases for which information was available.

[c] Significantly different from 50%.

[d] 'Any diarrhoea' includes the cases that were reported with either bloody or unspecified diarrhoea, or both types.

pre-outbreak period, 52/232 (22%) in the outbreak period and 21/108 (19%) in the post-outbreak period, were additionally excluded. Of the remaining 329 symptomatic sporadic cases, 62 were reported during the pre-outbreak period, 180 during the outbreak period and 87 during the post-outbreak period (Figure 1).

During the outbreak period, 20 sporadic symptomatic cases were notified per week on average, compared to four cases per week in the corresponding period of the five preceding years, which equals a 16/4 (400%) increase (Figure 2).

Demographics

Sporadic cases were reported from 68 different municipalities in Bavaria. The age distribution of the sporadic symptomatic EHEC cases did not differ between the pre- and post-outbreak periods. The cases notified during the outbreak period, however, were found to be statistically significantly older compared to the post-outbreak period (Table 1).

The proportions of females and males were similar among children (under 18 years-old) within all time periods. However, the adult cases notified in the post-outbreak period were more often female and the proportions differed statistically significantly from the outbreak period (Table 1).

Clinical features

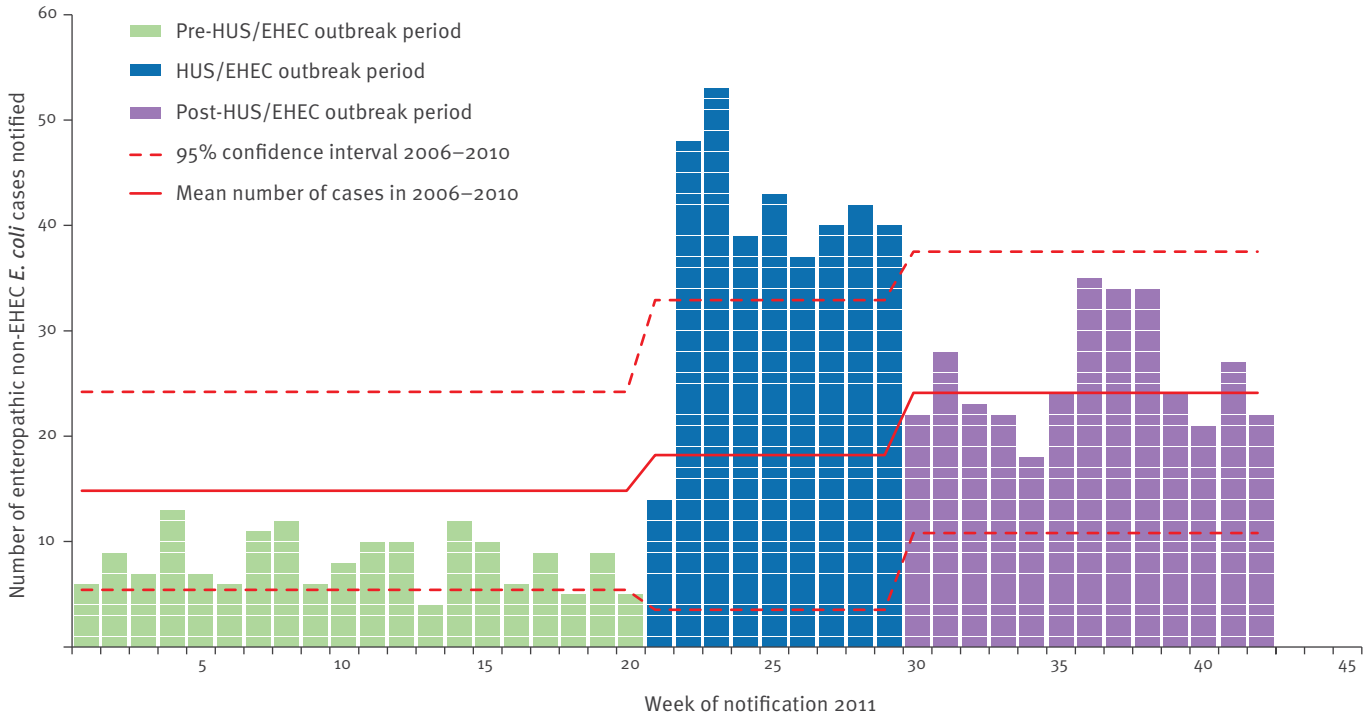
The proportion of cases reported with stomach cramps did not differ between the pre- and post-outbreak period; vomiting was however less often reported in the post-outbreak period compared to before the outbreak (p=0.007) (Table 1). During the outbreak period, bloody diarrhoea was more often reported than in both the pre- and post-outbreak periods, whereas unspecified diarrhoea was reported less often compared to the pre-outbreak period. The proportion of cases that was reported with any type of diarrhoea was however the same during all periods. Only five of the 329 symptomatic sporadic EHEC cases reported during weeks 1–42 2011 were reported with both types of diarrhoea.

