



# Shiga toxin-producing *Escherichia coli* burden in the Netherlands

**Authors:** M. Petrigani<sup>1,2</sup>, C.H.F.M. Waegemaekers<sup>2</sup>, P.D. Croughs<sup>3</sup>, W. Niessen<sup>4</sup>, J.W.A. Rossen<sup>5</sup>, A.W. Friedrich<sup>5</sup>, R.F. de Boer<sup>6</sup>, A.M.D. Kooistra-Smid<sup>5,6</sup>, I.H.M. Friesema<sup>2</sup>

- 1 Municipal Health Service Rotterdam-Rijnmond, Rotterdam, the Netherlands
- 2 National Institute for Public Health and the Environment, Bilthoven, the Netherlands
- 3 Star-MDC, Rotterdam, the Netherlands
- 4 Municipal Health Service Groningen, Groningen, the Netherlands
- 5 Department of Medical Microbiology, University of Groningen, University Medical Center Groningen, Groningen, the Netherlands
- 6 Certe, Medical Microbiology, Groningen, the Netherlands.

## Background

Clinical manifestations of Shiga toxin-producing *Escherichia coli* (STEC) range from mild diarrhea to extraintestinal severe complications, such as hemolytic uremic syndrome (HUS). Surveillance is needed for early detection of clusters and source tracing in order to prevent transmission. In the Netherlands, surveillance was extended from O157 to all STEC serotypes in 2007, when molecular methods for detection of STEC became available. Consequently, a sharp increase in STEC notifications took place, which led to an increased workload for public health services and often missing epidemiological and serotyping information.

## STEC-ID-net

This multicenter prospective study to investigate the virulence of STEC and the public health relevance of *stx1/stx2/escV* genes detected in stool, consists of a laboratory and a public health component and was performed in two Dutch regions. Stool samples from patients with presumed infectious gastroenteritis arriving at one of the two participating laboratories between April 1, 2013 and March 31, 2014 were screened using qPCR targeting the *stx1/stx2/escV* genes. Samples testing positive for these genes were further tested for additional virulence factors and serotyped. Patients with *stx*-positive stool were interviewed by phone. If patients could not be reached, the questionnaire was sent by mail.

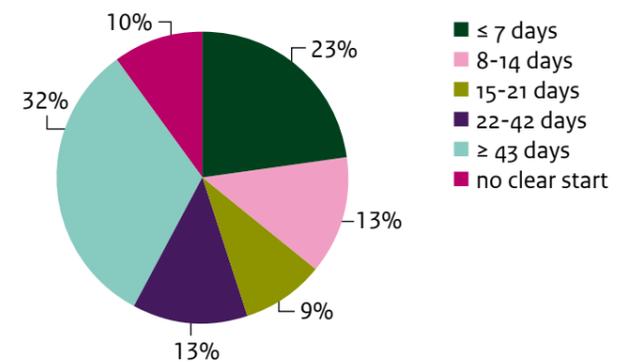
## Results

- *Stx*-genes were detected in 425 of 23153 stool samples (1.8%). The median age of the STEC-patients was 40 years (0-92 years; n=425), and 59% were female.
- One participating laboratory serves a population of over one million inhabitants, including both community-based and hospitalized patients. Incidence of STEC-infections in that area was 19.6 cases per 100.000 inhabitants.
- A questionnaire was obtained from 246 patients (58%). Median age of these STEC-patients was 36 years (0-87 years; n=246), and 60% were female. Only 1 HUS-case was reported.

