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Assessing the risk of a community outbreak of hepatitis A on blood safety in Latvia, 2008

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Post-transfusion hepatitis A virus (HAV) infection worldwide is considered a sporadic event. An outbreak of HAV infection occurred in Latvia between the end of 2007 and throughout 2008 with more than 2,800 confirmed cases reported over a 13-month period (incidence of 123 per 100,000 population). The majority of reported HAV infection cases were in people over 18 years of age and in people living in the capital city, Riga. We estimated that the crude risk for HAV contamination of whole blood supplies in Riga between February and October 2008 ranged from 1.4 to 10.6per 10,000 donated units. In people under 40 years of age, the risk of receiving an infectious blood transfusion was more than 3.0 per 10,000 recipients between August and October 2008 during the peak of the outbreak. We conclude that there is a previously under-recognised impact of HAV on blood safety during widespread outbreaks of this disease. Estimating the risk of contamination of blood supplies during an infectious disease outbreak scenario is important for fine tuning risk assessments and potentially improving public health practices. `

Introduction

Hepatitis A virus (HAV) infection is an acute viral illness usually acquired through the faecal–oral route. Outbreaks have been associated with contaminated food and water supplies, and have also been identified in specific communities such as injecting drug users (IDUs) and men who have sex with men (MSM). The level of endemicity of HAV infection varies worldwide, with higher seroprevalence reported in resource-poor countries and lower seroprevalence in developed regions such as northern Europe and Japan [1]. In the European Union (EU), the overall notification rate for HAV infection decreased from 15.1 to 2.81 cases per 100,000 from 1996 to 2007 [2]. Despite improved sanitary conditions, but with the lack of universal HAV vaccination programmes in the majority of countries, this disease remains endemic in the EU. However, its epidemiology is changing: EU Member States that were considered previously highly endemic, mostly former east-European countries [3], are now demonstrating moderate endemicity. Such changes in epidemiology are usually characterised by shifts in the population affected from children where HAV infection is asymptomatic or mild, to young adults, in whom the disease is more severe.

Post-transfusion HAV infection has been documented after a person has received whole blood and plasma [4-8], as well as in haemophiliac patients who have received concentrated blood products such as Factor VIII [6,9-17]. In India, blood product recipients are recommended to receive HAV vaccination and in the United Kingdom, the Department of Health recommends HAV vaccination for haemophiliacs [18,19]. Current methods for inactivation of viruses and partition methods for long-lasting blood products are less effective for HAV [20] and parvovirus B19 [21], than for hepatitis B and C viruses, HIV and dengue virus, because HAV and parvovirus B19 are non-enveloped protein viruses. However, the general assumption is that blood safety is not greatly affected by HAV and that post-transfusion infection with the virus is a sporadic event, especially in endemic countries where immunity is high.

In Latvia, HAV infection is a notifiable disease through the national surveillance system, using the EU case definition [22]. The incidence of the disease has decreased substantially over the last 20 years, with more than 6,000 cases reported in 1990 (incidence of 263 per 100,000 population), compared with a mean of 87 cases per year between 2000 and 2007 (incidence of four per 100,000 population) [23,24].

In late 2007, surveillance data indicated an increase of reported HAV cases in the country. By December 2008 a total of 2,817 cases had been reported, with 17 deaths [25] (incidence of 123 per 100,000 population). This outbreak was noteworthy in several aspects. Firstly, it was a community-wide outbreak that was concentrated in the capital city, Riga, where 76% of the cases were reported. Furthermore, the proportion of IDUs among the reported HAV cases was more than 20% up to July 200; after that, the proportion decreased as the outbreak became increasingly established in the community [25]. Finally, adults were the most affected

age group of the 1,701 cases reported in Riga between February and October 2008: 1,344 (79%) cases were aged between 18 and 65 years.

Because of the geographical and age distribution of the majority of cases in this outbreak, we hypothesised that there was a potential impact on blood safety, as the majority of blood donors come from urban areas and are older than 18 years (the minimum age for blood donation, which in Latvia is voluntary). Around 1.3% of the population regularly donates blood (unpublished data). For this reason we decided to estimate the impact of HAV infection on blood donations during this community-wide outbreak in Latvia.

Methods

As the majority of HAV infections in Riga were reported between February and October 2008, we divided this time into three distinct outbreak periods (Figure 1): February – April (Period 1), May – July (Period 2) and August – October (Period 3), the last being the peak of the outbreak. On the assumption that 70% of HAV infections are asymptomatic [26,27] and that all symptomatic infections were reported through the Latvian surveillance system, we calculated the total number of HAV infections in Riga for each of the three outbreak periods (incidence). We also further restricted this analysis to people over 18 years of age (the lower age limit for blood donation in Latvia).

The method used to calculate the risk of HAV contamination of the supply of whole blood in Latvia was based on previous calculations conducted by Biggerstaff and Petersen [28,29] to estimate the impact of West Nile fever outbreaks in the United States on national blood safety. This method considers the proportion of symptomatic and asymptomatic infected cases, the duration of the viraemic period in asymptomatic and symptomatic cases before they develop symptoms (i.e. when they could donate blood) and the duration and attack rate of the outbreak.

The formula used to calculate the mean risk to blood donations is:

$$\text{Mean risk} = \text{Incidence during the outbreak (per 100,000 population)} \times \frac{\text{Mean duration of asymptomatic viraemia (days)}}{\text{Duration of the outbreak (days)}}$$

In order to calculate the mean duration of asymptomatic viraemia, we use the following formula:

$$\text{Mean duration of asymptomatic viraemia} = (P_{sympto} \times V_{sympto}) + (P_{asympto} \times V_{asympto})$$

where:

- P*sympto* = Proportion of symptomatic cases
- V*sympto* = Duration of viraemia in symptomatic cases (days)
- P*asympto* = 1 – P*sympto* = Proportion of asymptomatic cases
- V*asympto* = Duration of viraemia in asymptomatic cases (days).

To our knowledge, this method has only been used once for other situations, to estimate the impact of a local HAV outbreak on blood safety in France [27]. In order to ensure that our data are comparable, we used the same parameters and assumptions as the French study. On the basis of the parameters from that study and other literature, we assumed that in the Latvian outbreak 70% of cases were symptomatic, all symptomatic cases were reported through the surveillance system, the duration of pre-symptomatic viraemia in symptomatic cases was 16 days and that the duration of viraemia in asymptomatic cases was 70 days [26,27,30]. The crude risk of HAV contamination in blood supplies was then calculated for each of the three outbreak periods.

In order to estimate the risk that a blood transfusion recipient would be susceptible to HAV infection during this outbreak, we took into account the underlying immunity for HAV in the Latvian population and the screening procedures used at the Latvian blood bank. The anti-HAV seroprevalence of the population was determined in 1998 (unpublished data). In order to estimate the underlying HAV immunity, we extrapolated the seroprevalence data from 1998 by 10 years to estimate seroprevalence levels in 2008 (e.g. we assumed that the seroprevalence of the age group 30–39 years in 1998 would be the level of the 40–49 years age group in 2008, etc.). We did not take into consideration any additional population immunity resulting from HAV vaccination as this vaccine is not routinely included in the Latvian vaccination schedule and is only available upon individual request. Therefore, we assumed that any population immunity resulting from HAV vaccination would be negligible. Furthermore, blood will not be taken from potential donors at any Latvian blood bank if they report that they have had contact with a person with any infectious disease (including hepatitis A). For those reporting close contact with an HAV-infected person, their blood donation will be deferred for 50 days.