Of the 180 symptomatic sporadic cases notified during the outbreak period, 73 (41%) were hospitalised, which was a statistically significantly higher proportion than in the pre-outbreak period (Table 1). The proportion of children hospitalised did not differ between time periods. Adults, however, were more likely to have been hospitalised during the outbreak period (OR: 6.2, 95% confidence interval (CI): 1.9–20.2; p<0.001) and post-outbreak period (OR: 4.4, 95% CI: 1.2–16.1; p<0.016) compared to the pre-outbreak period.

The median duration of hospitalisation did not differ between comparison periods (Table 1). Ten (14%) of

Figure 3

Symptomatic enteropathic non-EHEC *Escherichia coli* cases (n=855) by week of notification, Bavaria, Germany, 2011, and mean number of cases reported weekly in Bavaria in 2006–2010



E.coli: *Escherichia coli*; EHEC: enterohaemorrhagic *Escherichia coli*; HUS: haemolytic-uraemic syndrome.

Table 2

Demographic and clinical features of symptomatic non-EHEC *Escherichia coli* cases notified during the HUS/EHEC outbreak period, compared to the preceding and following periods, Bavaria, Germany, 2011 (n=855)

Characteristics of cases	Pre-outbreak period (weeks 1–20) n=165		Outbreak period (weeks 21–29) n=356	Post-outbreak period (weeks 30–42) n=334	
	n/N(%)[a]	p	n/N(%)[a]	n/N(%)[a]	p
Median age in years (range)	2 (0–89)	<0.001	18 (0–88)	2 (0–88)	<0.001
Children <18 years-old	117/165 (71)	<0.001	173/356 (49)	230/334 (69)	<0.001
Adults ≥18 years-old	48/165 (29)	<0.001	183/356 (51)	104/334 (31)	<0.001
Females	85/165 (52)	0.914	178/349 (51)[b]	162/328 (49)[b]	0.675
Among children <18 years-old	57/117 (49)	0.356	73/169 (43)[b]	104/224 (46)[b]	0.524
Among adults ≥18 years-old	28/48 (58)	1.000	105/180 (58)[b,c]	58/104 (56)	0.674
Diarrhoea, unspecified	159/165 (96)	0.877	344/356 (97)	313/334 (94)	0.073
Stomach cramps	68/165 (41)	0.335	131/356 (37)	128/334 (38)	0.679
Hospitalisation	23/164 (14)[b]	0.022	80/353 (23)[b]	64/327 (20)[b]	0.324
Median duration of hospitalisation in days (range)	4 (2–20)	0.086	4 (1–24)	4 (2–15)	0.633

EHEC: enterohaemorrhagic *Escherichia coli*; HUS: haemolytic-uraemic syndrome.

[a] Unless otherwise specified.

[b] For cases for which information was available.

[c] Significantly different from 50%.

the 73 hospitalised cases notified during the outbreak period were treated for two days or less in a hospital. The duration of hospitalisation was missing for 28 (38%) cases.

Persons with bloody stools were almost eight times more likely to be hospitalised than persons where this symptom had not been reported (OR: 7.8, 95% CI: 5.1–12.0; p<0.001). This correlation was the same in all comparison periods.

Laboratory features

The reported laboratory methods used and types of stool cultures analysed did not differ between time periods; in 25–30% of case reports, culture-based methods were reported. A Shiga toxin gene had been detected in 54–66% of samples in a mixed culture and in 22–34% of samples in an isolate. Shiga toxin had been detected in the culture of 16–23% of samples. Many different combinations of Shiga toxins or Shiga toxin genes were reported among the symptomatic laboratory-confirmed sporadic cases. The proportion of cases with undifferentiated Shiga toxins was lower during the outbreak period, whereas toxin-combinations with intimin were reported more frequently; eleven percent of cases were reported with intimin in the pre-outbreak period, compared to 32% of the cases of the outbreak and post-outbreak periods (p=0.001).

Non-enterohaemorrhagic Escherichia coli

A total of 948 cases of enteropathic non-EHEC *E. coli* were notified during weeks 1–42 2011. Ninety-three cases, corresponding to 11/176 (6%), 34/390 (9%) and 48/382 (13%) in each of the respective time periods, were asymptomatic and excluded. The proportion of asymptomatic cases was higher in the post-outbreak period compared to the pre-outbreak period (p=0.024). Nine asymptomatic cases, within two clusters, were diagnosed because they had had contacts with EHEC cases and therefore had been tested for enteropathic E. coli.

The notification rate of symptomatic cases increased markedly from week 22 (Figure 3). During the outbreak period 40 symptomatic cases were notified per week on average, which is 22 cases more than the average weekly number in the corresponding period of the five preceding years; this equals a 22/18 (122%) increase. In the pre- and post-outbreak periods 2011, the number of cases was within the expected range (Figure 3).

Demographics

Cases were reported from 87 different municipalities in Bavaria. The age distribution of cases notified in the pre- and post-outbreak periods did not differ, but the cases notified during the outbreak period were considerably older (Table 2).

There was no difference in the distribution of cases with regard to sex overall (weeks 1–42) or in any of the time periods. Among children overall, 46% (234/510) were girls, but this was not a statistically significantly different sex distribution (p=0.069). Among adults overall, women constituted 58% of the cases (191/332) and were thereby disproportionally represented (p=0.007); this discrepancy could be perceived in all time periods, although not always statistically significant (Table 2).

