# 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

**H Englund (helene.englund@lgl.bayern.de)[1,2], W Hautmann[1]**
1. Bayerisches Landesamt für Gesundheit und Lebensmittelsicherheit, Oberschleissheim, Germany
2. European Programme for Intervention Epidemiology Training (EPIET), European Centre for Disease Prevention and Control (ECDC), Stockholm, Sweden

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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.

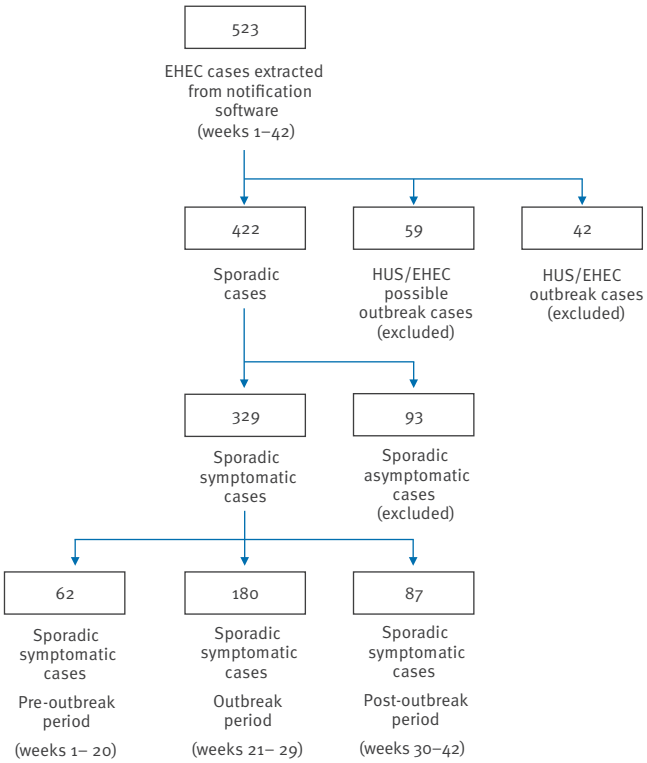
## Results

### 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**

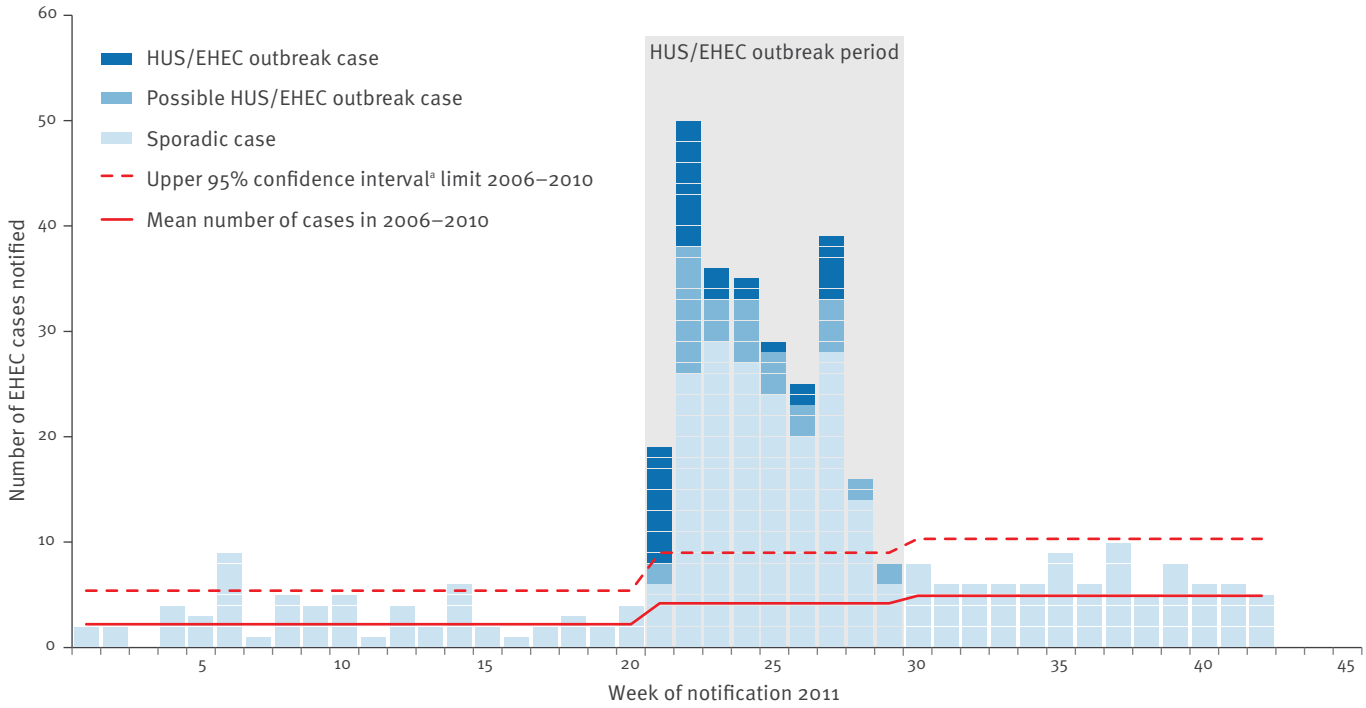
Flowchart of exclusion of particular EHEC cases among those reported between notification weeks 1 and 42 and assignment of remaining cases (n=329) into study periods, Bavaria, Germany, 2011