In addition, blood units are tested for alanine aminotransferase (ALT) levels: any donation that contains greater than 90 international units per litre (IU/L) is rejected for donation, as it indicates impaired liver function associated with all types of hepatitis. We assumed that in asymptomatic HAV-infected donors, the ALT levels would reach this threshold after 16 days of infection (i.e. the duration of pre-symptomatic viraemia in symptomatic patients) and that their donations would be excluded from the central blood bank. Using the Biggerstaff and Petersen formula we calculated the risk of contamination of blood with HAV using the adjusted asymptomatic viraemic period. This risk was multiplied by the proportion of the population that is

not immune to hepatitis A, i.e. 1 – [anti-HAV seroprevalence proportion], for a specific age group to obtain the risk of receiving an infectious donation per age group.

Results

The incidence (per 100,000 population), taking into account asymptomatic and symptomatic cases of HAV infection in Latvia during the three outbreak periods, were calculated to be 32 for Period 1, 52for Period 2 and 290 for Period 3. The estimated crude risk for HAV-contaminated whole blood supplies in Latvia between February and October 2008 ranged from 1.4 to 10.6 units per 10,000 donated units (Table 1).

The extrapolated anti-HAV seroprevalence (i.e. immunity) in Latvia in 2008 increased with age, from 15% in people younger than 15 years to 60% in people older than 40 years of age (Figure 2 and Table 2). When considering the underlying immunity and the ALT screening at the blood bank, the risk of receiving a contaminated donation and being susceptible for infection was greater than 3.0 per 10,000 transfusions for people younger than 40 years in Riga (Table 2).

The Latvian central blood bank received 24,727 valid donations between February and October 2008. Of these, 1.5% (range: 1.0–2.0%) per month had ALT levels greater than 90 IU/L and were therefore rejected for use. These numbers are similar to those rejected for use before the outbreak was identified. There was one report of possible post-transfusion hepatitis A during the 2008 HAV outbreak, in a hospital in Riga. This person received blood from 28 different donors, none of whom were symptomatic for infection at the time of donation. No further investigations (trace-back or epidemiological) were conducted with the donors to determine their anti-HAV status.

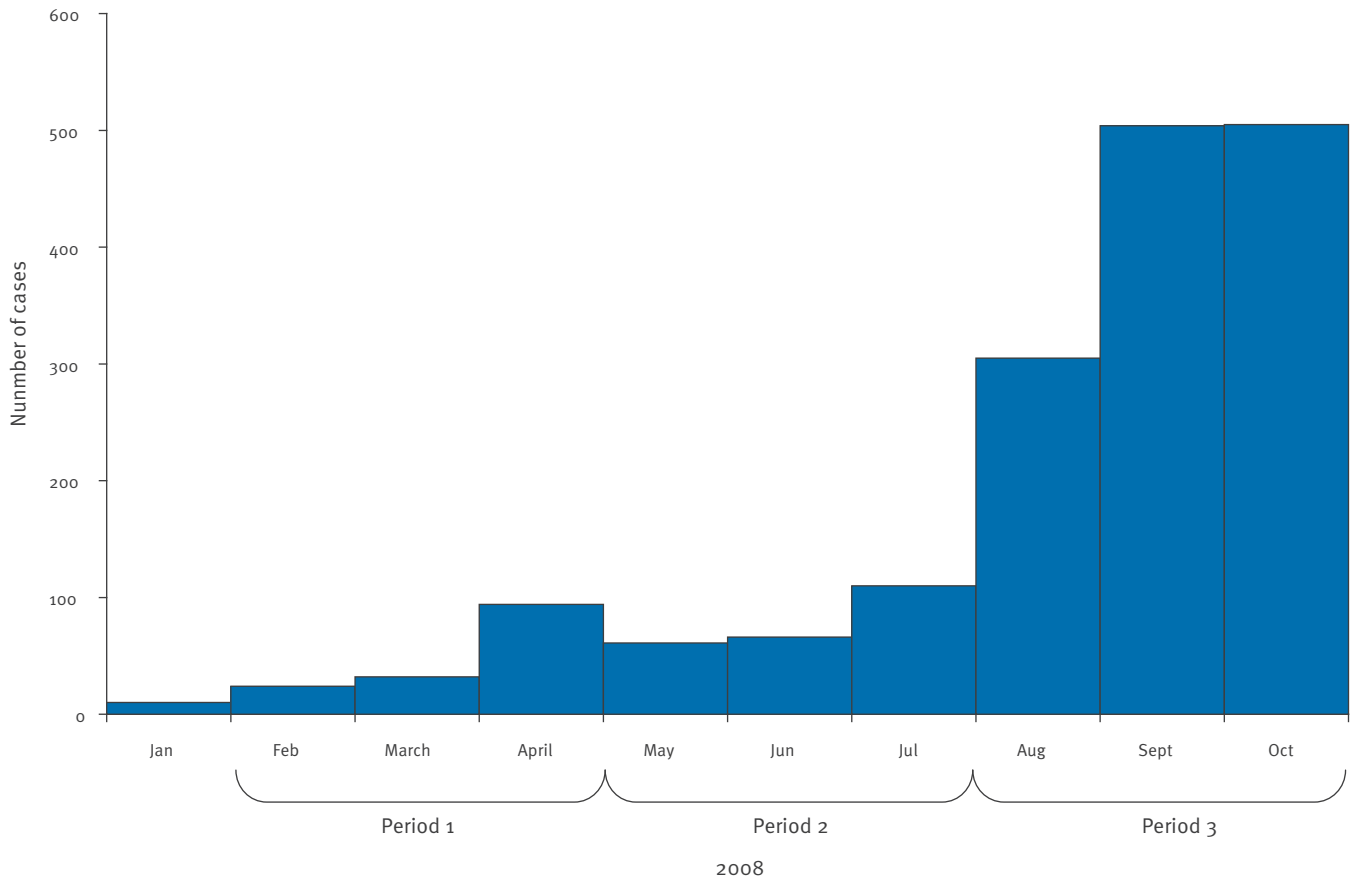
Discussion

To the best of our knowledge, this is the first time that a national risk assessment of blood safety following a widespread community outbreak of HAV infection in a European country has been conducted. Our study shows that large community outbreaks of an infectious disease such as hepatitis A in a country with a moderate endemicity can have an important and under-recognised impact on blood safety.

There are several limitations in the estimation of risk of contaminated whole blood products with HAV. It is possible that the crude and adjusted risk calculations were overestimated as we considered the overall attack rate of HAV infection in Riga and did not exclude reported cases in infecting drug users. As blood donations from these people would be deferred, they would probably not contribute to contaminated blood supplies. Also,

Figure 1

Confirmed cases of hepatitis A virus infection, Riga, Latvia, January – October 2008 (n= 810)



The three outbreak periods considered in the current study are indicated.

the calculations were unable to take into account the effectiveness of screening procedures that are implemented at the blood bank in Latvia to defer donations from people with a history of contact with someone with an infectious disease. We did not take into consideration the effect of neutralising antibodies in potential donors on reducing the infectious capability of their donated blood, as all available evidence suggest that such antibodies only appear and continue to increase once the person has become symptomatic [30,31]. Their presence would therefore not affect our current risk estimates as a symptomatic potential donor would be excluded from donation at that point. We also could not quantify the effect of HAV-immune donors on the current risk estimates. Furthermore, we were not able to estimate the residual viraemic potential of HAV in blood units or the immunological response of transfusion recipients. Both these factors would modify the risk of post-transfusion HAV infection.

Table 1

Risk of hepatitis A virus contamination of blood donation from donors aged 18–65 years, Riga, Latvia, 2008

Period, 2008	Number of HAV-positive blood donations per 10,000 blood donations	95% CI
1. February – April	1.36	1.16–1.56
2. May – July	2.03	1.80–2.27
3. August – October	10.59	10.05–11.13

CI: confidence interval; HAV: hepatitis A virus.