Clinical features

A majority of the symptomatic cases (98%) were reported without an epidemiological link to another case.

Unspecified diarrhoea was reported for a majority of symptomatic cases. Diarrhoea and stomach cramps were equally often reported in all comparison periods (Table 2). Of the 844 symptomatic cases where information regarding hospitalisation was known, 167 cases (20%) had been hospitalised. Higher proportions of symptomatic cases were hospitalised during the outbreak and post-outbreak periods in comparison to the pre-outbreak period (Table 2). The median duration of hospitalisation did not differ between time periods (Table 2).

Laboratory features

Laboratory information was available for 844/855 non-EHEC *E. coli* cases. EPEC was the dominating pathovar reported among non-EHEC *E. coli* cases during all periods. Of 790 cases reported with a specific pathovar 721 (91%) were classified as EPEC.

The proportion of cases where isolation of *E. coli* was stated as the diagnostic method used was lower during the outbreak and post-outbreak periods (64% and 55%, respectively), compared to the pre-outbreak period (82%, $p<0.001$). The use of polymerase chain reaction (PCR) however was more often reported in the outbreak and post-outbreak periods (in 46% and 56% of the cases, respectively) compared to the pre-outbreak period (26%, $p<0.001$).

Discussion

Testing practices influence the surveillance

The sudden increase in EHEC cases not related to the HUS/EHEC-outbreak and the fact that reports of other enteropathic *E. coli* cases increased in parallel indicates that the case numbers were unlikely to be the result of an increasing secular trend. The increase could not be attributed to system-specific changes either, as neither the case definitions nor the law regulating the reporting of suspected and confirmed cases from laboratories to local health authorities changed in 2011. Furthermore, the EHEC cases in our analysis were reported with a variety of toxins, from a number of different municipalities in Bavaria and not as epidemiologically linked. At the time of the HUS/EHEC-outbreak, all EHEC-cases were also interviewed about their exposures by the local health authorities. The combined evaluation did not indicate that the increase seen in Bavaria was due to another, regional, outbreak.

We hypothesised that the increase was due to an increase of symptomatic persons seeking healthcare, being asked to leave a stool sample and the sample being tested for EHEC, and that the observed increase was an effect of increased testing. Supporting this theory is that the proportion of symptomatic to asymptomatic EHEC cases was the same before and during the outbreak, indicating that mass screening of asymptomatic individuals was not a major driving force for the increase. Furthermore, intimin was more frequently reported among EHEC cases in the outbreak and post-outbreak periods. We do not believe that this represents an increase in incidence of intimin-positive strains, but rather an increased detection of such strains. Because the strain responsible for the HUS/EHEC-outbreak was intimin-negative, laboratories may more often have conducted this additional analysis. This could also explain the increase seen in non-EHEC E. coli, mainly dominated by EPEC. However, because the surveillance data does not include the basis for the pathovar assignment for non-EHEC E. coli, such as detected virulence factors, we cannot conclusively say that the increase in non-EHEC *E. coli* was due to an increase in intimin-positive EPEC cases.

In October 2009, the United States (US) Centers for Disease Control and Prevention (US CDC) recommended that 'all stools submitted for routine testing from patients with acute community-acquired diarrhoea (regardless of patient age, season of the year, or presence or absence of blood in the stool)' should be tested for Shiga toxin-producing *E. coli* [7]. One of the stated reasons was that the use of selective criteria for testing results in cases being missed, with negative impact on secondary transmission, outbreak identification, treatment and the monitoring of epidemiological trends. The use of different screening criteria and laboratory methods has also been identified as a possible cause for regional differences in EHEC-incidence in Australia [8]. Other authors have argued that such general screening is not suitable in low-prevalence settings [9]. We estimated the incidence of symptomatic sporadic EHEC infections in Bavaria during the outbreak period to 8.3 cases per 100,000 inhabitants, i.e. higher incidences than those that prompted the US CDC to issue their recommendation, which would justify such recommendations also in Bavaria [4]. However, as laboratories in Germany are not reimbursed for additional analyses, they would not be likely to implement such a recommendation.

Finally, mixed clusters of EHEC and non-EHEC *E. coli* cases were also reported. On more than one occasion this was due to contact tracings surrounding EHEC cases that concomitantly detected persons infected with EPEC, indicating that a broader analysis not only focused on EHEC was carried out. Identification of EPEC cases during similar investigation has also been reported in other studies [10].

The sensitivity of the surveillance system is low

During the outbreak period, almost five times as many sporadic EHEC cases and more than two times as many non-EHEC *E. coli* cases were notified per week compared to previous years, corresponding to incidences of 8.3 and 16.3 cases per 100,000 inhabitants. If these notification rates represent a closer estimate of the

true incidence of EHEC and non-EHEC E. coli, then the surveillance system is only capturing a fraction of the enteropathic *E. coli* cases.

We defined cases notified during the outbreak period where the serogroup and/or toxins were unknown as possible outbreak cases and excluded them from the analysis. If they were to be considered sporadic cases, the estimate of the sensitivity of the surveillance system decreases further.