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

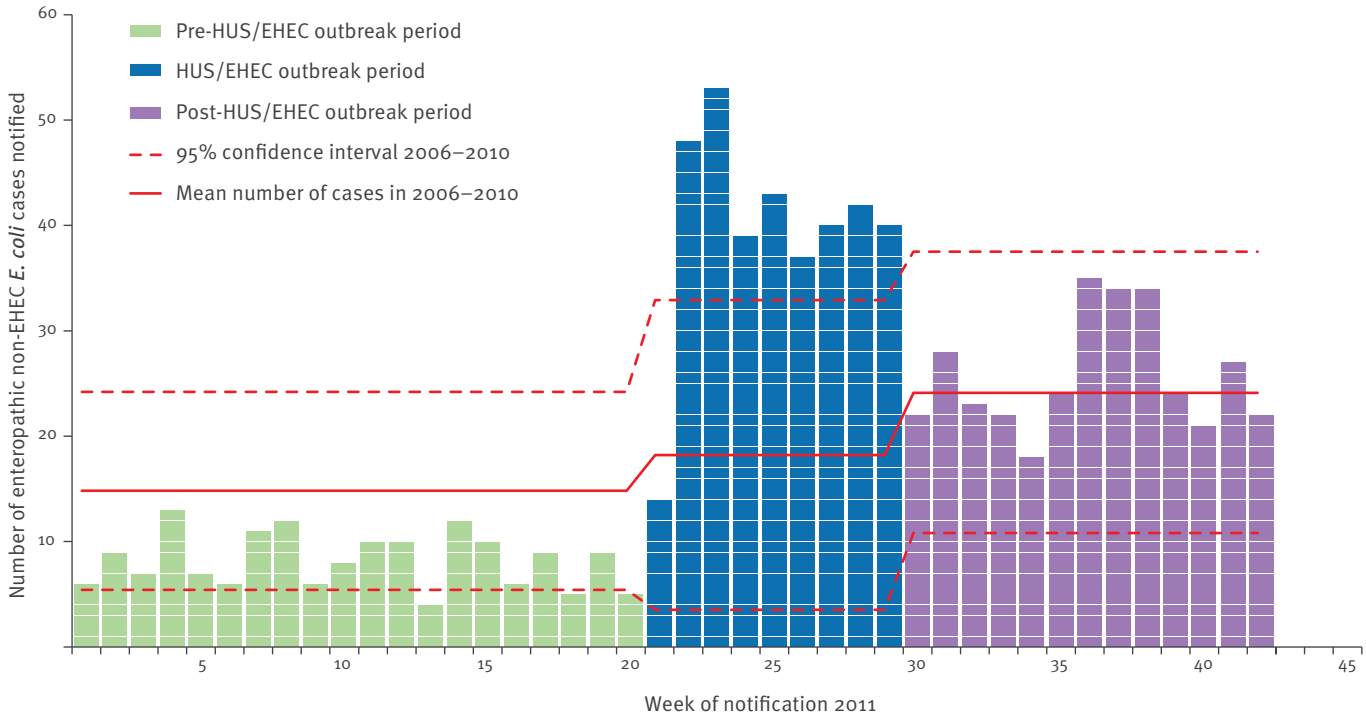
The proportion of cases reported with stomach cramps did not differ between the pre- and post-outbreak period; vomiting was however less often reported in the post-outbreak period compared to before the outbreak (p=0.007) (Table 1). During the outbreak period, bloody diarrhoea was more often reported 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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## References