Figure 2

Anti-hepatitis A seroprevalence in 1998 and extrapolated seroprevalence in 2008, by age group, Latvia

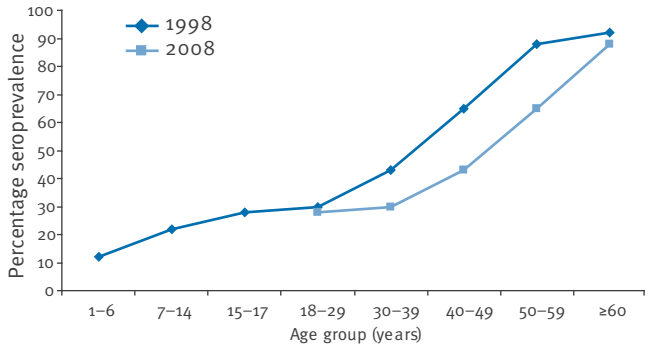


Table 2

Risk of hepatitis A virus infection in recipients of blood donation by age group, Riga, Latvia, August – October, 2008

Age group of recipients (years)	Percentage of population immune[a]	Number of HAV infections per 10,000 blood donation recipients	95% CI
0–14	15	4.47	4.24–4.70
15–39	30	3.68	3.49–3.87
≥40	60	2.10	1.99–2.21

CI: confidence interval; HAV: hepatitis A virus.

[a] Latvian seroprevalance data from 1998 adjusted for 2008.

This study focused only on contamination of whole blood. Long-lasting blood products are produced from pools of blood units (sometimes several thousands) and therefore the risk for contamination would potentially be increased. Also, long-lasting blood products undergo several deactivation steps to eliminate other infectious disease risks. Even though HAV is a non-enveloped virus and the deactivation steps are less effective for this type of virus, it is likely that most viral potential would be removed [26,30]. The real risk of contaminated long-lasting blood products during this outbreak in Riga in 2008 is therefore more complex to quantify.

At the peak of the outbreak between August and October 2008, the crude risk for contaminated whole blood supplies was 10.6per 10,000 donations and the adjusted risk for infective transfusions was greater than 3.0 per 10,000 recipients in people under 40 years. Between February and October 2008, a mean of 2,700 donations per month were made to the Latvian blood bank. Therefore, the calculated risk per 10,000 donations is very similar to the monthly contamination of whole blood supplies during this outbreak.

During a West Nile virus outbreak in the United States in 1999, the calculated risk for transmission of the virus was between 1.8 and 2.7 per 10,000 blood donations [28]. In the light of this estimate, the United States implemented pooled screening of all blood donations for West Nile virus [32]. For other viruses that cause infectious diseases, such as human immunodeficiency virus (HIV) and hepatitis C, the current estimated risk of contamination is one unit per two million donations; for hepatitis B it is one per 200,000 donations [33]. The calculated HAV contamination risk in Riga during this epidemic was significantly higher than the risk of contamination with any of the other mentioned viruses. Over the studied outbreak period, close to 30,000 blood donations were received in Latvia, and it is likely that some of these were contaminated and were not rejected for donation despite routine screening. It is unlikely that the current crude contamination estimation would be reflected in the proportion of donations that exceeded 90 IU/L of ALT (and would therefore be rejected at the central blood bank), as they only comprise 0.1% of the total number of donations.

Only one report of possible post-transfusion HAV infection in Latvia was received during the outbreak. This might be explained by the fact that HAV infection is generally not a severe disease and could therefore be missed in patients with serious underlying conditions who receive blood transfusion. Furthermore, it is unlikely that the resources necessary to conduct in-depth investigations around this single reported case could be liberated. A stricter follow-up of all transfusion recipients during the outbreak period would have allowed the actual incidence of post-transfusion HAV infection during this outbreak to be determined.

There are measures to prevent infections with HAV through blood transfusion, including vaccination,

immunoglobulin administration and more stringent screening procedures for possible blood donors. Such methods might need to be temporarily employed during large-scale community outbreaks in order to reduce the risk of HAV infection in transfused patients. However, their use would need to be carefully assessed by comparing the risk of acquiring the infection from contact with a hepatitis A case in the general population versus the risk of acquiring the infection through a blood transfusion as it is possible that the incidence is sufficiently high during the outbreak that a person would be more likely to become infected in the community.

The methods described in this study are one of the possible tools that could facilitate conducting a targeted risk assessment for the impact of an infectious disease on blood supplies during an acute period such as an epidemic. The calculations are simple and easily reproducible for other infectious diseases of epidemic potential. Even though the method has limitations, the estimations of crude and adjusted risks of contamination of whole blood supplies provide important information for the further management of blood donations during an infectious disease outbreak. Combining these rough calculations with other available epidemiological information about the outbreak and complementing these findings with close follow-up of transfusion recipients, the risk assessment might be even further fine-tuned, resulting in better public health practices.

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Laboratory-based surveillance for Cryptosporidium in France, 2006–2009

The ANOFEL Cryptosporidium National Network[1]
1. Details of the corresponding author and the list of members of the network are included at the end of the article

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In 2002, the French Food Safety Agency drew attention to the lack of information on the prevalence of human cryptosporidiosis in the country. Two years later, the ANOFEL *Cryptosporidium* National Network (ACNN) was set up to provide public health authorities with data on the incidence and epidemiology of human cryptosporidiosis in France. Constituted on a voluntary basis, ACNN includes 38 hospital parasitology laboratories (mainly in university hospitals). Each laboratory is engaged to notify new cases of confirmed human cryptosporidiosis, store specimens (e.g. stools, duodenal aspirates or biopsies) and related clinical and epidemiological data, using datasheet forms. From January 2006 to December 2009, 407 cryptosporidiosis cases were notified in France and 364 specimens were collected. Of the notified cases, 74 were children under four years of age, accounting for 18.2%. HIV-infected and immunocompetent patients represented 38.6% (n=157) and 28% (n=114) of cases, respectively. A marked seasonal pattern was observed each year, with increased number of cases in mid to late summer and the beginning of autumn. Genotyping of 345 isolates from 310 patients identified *C. parvum* in 168 (54.2%) cases, *C. hominis* in 113 (36.4%) and other species in 29 (9.4%), including *C. felis* (n=15), *C. meleagridis* (n=4), *C. canis* (n=4), *Cryptosporidium* chipmunk genotype (n=1), *Cryptosporidium* rabbit genotype (n=1) and new *Cryptosporidium* genotypes (n=4). These data represent the first multisite report of laboratory-confirmed cases of cryptosporidiosis in France.

Introduction

Cryptosporidium infection is increasingly recognised as a major cause of diarrhoeal disease worldwide, in all age groups [1]. The range of people affected is broad including immunosuppressed people and children, especially in developing countries. Sporadic or outbreak cases are also seen among immunocompetent individuals. Symptoms of the disease are diverse: 90% of patients have diarrhoea, which is often associated with other gastrointestinal symptoms such as vomiting, nausea or abdominal pain [1]. Asymptomatic infections are also reported. In immunocompromised individuals, such as people receiving immunosuppressive drugs and acquired immunodeficiency syndrome (AIDS) patients with low CD4 lymphocyte counts, cryptosporidiosis is often chronic, leading to important weight loss and cachexia. Currently, very few drugs are active against *Cryptosporidium* and none is curative: the only antiparasitic drug proven to be effective in immunocompetent adults and children is nitazoxanide, and none has proven effective in severely immunocompromised patients [2].