The incidence estimates, however, do not take into account the underreporting following from laboratories not analysing samples for non-EHEC *E. coli* or not being able to detect different *E. coli* pathovars. The increase in EPEC cases during the HUS/EHEC-outbreak suggests that the underreporting due to laboratory factors could be considerable. Furthermore, studies have shown that only approximately 20% of individuals with diarrhoea seek medical attention and that only 15–20% of those are asked to submit a stool sample [11-15]. Thereby, the true incidences of EHEC and non-EHEC *E. coli* are likely to be higher than those observed during the outbreak period.

The increase in asymptomatic non-EHEC *E. coli* cases in the post-outbreak period indicates that contact tracings might have been performed more often. As the frequency of performed contact tracings might have biased the comparison between periods and years, we chose to limit the analysis to symptomatic cases.

Adults and males are underrepresented

No sex difference could be seen among children, but adult females were overrepresented among EHEC cases in the post-outbreak period and among non-EHEC *E. coli* cases in the outbreak period. The early reports of the HUS/EHEC-outbreak indicated that adult women were a more affected group [4]. This might have influenced adults and especially adult women, to seek healthcare, leading to an increase in detection and a consequent increase in notifications.

EHEC and non-EHEC *E. coli* cases notified during the outbreak period were older compared to cases notified during the comparison periods. This suggests that adults might have been underrepresented among notified cases earlier, especially with regards to non-EHEC *E. coli* where the laboratory investigations are mostly limited to children below three years of age in accordance with guidelines from the German society for Hygiene and Microbiology (DGHM) [16]. That the median age of non-EHEC *E. coli* cases returned to its pre-outbreak level in the post-outbreak period indicates that testing practices have reverted and that adults may still be underrepresented.

Severity of disease in notified cases

Bloody diarrhoea and hospitalisation were more often present in the reports of EHEC cases notified in the outbreak period, indicating that cases were more severe. This was also noted in the post-outbreak period, suggesting a possible residual effect.

Severe symptoms, especially bloody stools, have been shown to be a predictor for both seeking medical attention and submitting stool samples [11-15]. It is also probable that hospitalised patients are more often investigated for the microbiological cause of the symptoms than non-hospitalised patients. Guidelines issued by the German Association for General Medicine and Family Medicine in June 2011 as a response to the HUS/EHEC-outbreak, recommended limiting laboratory investigation to cases with noticeable blood in the stools where the clinical picture was unclear [17]. Management guidelines for children with suspected acute infectious gastroenteritis also state that the identification of the causing organism of an uncomplicated gastroenteritis is unnecessary and recommends limiting laboratory confirmation to patients with severe bloody stools, severe or persistent duration of symptoms, HUS, immunodeficiency, age below three months, recent travel to risk countries, or where there is illness in the surroundings, and especially in order to guide antibiotic treatment [18]. In their quality standards for microbiological diagnostics, the German society for Hygiene and Microbiology also recommends that EHEC-analyses primarily be performed in outpatients with bloody-slimy stools or severe clinical picture and when HUS is suspected [16]. They further recommend performing EPEC-analyses in children below three years of age, with watery or bloody stools or severe symptoms. These testing algorithms aim to increase the specificity of laboratory analyses and serves cost-efficiency. Although the guidelines are not binding, it is likely that they influence the profile of the patients investigated, and may thus lead to severe and hospitalised cases being overrepresented among notified cases.

The argument against cases having been more severe during the outbreak period is that the prevalence of diarrhoea overall was the same in all time periods. Because of the increased public health focus on EHEC at the time, local health authorities might have inquired more thoroughly on the type of diarrhoea of the cases and thus identified more instances of bloody diarrhoea. Medical practitioners might also have taken a precautionary approach and recommended hospitalisation of persons presenting with EHEC-compatible symptoms. This is supported by the fact that 20 patients were hospitalised for two days or less. Furthermore, the median duration of hospitalisation was similar in all time periods. Thereby we cannot conclude that EHEC cases notified during the outbreak period were in fact more severe.

Conclusions and recommendations

We believe that our results support our hypothesis that the increase in EHEC cases and other enteropathic *E. coli* cases at the time of the HUS/EHEC outbreak was likely due to changes in health-seeking behaviour, especially among adults, in combination with altered

diagnostic methods and suggest that this was triggered by the attention from media and public health authorities during the HUS/EHEC-outbreak that was ongoing at the time.

All laboratory-confirmed cases of enteropathic *E. coli* are notifiable, but since mild cases are less likely to seek medical attention and the guidelines limit the proportion where a microbiological investigation is conducted, the surveillance system is likely to overestimate the proportion of severe cases and underestimate the total incidence, thus limiting the representativeness of the incidence estimates generated through the statutory surveillance system.

We estimate that the yearly incidences of EHEC and non-EHEC *E. coli* infections in Bavaria could be above eight and 16 cases per 100,000 inhabitants, respectively. Because of the high incidences, testing of all stool samples for enteropathic *E. coli* should be considered.