1. Gesetz zur Neuordnung seuchenrechtlicher Vorschriften (Seuchenrechtsneuordnungsgesetz - SeuchRNeuG) vom 20. Juli 2000. Artikel 1 Gesetz zur Verhütung und Bekämpfung von Infektionskrankheiten beim Menschen (Infektionsschutzgesetz - IfSG). [Act on the Reform of the Communicable Diseases Law (Communicable Diseases Law Reform Act) of 20 July 2000. Article 1. Act on the Prevention and Control of Infectious Diseases in Man (Protection against Infection Act)]. Bundesgesetzblatt (BGBl). I S. 1045. 2000. 20 Jul 2000. German. [Accessed 04 Jan 2012]. Available from: http://www.rki.de/EN/Content/Prevention/Inf_Dis_Surveillance/inf_dis_down.pdf?__blob=publicationFile
2. Robert Koch Institute (RKI). Falldefinitionen des Robert Koch-Instituts zur Übermittlung von Erkrankungs- oder Todesfällen und Nachweisen von Krankheitserregern - Ausgabe 2007. [Case definitions for the surveillance of notifiable infectious diseases in Germany – Edition 2007]. Berlin: RKI; 2007. German. [Accessed 04 Jan 2012]. Available from: http://www.rki.de/DE/Content/Infekt/IfSG/Falldefinition/Falldefinition.pdf;jsessionid=700F4F1C3FEFFF5081B89AB23933B2E0.2_cid241?__blob=publicationFile
3. Ochoa TJ, Barletta F, Contreras C, Mercado E. New insights into the epidemiology of enteropathogenic Escherichia coli infection. Trans R Soc Trop Med Hyg. 2008;102(9):852-6.
4. Robert Koch-Institut (RKI). SurvStat@RKI. Berlin: RKI. [Accessed 21 Apr 2012]. Available from: http://www3.rki.de/SurvStat
5. Frank C, Faber MS, Askar M, Bernard H, Fruth A, Gilsdorf A, et al. Large and ongoing outbreak of haemolytic uraemic syndrome, Germany, May 2011. Euro Surveill. 2011;16(21):pii=19878. Available from: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleID=19878
6. Faensen D, Claus H, Benzler J, Ammon A, Pfoch T, Breuer T, et al. SurvNet@RKI -- amultistate electronic reporting system for communicable diseases. Euro Surveill. 2006;11(4):pii=614. Available from: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=614
7. Gould LH, Bopp C, Strockbine N, Atkinson R, Baselski V, Body B, et al. Recommendations for diagnosis of Shiga-toxin producing Escherichia coli infections by clinical laboratories. MMWR Recomm Rep. 2009; 58(RR12):1-14.
8. Combs BG, Raupach JC, Kirk MD. Surveillance of Shiga toxigenic Escherichia coli in Australia. Commun Dis Intell. 2005;29(4):366-9.
9. Kiska DL, Riddell SW. Counterpoint: Should all stools be screened for Shiga toxin-producing Escherichia coli? J Clin Microbiol. 2011;49(7):2394-7.
10. Wahl E, Vold L, Lindstedt BA, Bruheim T, Afset JE. Investigation of an Escherichia coli O145 outbreak in a child day-care centre--extensive sampling and characterization of eae- and stx1-positive E. coli yields epidemiological and socioeconomic insight. BMC Infect Dis. 2011;11:238.
11. Scallan E, Majowicz SE, Hall G, Banerjee A, Bowman CL, Daly L, et al. Prevalence of diarrhoea in the community in Australia, Canada, Ireland, and the United States. Int J Epidemiol. 2005;34(2):454-60.
12. Scallan E, Jones TF, Cronquist A, Thomas S, Frenzen P, Hoefer D, et al. Factors associated with seeking medical care and submitting a stool sample in estimating the burden of foodborne illness. Foodborne Pathog Dis. 2006;3(4):432-8.
13. Hall G, Yohannes K, Raupach J, Becker N, Kirk M. Estimating community incidence of Salmonella, Campylobacter, and Shiga toxin-producing Escherichia coli infections, Australia. Emerg Infect Dis. 2008;14(10):1601-9.
14. Vally H, Hall G, Scallan E, Kirk MD, Angulo FJ. Higher rate of culture-confirmed Campylobacter infections in Australia than in the USA: is this due to differences in healthcare-seeking behaviour or stool culture frequency? Epidemiol Infect. 2009;137(12):1751-8.
15. Tam CC, Rodrigues LC, O'Brien SJ. The study of infectious intestinal disease in England: what risk factors for presentation to general practice tell us about potential for selection bias in case-control studies of reported cases of diarrhoea. Int J Epidemiol. 2003;32(1):99-105.
16. Kist M, Bockemühl J, Aleksic S, Altwegg M, Autenrieth IB, Bär W, et. al. MiQ 9: Infektionen des Darmes. [Infections of the gut]. In: Mauch H, Lütticken R, Gatermann S, editors. MIQ - Qualitätsstandards in der mikrobiologisch-infektiologischen Diagnostik. [Quality standards for microbiological and infection-diagnostics]. 1st edition. Munich - Jena: Urban & Fischer; 2000. German.
17. Kochen MM, Kaduszkiewicz H, Scherer M, Deutsche Gesellschaft für Allgemeinmedizin und Familienmedizin (DEGAM). S1-Leitlinie EHEC/HUS. [S1-Guidelines for EHEC/HUS]. Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften (AWMF)-Leitlinien-Register Nr. 053/025. Version: 10.06.2011. Valid through: 10.06.2016. Düsseldorf: AWMF; 2011. German. [Accessed 23 Aug 2011]. Available from: http://www.awmf.org/uploads/tx_szleitlinien/053-025_S1_EHEC-HUS_2011-06-10.pdf
18. Gesellschaft für Pädiatrische Gastroenterologie und Ernährung (GPGE). Akute infektiöse Gastroenteritis. [Acute infectious gastroenteritis]. Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften (AWMF)-Leitlinien-Register Nr. 068/003. Version: 01.04.2008. Valid through 01.04.2013. Düsseldorf: AWMF; 2008. German. [Accessed 23 Aug 2011]. Available from: http://www.awmf.org/uploads/tx_szleitlinien/068-003_S1_Akute_infektioese_Gastroenteritis_04-2008_04-2013.pdf