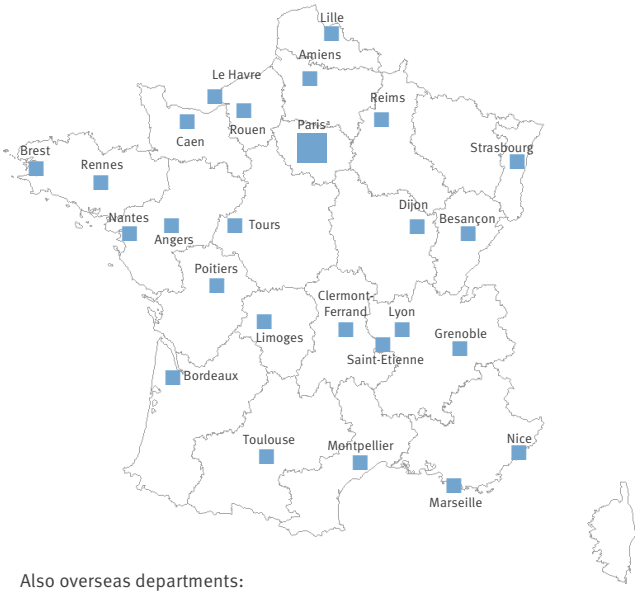
Over the past 20 years, *Cryptosporidium* has been responsible for numerous waterborne outbreaks of gastrointestinal disease, mainly in North America and the United Kingdom, but also throughout the world [3,4]. These outbreaks have been described in relation to drinking contaminated water or recreational use of contaminated water, consumption of contaminated food, person-to-person spread and animal-to-person contact [5]. *Cryptosporidium* species are of major concern for regulatory agencies, water industries and consumers [6], because they are widespread zoonotic pathogens and because oocysts (the transmissible form of the parasite) are resistant to chemical disinfectants used for treating drinking water.

Although the role of water and food in the epidemiology of cryptosporidiosis is now clearly recognised, the prevalence of *Cryptosporidium* spp. infection in humans is not well known. In several countries, notification of confirmed cases to public health agencies is an essential stage of national strategies to improve both prevention of *Cryptosporidium* infection and the understanding of cryptosporidiosis epidemiology [4,5,7-10]. In France, most laboratories do not test for *Cryptosporidium* in stool specimens submitted for routine parasitological examination and sporadic cases are not reported at regional or national level. For this reason, cryptosporidiosis remains underdiagnosed and underreported. Nevertheless, three cryptosporidiosis outbreaks have been documented in France. The first occurred in Sète (Hérault) in 1998, the second in Dracy-le-Fort (Saône et Loire) in 2001, and the last in Divonne-les-Bains (Ain) in 2003, involving 150, more than 480 and 727 estimated cases, respectively [11-13].

To deal with a recognised but poorly defined risk of cryptosporidiosis in immunocompetent and immunocompromised populations, the French Food Safety Agency (Agence française de sécurité sanitaire des aliments, Afssa) asked an expert group to assess the risk of food-borne and waterborne cryptosporidiosis in France. The group was set up in January 2001: on the basis of its final report in 2002, Afssa pointed out the lack of information on human cryptosporidiosis in France and strongly suggested improving surveillance by improving investigation means for *Cryptosporidium* in humans, animals and foods (including water resources) [14]. As a result of this report, a network of laboratories – the ANOFEL *Cryptosporidium* National Network (ACNN) – covering most of the French territory was established in October 2004 to provide public health authorities with information on the incidence and epidemiology of human cryptosporidiosis in France. It was set up on a voluntary basis by the French association of medical parasitologists (Association des enseignants et des praticiens hospitaliers titulaires de parasitologie et mycologie médicales, ANOFEL) with the support of Afssa and the national institute of disease surveillance (Institut de veille sanitaire, InVS). Established with 31 hospital parasitology laboratories (mainly university hospitals) distributed all over the national territory (metropolitan France and overseas departments of French Guiana, Guadeloupe and Martinique), the network initially focused on internal organisation and interlaboratory tests for microscopic diagnosis of cryptosporidiosis. Reporting of cryptosporidiosis cases and specimen collection started in January 2006.

Figure 1

Location of the 38 laboratories participating in the ANOFEL *Cryptosporidium* national network (ACNN), France, 31 December 2009



ANOFEL: French association of medical parasitologists.

[a] There are 10 laboratories in the network in Paris.

By the end of the year, there were 36 participating laboratories; a further two joined in 2008 (Figure 1). This article summarises the Cryptosporidium-related data, including genotyping, collected from 2006 to 2009.

Since testing for *Cryptosporidium* is not included in routine parasitological stool tests in France, it is only performed at the physician's request or following the recommendation of the director of a laboratory, on the basis of available clinical or epidemiological patient data suggesting *Cryptosporidium* infection. An ACNN internal survey carried out in February 2010 revealed that routine testing for *Cryptosporidium* in stools of HIV-infected patients is performed by 27 participating laboratories (almost three quarters), by 50–60% of laboratories in stool samples from patients with organ transplantation (n=18), stem cell transplantation (n=21) or lymphoproliferative disorder (n=19) and by around 40% of laboratories in faecal samples from immunocompetent patients with diarrhoea (n=15 for samples from children; n=13 for samples from adults).

Methods

Data and specimen collection

Each laboratory in the ACNN was engaged to notify every new case of laboratory-confirmed human cryptosporidiosis. Diagnosis was based on the demonstration of *Cryptosporidium* spp. in stools, duodenal aspirates or intestinal biopsies (or in other sample in case of extraintestinal cryptosporidiosis) by microscopy, using modified Ziehl–Neelsen stain alone or in conjuction with polymerase chain reaction (PCR) (36 laboratories), Heine stain (one laboratory) and auramine stain (one laboratory) [15]. Diagnostic laboratory staff were asked to provide details (including age, sex and sample collection date) of cryptosporidiosis cases upon notification, using a standardised form. Related clinical and epidemiological data were also collected: patient's place of residence, history of recent foreign travel, animal and water exposure and whether the case was considered to be part of a family or household cluster or an outbreak. Faecal samples were collected, preserved in 2.5% (volume by volume) potassium dichromate solution and stored at +4 °C until they were sent to the Lille or Lyon laboratories, which were in charge of *Cryptosporidium* spp. sample collection. More rarely, DNA extracts were sent to the collection and stored at –20 °C.

Molecular characterisation of isolates

Except for two laboratories that carried out genotyping by themselves (Dijon and Paris Pitié Salpétrière), molecular characterisation of isolates from other laboratories was performed in Lille. Genomic DNA was extracted from stool samples using the UltraClean Fecal DNA Kit (MoBio, Ozyme) according to the manufacturer's protocol. The species and genotype were determined using 18S ribosomal DNA sequence analysis [16].

Data analysis

Case notifications were centralised in one laboratory (Lille). All collected information was entered into

a Microsoft Excel database. Epidemiological analysis was published each year for members of the network. The comparative distribution of *C. parvum* and *C. hominis* cases in the dataset was analysed by Fisher's exact test.