A better estimate of the burden of disease in different age groups would be to use the positivity rate, which would take into account the number of persons tested. However, this information is not available in Bavaria today. A syndromic data source could also supplement the notification data and help us to better estimate the burden of disease. In addition, if a sample of these syndromic cases were tested for intestinal pathogenic E. coli, as well as other gastrointestinal pathogens, in a systematic way, we could verify the representativeness of the data collected by the statutory surveillance system by comparing the incidence estimates of the two systems.

Finally, if the case definitions for non-EHEC *E. coli* required that detected virulence factors such as intimin were reported, we would be better able to interpret the notification data.

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Prevalence and determinants associated with healthcare-associated infections in long-term care facilities (HALT) in the Netherlands, May to June 2010

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HAIs (healthcare-associated infections) are likely to become an increasing public health problem. Therefore, a point-prevalence study called HALT (Healthcare-associated infections in long-term-care facilities) was set up by the European Centre for Disease Prevention and Control to determine the prevalence, antibiotic use and determinants associated with HAIs. In the Netherlands, 10 nursing homes (in total 1,429 elderly residents) participated in the study between May and June 2010. Risk and protective factors were determined by calculating relative risks (RRs) and performing multilevel Poisson regression. An overall infection prevalence of 2.8% was found and 3.5% of the residents used antibiotics. Residents' characteristics such as the presence of pressure wounds (RR: 2.58; 95% CI: 1.04–6.39) and other wounds (RR: 5.70; 95% CI: 2.99–10.86) were risk factors for an HAI, whereas being male (RR: 0.43; 95% CI: 0.21–0.91) was protective. Nursing home characteristics, such as the percentage of shared rooms (≥32%) (RR: 0.49; 95% CI: 0.39–0.62) and percentage of incontinent residents (≥63%) (RR: 0.72; 95% CI: 0.61–0.85) were protective determinants in a multivariate analysis. Special attention is therefore needed for female residents and residents with pressure and other wounds for the prevention of HAIs in Dutch nursing homes.

Introduction

The European Centre for Disease Prevention and Control (ECDC) defines healthcare-associated infections (HAIs) as infections occurring after exposure to healthcare, often, but not always, as a consequence of this exposure [1]. HAIs are a major challenge: in Europe, they are a frequent source of morbidity and mortality and the leading reason for residents of long-term-care facilities (LTCFs) to be hospitalised [2-4]. In Norway, the mortality rate and hospital admission rate due to HAIs during October 2004 and May 2005 were assessed at respectively 0.16 per 1,000 resident-care days and 0.35 per 1,000 resident-care days [5]. HAIs may also have an impact on the quality of life of the residents in LTCFs [4,6], but this hypothesis needs more research.

Elderly people are especially prone to HAIs because their immune response may be diminished due to malnutrition, polypharmacy and the presence of multiple chronic diseases [4,7]. The most common HAIs reported are respiratory, urinary, gastrointestinal, skin and tissue infections [2].

It is estimated that there are about 4 million HAIs per year in hospitals and LTCFs in the European Union, leading to 37,000 deaths per year [1]. Meanwhile, the average age of the European population is rising: by 2060, persons aged 60 years and above will account for 30% of the European population, compared with 17% in 2008 [8]. Moreover, persons aged 80 years and above will account for 12% of the European population in 2060 [8]. Of elderly people, this group have the most physical limitations and are therefore most likely to be moving into a nursing home [9]. As the aging of the European population will lead to more elderly people residing in nursing homes, it could be expected that the burden of HAIs will rise [1]. Due to the interaction between populations inside and outside nursing homes, HAIs in such homes are linked with infections in the general population and will become an increasing public health problem [10]. Furthermore, because of the HAIs, antibiotics are used to a considerable extent in LTCFs [11,12]: such use leads to the occurrence of antibiotic-resistant pathogens in LTCFs [12,13]. Due to the frequent transfer of residents to hospitals, resistant pathogens can also be transferred from hospitals to nursing homes and vice versa [7].

In the Netherlands, LTCFs are homes for people who need intensive care, nursing, treatment, constant assistance due to chronic physical and mental problems and who are dependent in their activities of daily life. In Italy (winter months, published in 2007), Norway (June–October 2002 and June–October 2003), Ireland (May, 2010) and Germany (May–September 2010), the prevalence of HAIs in such facilities has been shown to be 10.8%, 6.6–7.6 %, 11.3% and 1.6%, respectively [14-17]. Eikelenboom-Boskamp et al. found a mean HAI

prevalence of 7.3% in nursing homes in the region of Nijmegen in the Netherlands from 2007 to 2009 (season unknown) [18].
In the Netherlands, a surveillance network has been set up to monitor the incidence of HAIs in Dutch nursing homes, called SNIV (Surveillance Netwerk Infectieziekten Verpleeghuizen [Surveillance network infectious diseases nursing homes]) [19,20]. Participation in this network is voluntary.

Determinants associated with HAIs have been identified in Italy, France/Switzerland, Germany and [14,21,22]. In order to gain more insight in HAIs, a European point prevalence study was planned for 2009 to 2011 by ECDC, called HALT (Health-care associated infections in long-term care facilities). The aim of this project was 'to develop and implement a protocol for surveillance of HAI, antimicrobial use and resistance in European LTCFs in order to establish baseline rates and identify priorities for improvement' [23]. This article presents the results of the HALT study in the Netherlands.