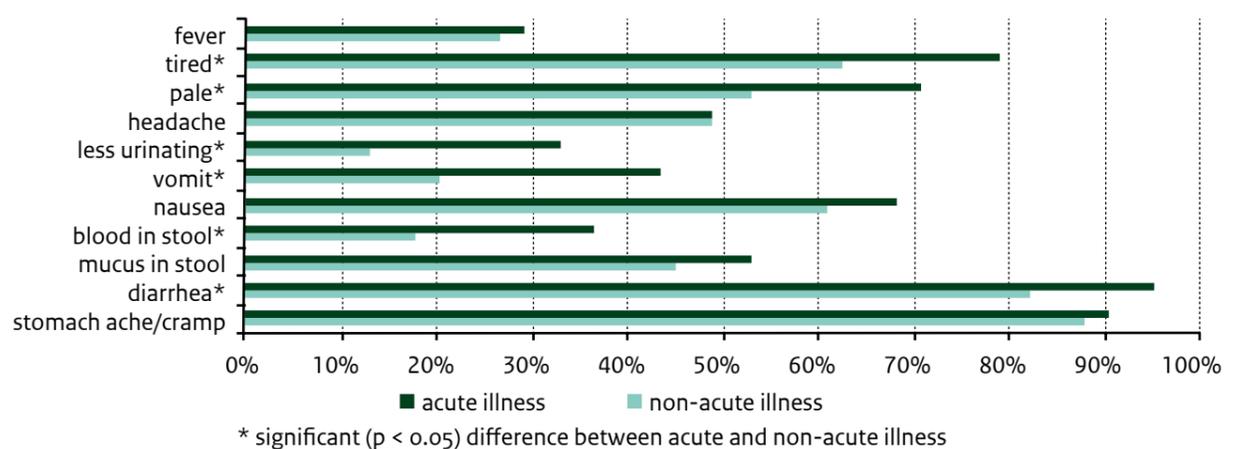
- Ten percent of the patients could not pinpoint a day of onset of disease, whereas in 23% of the cases a feces sample arrived at the laboratory within 7 days after start of the symptoms (Figure 1). A sample was sent in within 3 weeks after onset in 45% of the patients, further referred to as "acute illness".
- Diarrhea and stomach ache/cramps were the most commonly reported symptoms (Figure 2). Diarrhea, blood in stool, vomiting, less frequent urination, paleness and tiredness were significantly more often reported by patients with acute illness.
- Median duration of illness was 9 days (range 3-28 days; n=48) for patients with acute illness; when completing the questionnaire, 44 cases with acute illness (41%) still had some, mostly mild, symptoms, such as diarrhea, tiredness and stomach ache. Thirteen cases with acute illness (12%) were hospitalized for a median of 3 days (range 1-10 days; n=12). Median age of these hospitalized patients was 36 years (10-87 years; n=13), and 9/13 (69%) were female.
- 23% of the cases who vomited reported secondary cases compared to 10% of the cases without vomiting; odds ratio 2.8 (95% CI: 1.3-6.1).
- In almost half of the patients with acute illness (51/108; 47%) a feces sample was sent in during the months June-August (Figure 3). For patients with non-acute illness, most samples were sent in between July and September (58/138; 42%).
- Presence of the *escV* gene was associated with acute illness: the gene was present in 67% of the isolates of patients with acute onset versus 47% of non-acute illness; odds ratio 2.2 (95% CI: 1.3-3.8). Presence of the *stx2* gene was only associated with acute onset in combination with the *escV* gene: both genes were present in 40% of the isolates of patients with acute illness versus 17% of non-acute illness; odds ratio 3.3 (95% CI: 1.8-6.0).

## Discussion and conclusions

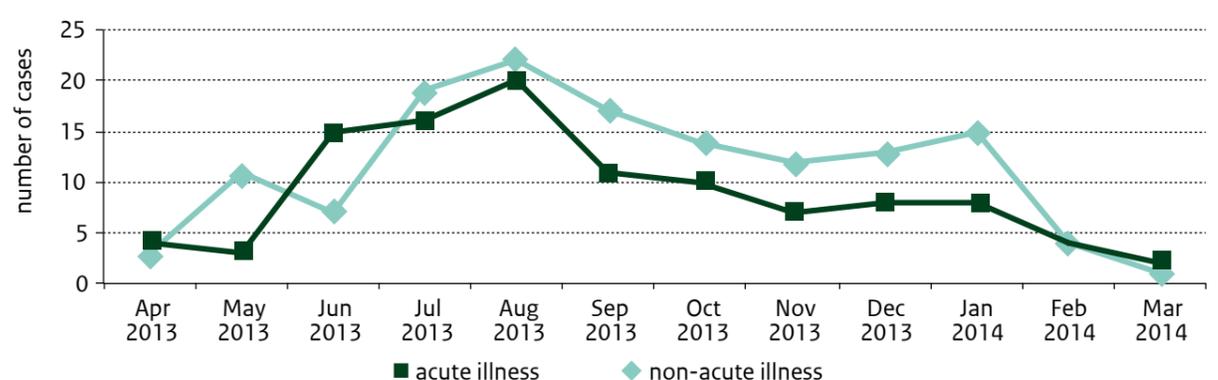
STEC-infections are notifiable in the Netherlands as STEC can cause serious illness, thus early detection of clusters, source tracing, and prevention of spread of the infection is important. When notified, public health workers can search for sources of infection to prevent further cases and give advice to prevent secondary cases. The current study shows that about half of the patients with *stx*-genes in their stool did not have acute illness. Overall, these patients also reported less symptoms, especially gastroenteritis-specific symptoms of diarrhea, vomiting and blood in stool. For public health aims, this group without acute illness is of lesser importance. The current study also shows that the presence of the *stx2* gene in combination with the *escV* gene is associated with acute onset. Finally, a result that needs further investigation is the association found between vomiting and the occurrence of secondary cases. The results of STEC-ID-net will be used to develop a laboratory algorithm and to revise the notification criteria for STEC infections in the Netherlands in order to distinguish the public health relevant infections from the non-relevant.



**Figure 1.** Number of days between onset of illness and arrival of feces sample at the laboratory



**Figure 2.** Prevalence of symptoms in patients with and without acute illness



**Figure 3.** Number of cases with and without acute illness per month (of arrival of feces sample)