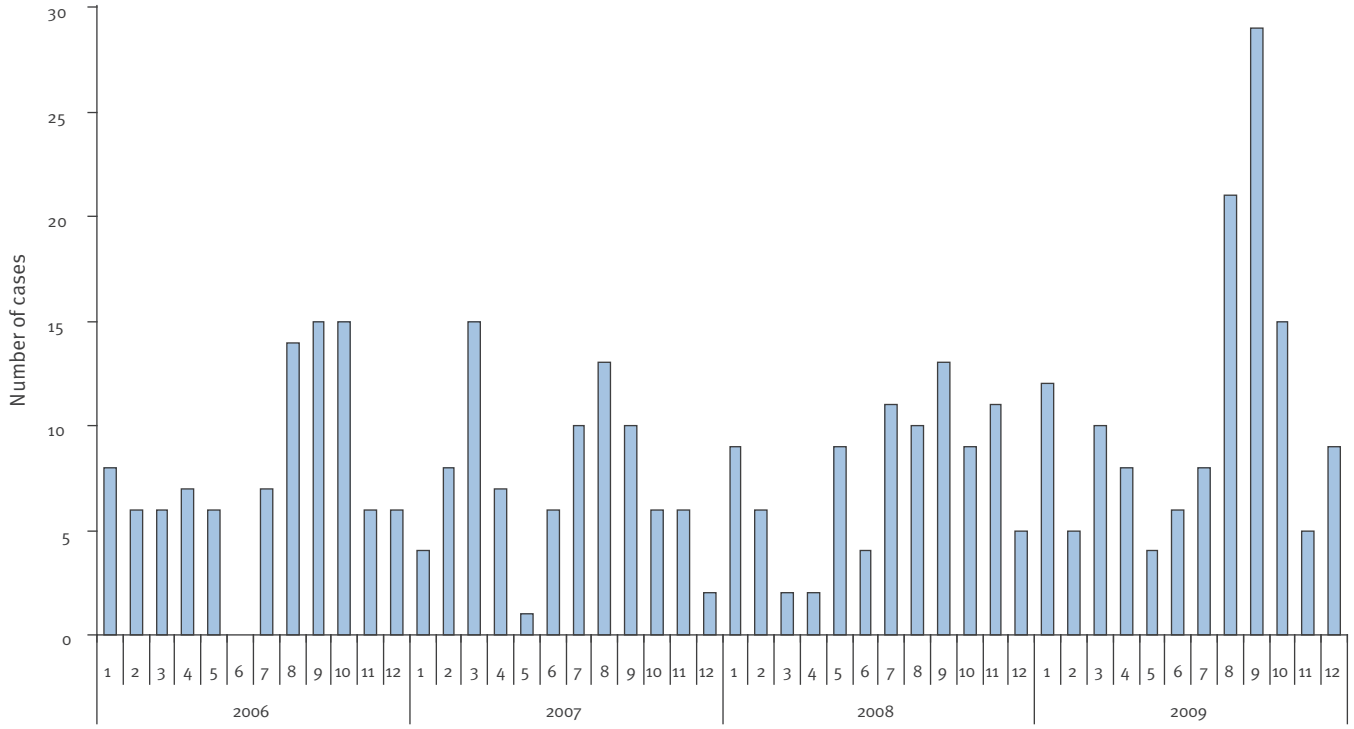
Results

Details of laboratory-confirmed cryptosporidiosis cases

During the four-year study period, 42,004 stools samples from 24, 915 patients were tested for *Cryptosporidium* oocysts. A total of 407 laboratory-confirmed cases of cryptosporidiosis were notified.

Figure 2

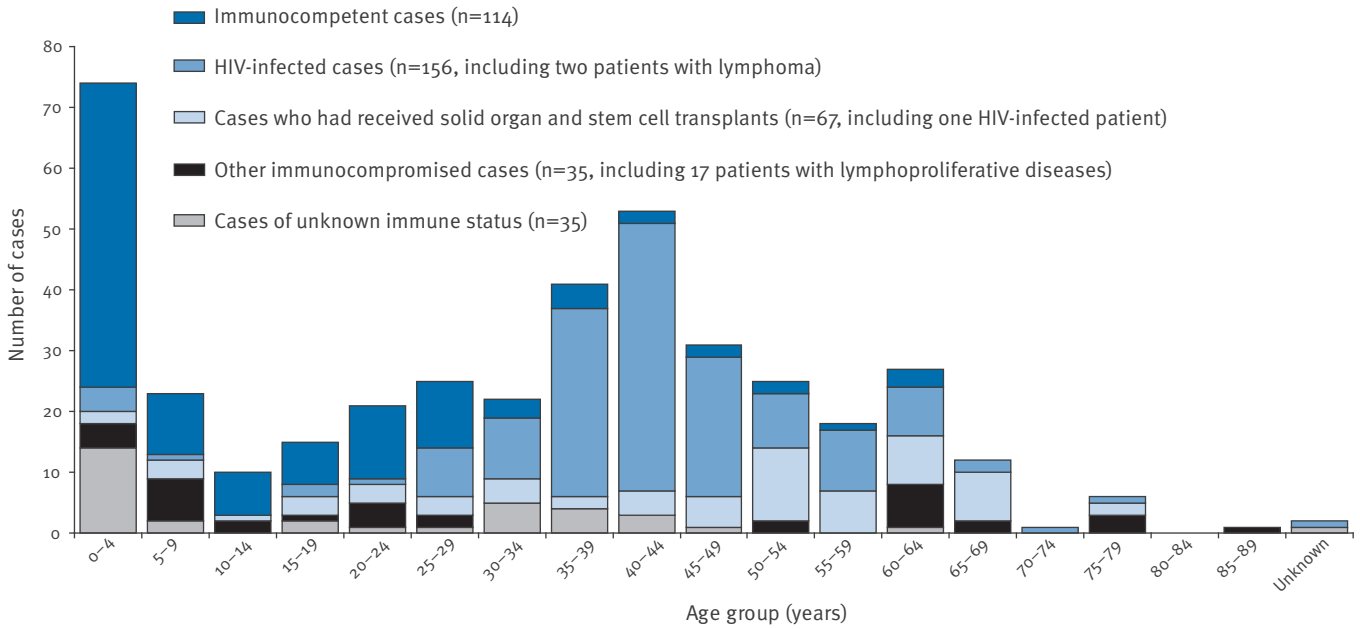
Reported cryptosporidiosis cases, ANOFEL *Cryptosporidium* national network (ACNN), France, 2006–2009 (n=407)



ANOFEL: French association of medical parasitologists.

Figure 3

Age distribution of cryptosporidiosis cases by immune status, ANOFEL *Cryptosporidium* national network (ACNN), France, 2006–2009 (n=407)



ANOFEL: French association of medical parasitologists; HIV: human immunodeficiency virus.

The number of cases was fairly similar over the first three years: 96 in 2006, 89 in 2007 and 92 in 2008; in 2009, the number was higher, with 135 cases reported (five cases were reported twice, in two different years, and were therefore removed from the total). Cases were reported in almost all months of the study period, with peaks from mid/late summer to autumn each year (Figure 2). In 2007, the high number of notifications in March was related to a suspected outbreak in French Guiana.

Of the 407 cases, 253 (62%) were male, 148 (36%) were female (the sex of six patients was not documented). Overall, the male to female ratio was 1.7 (2.2 in 2006, 2.1 in 2007, 1.5 in 2008 and 1.4 in 2009). All age groups were represented (Figure 3). The age distribution was bimodal, with the greatest number of cases reported among children under the age of four years (n=74, 18.2% of cases), and among adults aged 35–49 years (n=125, 30.7% of cases). In 2007, the cases in the age group 0–4 years included clustered cases (n=9) of the suspected outbreak in Guiana (discussed below).

Information about immune status was available for 372 patients. Immunocompetent patients accounted for 28% (n=114), mainly children and young adults (under 24 years old) (Figure 3). A large proportion of the reported cases were HIV infected (38.6%, n=157), accounting for 58.3% (56 of 96), 39.8% (35 of 88), 34.1% (31 of 91) and 26.5% (35 of 132) of reported cases in 2006, 2007, 2008 and 2009, respectively. Most of the HIV-infected patients had CD4+ lymphocyte counts of less than 200 per mm^3 (data not shown) and were in the age group 35–49 years (Figure 3). Other causes of immunosuppression accounted for 11.5% (n=11), 18.2% (n=16), 27.5% (n=25) and 39.4% (n=52) of cases in 2006, 2007, 2008 and 2009, respectively.

A total of 372 (91.4%) cases had diarrhoea; 19 did not (unknown for 16 patients).

Table 1

Cryptosporidium species and genotypes detected by the ANOFEL *Cryptosporidium* National Network (ACNN), France, 2006–2009 (n=310)

Cryptosporidium species or genotype	Number detected				
	2006	2007	2008	2009	Total
C. parvum	32	33	51	52	**168**
C. hominis	30	22	14	47	**113**
C. felis	7	2	3	3	**15**
C. meleagridis	2	0	1	1	**4**
C. canis	1	0	1	2	**4**
Chipmunk genotype	0	0	1	0	**1**
Rabbit genotype	0	0	0	1	**1**
Other genotypes	1	0	2	1	**4**
Total	**73**	**57**	**73**	**107**	**310**

ANOFEL: French association of medical parasitologists.