Methods

Study design

A total of 10 nursing homes of the 325 nursing homes in the Netherlands participated in the HALT study. At the time of the study, there were 25 nursing homes participating in the SNIV surveillance network: all 25 were invited to participate in the study, of which 10 agreed.

Data were collected at one point in time in each home between May and June 2010, following the HALT protocol [23]. One researcher visited all 10 homes, accompanied by one other researcher. All patients staying longer than 24 hours in the nursing home at the time the data were collected were included. Two questionnaires were used: one on the institution and one on the residents. The former, dealing with the characteristics of the home, was filled in by the nursing staff. The latter, completed by the researchers and nursing staff together, focused on characteristics of residents who had signs of an infection and/or used antibiotics.

In deviation from the HALT protocol, we defined having an infection as suspicion of infection. Suspicion of infection was defined as having at least one symptom or sign on the HALT score list [23]. We followed the HALT protocol in that three other criteria also had to be met: (i) all symptoms and signs had to be new or acutely worse; (ii) non-infectious causes of signs and symptoms were excluded; and (iii) identification of a sign or symptom was not based on a single piece of evidence. The signs and symptoms of infection in this study were recorded by the nursing staff who were present on each floor of the home. After collecting all the data, the presence of infection was also verified with the nursing home's general practitioner.

The following infections were recorded: gastrointestinal, urinary tract infections, systemic infections, respiratory tract infections, pneumonia/bronchial infections, unexplainable fever episodes, otorhinolaryngological infections and other infections.

Data analysis

For the purposes of data analysis, a resident was considered as having an infection or not (i.e. the type or number of infections was not taken into account). For urinary tract infections, a separate analysis was also performed. We included only the determinants that were described in the HALT protocol to identity any risk factors.

Using data from the resident and institutional questionnaires, the prevalence of infection and the use of antibiotics were determined. They were also used to identify resident characteristics as possible determinants. Data from the institutional questionnaire were used to identify nursing home characteristics as possible determinants.

The proportion of the nursing home characteristics (possible risk factors) was calculated using the total number of residents per nursing home. Then, the nursing home characteristics were dichotomised according to the mean values.

The proportions of residents who were incontinent, immobile or disorientated – which were considered as indicators of the burden of care – were included in the analysis to take into account any differences between the nursing homes. In the homes that participated in the study, the burden of care of their residents was found to be quite similar for incontinence and immobility; therefore, we chose to include only disorientation in the multivariate analysis as an indicator of the burden of care.

Poisson regression with a multilevel analysis was used to perform a multivariate analysis. The multilevel analysis consisted of including a nursing home identifier variable in the Poisson regression to take into account any differences that may have been present in the different nursing homes besides the variables we included to consider these differences. A Poisson distribution was used because the number of infections could be considered count data and no overdispersion was present.

Resident characteristics could not be analysed by regression analysis because no data were available on residents who did not show any signs of infection. Therefore, relative risks (RRs) were calculated from cross tabulation tables.

Characteristics that had p values of ≤0.05 in the univariate analysis were included in the multivariate analysis. A variable was considered a confounder when the regression coefficient changed more than 10%. P values of ≤ 0.05 were considered significant when

Table 1

Characteristics of residents of 10 nursing homes, HALT study, the Netherlands, May–June 2010 (n=1,429)

Characteristic	Number (%)
Male	451 (32)
Aged >85 years	572 (40)
Had a urinary catheter	165 (12)
Had a vascular catheter	0 (0)
Had pressure wounds	75 (5)
Had other wounds	100 (7)
Disorientated	840 (59)
Incontinent	871 (61)
Wheelchair bound or bedridden	819 (57)
Had an operation in the past 30 days	45 (3)
Had been admitted to hospital in the past 3 months	3 (0.2)

HALT: health-care associated infections in long-term care facilities.

investigating potential effect modifiers. For the analyses, SAS software version 9.2 and Excel 2007 were used.

Results

Study population

In total, 1,429 elderly people (living in 10 nursing homes across the Netherlands) were included in the study. Table 1 shows their characteristics. The nursing homes were quite similar regarding the proportions of incontinent (median: 67%; range: 47–76) and immobile (median: 58%; range: 44–67) residents, but not for those with disorientation (median: 58%; range: 47–93).

In total, 40 residents showed signs of an HAI, giving an overall prevalence of 2.8% (range between the homes: 0.10–5.6%). Urinary tract infection was the most prevalent diagnosed infection, with 10 cases, giving an overall prevalence of 0.7%. On average, antibiotics were used by 50 residents (range between nursing homes: 0–7%). Moreover, of the 40 residents who showed signs of an HAI, 24 did not use antibiotics.

Of the 40 residents who had an infection, 31 were women and 9 were men. Of the 50 residents who used antibiotics, 32 were women and 18 were men. Female residents used significantly more antibiotics than men (p=0.003) but did not show significantly more signs of infections (p=0.50).