Cryptosporidiosis clustered cases

During March and April 2007, 10 laboratory-confirmed cryptosporidiosis cases were passively reported in Cayenne, French Guiana. Nine were children under the age of two years and one adult. No epidemiological link between the cases was found (such as exposure to contaminated water or infected animals, or the location of the cases' homes) and the causative species of *Cryptosporidium* could not be identified (as samples were not sent for genotyping).

Isolate collection and genotyping

Over the study period, a total of 364 faecal specimens (or DNA extracts) from 328 patients were collected, corresponding to 80.6% of the notified cases. Of the 364 samples, 345 (94.8%) were genotyped from DNA by PCR-sequencing of the 18S rDNA locus. Among these, 35 specimens were received from 14 patients who were sampled at different dates during their cryptosporidiosis episode. In all these cases, the *Cryptosporidium* species identified in the sequential samples was indistinguishable from that of the initial specimen. Molecular characterisation of *Cryptosporidium* species in the 310 first specimens identified *C. parvum* in 168 (54.2%) and *C. hominis* in 113 (36.5%) (Table 1).

Other species or genotypes were identified in 29 patients (9.4%). They were *C. felis* (n= 15), *C. meleagridis* (n=4), *C. canis* (n=4), *Cryptosporidium* chipmunk genotype (n=1), *Cryptosporidium* rabbit genotype (n=1) and four different *Cryptosporidium* new genotypes (for each, n=1). 18S rDNA sequences of the four new genotypes presented 97% homology with both *C. parvum* and *C. meleagridis*, 99% with both *C. hominis* and *Cryptosporidium* rabbit genotype, 99% with *Cryptosporidium* cervine genotype and 96% with *C. hominis*. Species other than *C. parvum* and *C. hominis* were mostly found in patients with immune deficiencies (24 of 29); they were found in only five immunocompetent patients (Table 2).

The proportion of cases infected with *C. parvum* and *C. hominis* varied during this study. In 2006, each species was almost equally represented: 32 patients with *C. parvum* and 30 with *C. hominis*. In 2007, cases with *C. parvum* infection were present in a higher proportion (33 cases with *C. parvum* versus 22 with *C. hominis*) whereas cases with *C. parvum* were markedly over-represented in 2008 (51 with *C. parvum* versus 14 with *C. hominis*) (Table 1). The 2008 distribution could not be related to an outbreak or another identified cause. In 2009, the proportion of cases with *C. parvum* (48.6%, n=52) and *C. hominis* (43.9%, n=47) was again similar. The monthly distributions of *C. parvum* and *C. hominis* cases did not reveal any specific seasonal pattern, but the case numbers per month were too small to determine seasonality (data not shown).

The comparative distribution of *C. parvum* and *C. hominis* cases was analysed, looking at the following parameters: age, sex, immune status, symptoms (diarrhoea, nausea, abdominal pain, fever and weight loss),

location (rural or urban), whether the patient was part of a household cluster, and animal and water exposure (data not shown). *C. parvum* was more prevalent than *C. hominis* in patients above 60 years of age (p=0.01) and weight loss was more frequently reported by patients infected with *C. parvum* than by those infected with *C. hominis* (p<0.03). No difference in the distribution of *C. parvum* and *C. hominis* was found between immunocompetent and immunocompromised patients. Within the group of immunocompromised patients, *C. parvum* was more prevalent than *C. hominis* in patients with haematological disorders (lymphoproliferative diseases and stem cell transplantations) (p<0.001). *C. hominis* was more frequently associated than *C. parvum* with travel-related cryptosporidiosis (p<0.001), untreated drinking water (p<0.02) and the presence of diarrhoea in household contacts (p=0.001).

Discussion

This article constitutes the first human cryptosporidiosis epidemiological report in France, based on a four-year national survey. Data analysis indicates that *Cryptosporidium* spp. are geographically widespread in France and can infect both sexes in all age groups. As already reported but not explained in other surveillance studies, males were more frequently infected than females. In our study, this could be related in part to the over-representation of HIV-infected patients, who were mainly male.

Cryptosporidiosis affected particularly children under four years of age. A high incidence of the disease in this age group has been reported in Canada [7], the United States [10], New Zealand [9] and Europe [4], particularly in England and Wales [5,8]. The reason for this high incidence is unknown. It is possible that children are less likely to have pre-existing immunity and would therefore tend to have relatively more symptomatic

Table 2

Characteristics of patients infected with *Cryptosporidium* species other than *C. parvum* and *C. hominis*, ANOFEL *Cryptosporidium* National Network (ACNN), France, 2006–2009 (n=29)

Cryptosporidium species or genotype	Patient characteristics					
	Sex	Age (years)	Immune status (CD_4 counts per mm3)[a]	Household contacts with diarrhoea	Animal contact (type of animal)[a]	Travel history outside of France (travel location)
C. felis	M	19	HIV-infected (1)	No	No	No
	M	36	HIV-infected (58)	ND	No	No
	F	40	HIV-infected (70)	No	No	Yes (Central African Republic)
	M	33	HIV-infected (116)	No	No	ND
	F	54	HIV-infected (<200)	Yes	No	No
	M	64	HIV-infected (856)	ND	Yes	Yes (Madagascar)
	F	41	HIV-infected	No	No	No
	M	61	HIV-infected	No	Yes	No
	M	41	HIV-infected	No	No	ND
	M	43	HIV-infected (59)	No	No	No
	M	41	Transplant recipient	No	No	No
	F	31	Transplant recipient	Yes	No	No
	F	52	Transplant recipient	No	Yes	No
	M	22	Immunocompetent	No	ND	Yes (Benin)
	M	36	Immunocompetent	Yes	ND	Yes (Canary Islands, Spain)
C. meleagridis	M	44	HIV-infected	No	No	Yes (England)
	ND	1	Immunocompetent	ND	ND	Yes (Cape Verde)
	M	47	Immunocompetent	No	Yes (wild animals)	Yes (Congo)
	M	43	HIV-infected (4)	No	No	ND
C. canis	M	36	HIV-infected (27)	No	No	No, but living in Martinique
	M	26	Immunocompetent	ND	Yes	Yes (Niger)
	M	49	HIV-infected (<100)	No	No	No
	F	41	HIV-infected (3)	No	ND	Yes (Africa)
Chipmunk genotype	M	41	HIV-infected	ND	ND	ND
Rabbit genotype	M	30	HIV-infected (300)	ND	ND	ND
New genotype (a)	M	34	HIV-infected (21)	No	ND	Yes (Senegal and Guinea)
New genotype (b)	M	57	HIV-infected (15)	No	No	No
New genotype (c)	M	86	Myelodysplasia	No	ND	ND
New genotype (d)	M	43	HIV-infected (35)	No	Yes (bovines)	No

ANOFEL : French association of medical parasitologists; F: female; M: male; ND: not documented.

[a] If known.

disease than adults. Moreover, young diarrhoeic children attend a physician more frequently and are also more easily hospitalised for rehydration therapy, thus increasing the chance of *Cryptosporidium* detection and notification.

Data reported here suggest a seasonal trend of cryptosporidiosis in France. Seasonal variations have also been seen in other countries [4,5,10] and could be related to seasonal changes in the environment (e.g. the birth of farm animals) or to human behaviour that increase the risk of exposure (e.g. bathing in recreational water). Differences between the epidemiology of *C. parvum* and *C. hominis* are known [8,17]. Travel abroad, household contact with diarrhoea and untreated drinking water, already known to be significant risk factors for *C. hominis* infection [8,17], were found in this study to be more frequently associated with *C. hominis* than *C. parvum* infection.

Cryptosporidium species other than *C. parvum* and *C. hominis* were identified in 9.4% of the patients analysed: most of them were HIV-infected. This proportion is in agreement with data from Caccio *et al.*: approximately 3% of 3,500 immunocompetent cryptosporidiosis cases and 19% of 600 immunocompromised cases, were infected with less common *Cryptosporidium* species (*C. meleagridis, C. felis*, *C. canis*, cervine genotype and monkey genotype) [18]. We also report here the first cases of human infection by *C. canis* and *Cryptosporidium* chipmunk genotype in France.

Our study has limitations associated with the hospital-based structure of the ACNN. The patients studied by the network are probably more clinically patent cases of cryptosporidiosis as well as immunocompromised patients, who are admitted to hospital or who attend as outpatients from the surrounding towns. In the study, 70% of patients were hospitalised and 24.3% were not (not documented for 5.7% of patients, data not shown). This accounts for the overrepresentation of HIV-infected (although the proportion of cases with HIV infection halved over the study period) and immunocompromised patients and the probable patient age imbalance in our study. Indeed, from the annual record of the number of parasitological examinations that were performed by participating laboratories, which included the search of *Cryptosporidium*, the incidence of cryptosporidiosis in the population studied by the network can be estimated at 2.3% in 2006, 1.48% in 2007, 1.1% in 2008 and 1.96% in 2009. But we cannot assume such incidence in the general population in France.

There are, in fact, several major difficulties in defining the real prevalence or incidence of cryptosporidiosis in France. First, the search for *Cryptosporidium* oocysts in stools is not routinely performed by laboratories unless requested by the treating physician. This probably accounts for misdiagnosis since healthcare practitioners may be not familiar with this practice and since cryptosporidiosis is still considered a rare disease in France, far less frequent than some other causes of diarrhoea. Obviously, there is a need for wide dissemination of comprehensive information on the epidemiology, risk factors and diagnosis of cryptosporidiosis among general practitioners and laboratory staff. The second reason is more technical, due to the difficulties encountered routinely by laboratories in the diagnosis of cryptosporidiosis, which requires skills and experience [19]. Interlaboratory tests performed within the ACNN (which comprise only experienced parasitology laboratories) initially showed some discrepancies between laboratories for diagnosis and parasite burden estimates (data not shown) and several interlaboratory blind tests were necessary to improve the sensitivity of detection when the level of oocyst shedding was low. Setting up interlaboratory tests at a national or European level would probably substantially improve the detection rate of *Cryptosporidium* in all laboratories. Alternatively, or to complement microscopy, other methods such as PCR or antigen detection could be used (several commercial test kits are available), but they are costly and the ability of some of these tests to detect all *Cryptosporidium* species needs to be ascertained.

This study, while providing new information about *Cryptosporidium* infection in hospitalised patients in France, does not provide sufficient denominator or comparative data to estimate the burden of disease. Extension of this study to a more representative sample of the French population, provision of information on diagnosis to practitioners, assessment of how well diagnosis is performed in laboratories and extension of the network to veterinarians is expected to lead to a better understanding of the epidemiology and transmission of cryptosporidiosis.

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Value of syndromic surveillance in monitoring a focal waterborne outbreak due to an unusual Cryptosporidium genotype in Northamptonshire, United Kingdom, June – July 2008

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The United Kingdom (UK) has several national syndromic surveillance systems. The Health Protection Agency (HPA)/NHS Direct syndromic surveillance system uses pre-diagnostic syndromic data from a national telephone helpline, while the HPA/QSurveillance national surveillance system uses clinical diagnosis data extracted from general practitioner (GP)-based clinical information systems. Data from both of these systems were used to monitor a local outbreak of cryptosporidiosis that occurred following *Cryptosporidium* oocyst contamination of drinking water supplied from the Pitsford Reservoir in Northamptonshire, United Kingdom, in June 2008. There was a peak in the number of calls to NHS Direct concerning diarrhoea that coincided with the incident. QSurveillance data for the local areas affected by the outbreak showed a significant increase in GP consultations for diarrhoea and gastroenteritis in the week of the incident but there was no increase in consultations for vomiting. A total of 33 clinical cases of cryptosporidiosis were identified in the outbreak investigation, of which 23 were confirmed as infected with the outbreak strain. However, QSurveillance data suggest that there were an estimated 422 excess diarrhoea cases during the outbreak, an increase of about 25% over baseline weekly levels. To our knowledge, this is the first time that data from a syndromic surveillance system, the HPA/QSurveillance national surveillance system, have been able to show the extent of such a small outbreak at a local level. QSurveillance, which covers about 38% of the UK population, is currently the only GP database that is able to provide data at local health district (primary care trust) level. The *Cryptosporidium* contamination incident described demonstrates the potential usefulness of this information, as it is unusual for syndromic surveillance systems to be able to help monitor such a small-scale outbreak.

Introduction

As syndromic surveillance systems usually capture data already collected for other purposes, and monitor generic symptoms and/or clinically diagnosed disease, they provide information at an earlier stage of illness (compared with laboratory-confirmed diagnoses), so that action can be taken in time to substantially reduce the impact of disease. Some systems, for example, the Royal College of General Practitioners Weekly Returns Service, are now well established, with many years of historical data that allow monitoring of longer-term disease trends [1]. They have the ability to provide early warning of, for example, seasonal rises in influenza and can trigger public health action, such as a recommendation to prescribe antiviral drugs in line with national guidance [2-4]. They can also provide reassurance to incident response teams and the general public that an incident has not caused adverse health effects – for example, following an explosion at the Buncefield oil storage depot in Hemel Hempstead, United Kingdom (UK), in 2005, syndromic surveillance confirmed that there were no unusual rises in community-based morbidity linked to the incident [5]; following the eruption of the Eyjafjallajökull volcano in Iceland in April 2010 similar assurance was given about lack of impact on community morbidity [6].

Health departments are increasingly expected to monitor health effects of natural events such as heat wave or flooding, or implement surveillance – of which syndromic surveillance plays a major role – for mass gatherings such as the Olympics or football World Cup [7-9]. Systems in France, Australia and Taiwan use

data from emergency departments [10-12], a Canadian system uses over-the-counter pharmacy sales [13,14], and in the Netherlands data from both syndromic and surrogate data sources, such as employee absence records and prescription medications dispensed by pharmacies, are included in surveillance systems [15,16]. Currently systems based on Internet searches via search engines or on queries submitted to medical websites are being developed [17,18].

In the UK, the HPA/NHS Direct syndromic surveillance system uses pre-diagnostic syndromic data collected from the NHS Direct telephone helpline [19], while the HPA/QSurveillance national surveillance system uses clinical diagnosis data extracted from general practitioner (GP)-based clinical information systems [20].