Individual determinants

Table 2 shows the results of the univariate analysis at the individual level. Sex, with male being a protective factor (RR: 0.43; 95% CI: 0.21–0.91), the presence of pressure wounds (RR: 2.58; 95% CI: 1.04–6.39) and the presence of other wounds (RR: 5.70; 95% CI 2.99–10.86) were statistically significantly associated with having an HAI.

Nursing home determinants

Table 3 shows the univariate and multivariate Poisson regression analysis at nursing home level. The univariate model showed that residents in the homes that had 32% or more shared rooms had a statistically significant lower risk of an HAI than residents in homes with less than 32% shared rooms (RR: 0.46; 95 CI: 0.34–0.62). The same was the case for residents in homes that had 3% or more residents who had had an operation in the past 30 days (RR: 0.62; 95% CI: 0.44–0.88). Furthermore, residents in homes with 63% or more incontinent residents had a statistically greater risk of HAIs than residents in homes with less than 63% of their residents incontinent (RR 1.59; 95% CI: 1.01–2.49).

The multivariate model for the nursing home characteristics showed that residents in nursing homes that had 32% or more shared rooms were less at risk of acquiring an HAI (RR: 0.49; 95% CI: 0.39–0.62). Similarly, residents in nursing homes where 63% or more of the residents were incontinent were at less risk of acquiring an HAI (RR: 0.72; 95% CI: 0.61–0.85) (Table 3).

Discussion

In this study, the percentage of antibiotic use turned out to be higher than the prevalence of HAIs. This could indicate a contribution to the existing antimicrobial resistance in nursing homes [12]. Other explanations could be that the residents without signs or symptoms were finishing their antibiotic treatment in order to prevent antibiotic resistance or that the antibiotics were being used prophylactically.

Table 2

Univariate analysis of potential determinants for healthcare-associated infections at individual level, HALT study, the Netherlands, May–June 2010

Potential determinant	Relative risk (95% CI)
Sex (men vs women)*	0.43 (0.21–0.91)
Aged >85 years	1.62 (0.87–2.99)
Had a urinary catheter	1.62 (0.83–2.42)
Had pressure wounds*	2.58 (1.04–6.39)
Had other wounds*	5.70 (2.99–10.86)
Disorientated	0.58 (0.31–1.07)
Incontinent	0.96 (0.51–1.79)
Had an operation in the past 30 days	2.49 (0.80–7.79)
Wheelchair bound or bedridden	NA[a]

HALT: health-care associated infections in long-term care facilities; NA: not applicable.

[a] No residents with an infection were wheelchair bound or bedridden.

* Statistically significant (p<0.05).

Table 3

Univariate and multivariate multilevel Poisson regression analysis of potential determinants for healthcare-associated infections at nursing home level, HALT study, the Netherlands, May–June 2010

Potential determinant (mean cut-off value)	Univariate analysis	Multivariate analysis
	Relative risk (95% CI)	Relative risk (95% CI)
Male (≥32%)	0.75 (0.42–1.31)	–
Aged >85 years (≥39%)	0.64 (0.39–1.07)	–
Had a urinary catheter (≥11%)	0.86 (0.49–1.54)	–
Had pressure wounds (≥5%)	0.93 (0.54–1.60)	–
Had other wounds (≥7%)	1.15 (0.66–2.00)	–
Disorientated (≥60%)	0.74 (0.42–1.59)	0.92 (0.64–1.34)
Incontinent (≥63%)	1.59 (1.01–2.49)*	0.72 (0.61–0.85)*
Wheelchair bound or bedridden (≥57%)	1.50 (0.93–2.44)	–
Operation in past 30 days (≥3%)	0.62 (0.44–0.88)*	1.14 (0.81–1.59)
Admission to hospital in past 3 months (≥0.2%)	0.69 (0.36–1.33)	–
Shared rooms (≥32%)	0.46 (0.34–0.62)*	0.49 (0.39–0.62)*
No person present with training in HAI prevention	1.59 (0.96–2.61)	–
No protocol for MRSA infection	1.13 (0.83–1.54)	–
No vascular catheter protocol	0.76 (0.4–1.46)	–
No parenteral nutrition protocol	0.82 (0.47–1.44)	–
No use of hand alcohol	0.88 (0.38–2.02)	–
No use of disinfectant wipes	0.76 (0.4–1.46)	–

HAI: health-care associated infection; HALT: health-care associated infections in long-term care facilities; MRSA: meticillin-resistant *Staphylococcus aureus*.

* Statistically significant ($p<0.05$).

Pressure and other wounds at the resident level were associated with HAIs. Our hypothesis is that people with pressure or other wounds have a lower health status and are therefore more susceptible to an HAI. The percentage of incontinent residents was shown to be a risk factor in the univariate analysis of the nursing home characteristics, whereas in the multivariate model, it was found to be a protective factor. Incontinent residents may have higher risk of infection because urine and faeces irritate and damage the skin, which can lead to incontinence-associated dermatitis [24]. We did not expect to find the amount of incontinent residents (≥63%) to be protective. We think that the small size of the study population may have played a role. In addition, the amount of data is insufficient to allow stratified analyses, in order to determine more precisely how this can become a protective factor.

We also did not expect to find the amount of shared rooms (≥32%) to be protective. We hypothesise that residents who live in a single room possesses certain characteristics – other than those investigated in this study (e.g. presence of co-morbidities) – that make them more vulnerable to infection than residents who live in shared rooms. Such characteristics need further investigation. The small number of characteristics investigated in this study could therefore be seen as a limitation of this study. However, point prevalence studies using minimal resources can provide valuable information, freeing resources that can be used for other studies and developing interventions. Point prevalence studies are frequently used to determine HAI prevalence and use of antimicrobial agents in nursing homes [14,15,18,21,25,26].

There are other limitations to this study. We did not have details of the characteristics of residents who did not show signs of infection: such information would facilitate a multivariate analysis on the data collected in the resident questionnaire. This would give a better exploration of the potential determinants at the individual level. Moreover, the dichotomisation of the nursing home characteristics in our analysis causes (subtle) differences between nursing homes to be filtered out. Therefore, any effects that these differences would have on the risk of getting an infection are diminished. This is also another argument for collecting information in the future on additional characteristics of residents who do not show signs of infection. Furthermore, in the HALT study, a score list was used to determine the signs and symptoms of infection. In our analysis, we considered every sign and symptom of infection as an indicator of infection. This might have caused an overestimation of the prevalence. On the other hand, however, it is likely that we did not miss any infections this way. Lastly, the various HAIs seen in our study were analysed together: thus, the characteristics of an individual or nursing home cannot be associated with

a specific type of infection. Analysis of determinants of infection at the individual and nursing home level restricted to residents who were diagnosed with an urinary tract infection did not give reliable results: there seemed to be a lack of power (data not shown).

The mean HAI prevalence and level of antibiotic use seen in the study of Eikelenboom-Boskamp et al. in Nijmegen region in the Netherlands [18] were much higher than those seen in our study. In both studies, urinary tract infection was the most prevalent HAI. The prevalence of HAIs measured in Norway (2002–2004, Italy (published in 2007) and Ireland (2010) was also higher than that seen in our study, whereas in Germany (2010), the prevalence was lower [14-17].

In our opinion, there are four possible explanations for the differences between these studies. The first is confounding by indication: it is possible that the Dutch nursing homes that chose to participate in the HALT study had already paid a lot of attention to the prevention HAIs and therefore the prevalence was lower. The second is seasonality: performing a study in the winter could lead to different results compared with performing a study in the spring. Our study and in those carried out in Ireland and Germany were carried out in the spring/summer: the study in Norway was carried out in both spring and winter and the study in Italy in the winter. Third, nursing homes may differ across Europe: nursing homes in the Netherlands, for example, are very different from those in Italy and the United Kingdom (e.g. in terms of the population living in a nursing home and the function of the home) [27]. Last, the methodology of the studies were different, making it difficult to draw conclusions about differences in the results. The studies performed in Ireland and Germany were both part of the HALT study and the same methodology was used. In these two studies, infection (yes/no) was also defined as the presence of any sign or symptom of infection to estimate the HAI prevalence.

The determinants associated with HAIs in long-term care facilities or geriatric institutions in five European studies [14,16,21,22,28] are shown in Table 4.

Strikingly, the study in Ireland [16] found similar results for resident characteristics that were risk factors. Furthermore, having skin conditions (ulcers), found to be a risk factor in the Norwegian study [28], was also identified as a risk factor at the individual level in our study.

In the Netherlands, special attention should be given to female residents and residents with pressure wounds and other wounds in order to prevent HAIs in the nursing homes. Our results and those of other studies indicate that the overall health of a nursing home resident must be monitored and that specific control interventions must be developed in order to prevent HAIs in such residents. Initiatives to do this have already been set up in the Netherlands, in a surveillance system called PREZIES (Preventie van ziekenhuisinfecties door surveillance [Prevention of hospital acquired infection through surveillance]) [30,31] and SNIV.

For future studies, we consider it necessary to also take in consideration other factors (such as co-morbidities and nutrition status at resident level and use of infection prevention measures at nursing home level) in order to explore which other characteristics play a role in acquiring an HAI. Then, the appropriate indicators for infection control practices could be determined and prevention strategies developed.

Table 4

Protective and risk factors associated with healthcare-associated infections in other European studies

Country	Protective factors	Risk factors
Italy [14]	None	Degree of dependency[a], the presence of co-morbidities and invasive devices
Ireland [16]	None	Urinary catheter, incontinence, pressure sores, other wounds, surgery in the past 30 days
France, Switzerland [21]	Presence of a psycho-behavioural disorder	Nutrition abnormalities, diabetes, chronic bronchitis, swallowing disorders, intravenous catheter, urinary catheter and other catheters
Germany [22]	None	Urinary catheters, gastric tubes, age >80 years
Norway [28]	None	Bedridden or a stay of <28 hours in the facility, presence of chronic heart disease, urinary incontinence, an indwelling catheter, a skin ulcer

[a] The degree of dependency was derived from the number of disabilities for activities for daily living (ADL): 3–4 and 5–6 were risk factors [29].

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