The HPA Real-time Syndromic Surveillance Team is a small team that coordinates a number of syndromic surveillance systems within the HPA and takes a lead for syndromic surveillance in England [21]. This paper

Figure 1

Daily NHS Direct calls for diarrhoea in the East Midlands, compared with other regions, United Kingdom, 1 May – 31 August 2008

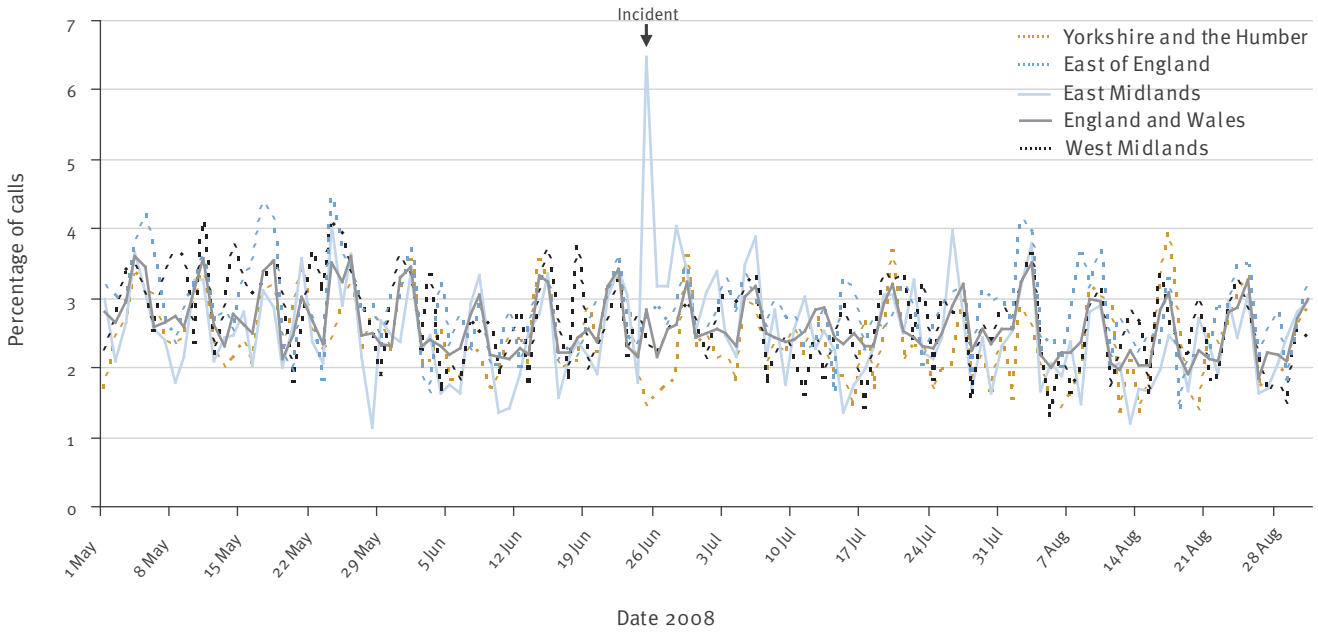
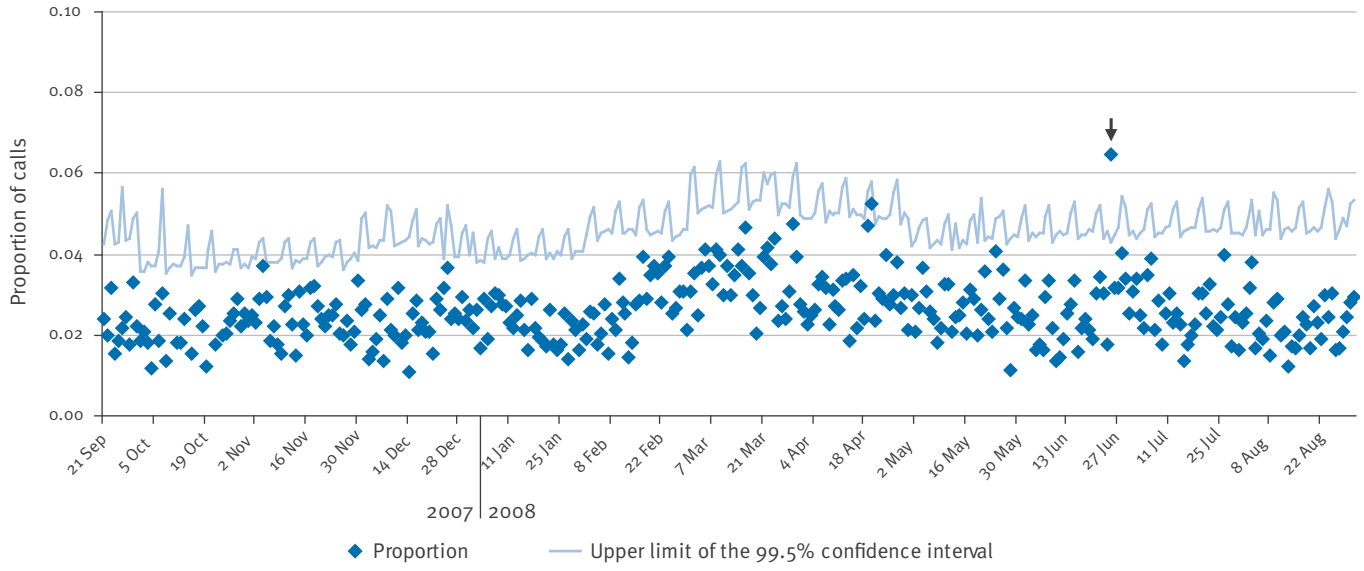


Figure 2

Control chart for NHS Direct calls for diarrhoea in the East Midlands region, United Kingdom, 21 September 2007 – 31 August 2008



The arrow demonstrates the high exceedance in the number of calls on 25 June 2008 following the contamination incident.

Table 1

QSurveillance general practitioner consultation rates for diarrhoea (all ages) per 100,000 practice population by week, Northamptonshire, United Kingdom, 16 June – 6 July 2008[a]

Surveillance region	Week 25 (16–22 June 2008)			Week 26: incident week (23–29 June 2008)			Week 27 (30 June – 6 July 2008)			
	Number of cases	GP consultation rate[b]	SIR[c] (95% CI)	Number of cases	GP consultation rate[b]	SIR[c] (95% CI)	QSurveillance denominator population[d]	Number of cases	GP consultation rate[b]	SIR[c] (95% CI)
East Midlands	617	33.2	113.3 (104.6–122.6)	599	34.1	113.0 (104.2–122.5)	1,922,622	656	34.1	112.8 (104.4–121.9
Trent SHA	284	32.0	109.3 (97.1–122.9)	267	31.8	105.6 (93.5–119.2)	930,841	276	29.6	98.0 (86.9–110.4)
Leicestershire, Northamptonshire and Rutland SHA	333	34.3	116.9 (104.8–130.3)	332	36.1	119.8 (107.4–133.5)	99,1821	380	38.3	126.7 (114.4–140.2)
Daventry and South Northants PCT	28	44.7	152.1 (102.4–222.1)	37	59.0	195.4 (139.0–271.5)	62,698	25	39.9	131.9 (86.6–196.9)
Northamptonshire Heartlands PCT	59	31.3	106.5 (81.6–138.1)	87	41.3	136.6 (109.9–169.1)	189,101	81	42.8	141.6 (113.0–176.7)
Northampton PCT	27	31.6	107.6 (71.9–158.2)	32	46.5	154.1 (106.6–219.5)	94,964	61	64.2	212.4 (163.4–274.2)
United Kingdom	**6,087**	**29.3**	**100.0**	**6,244**	**30.1**	**100.0**	**2,201,5291**	**6,658**	**30.2**	**100.0**

CI: confidence interval; GP: general practitioner; PCT: primary care trust; SHA: strategic health authority; SIR: standardised incidence ratio.

[a] Data are presented using the regional/SHA/PCT boundaries that were in place before October 2006.

[b] Per 100,000 practice population.

[c] Calculated using the United Kingdom as the standard population. If both the upper and lower limits of the 95% confidence interval are above 100, the SIR is considered to be significantly high. In the shaded cells, the standardised incidence ratio is significantly above that of the United Kingdom.

[d] The patient population of GP practices reporting to QSurveillance during week 27.

Source: HPA/Nottingham University National Surveillance System weekly bulletins 188, 189 and 190.

Table 2

QSurveillance general practitioner consultation rates for gastroenteritis (all ages) per 100,000 practice population by week, Northamptonshire, United Kingdom, 16 June – 6 July 2008[a]

Surveillance region	Week 25 (16–22 June 2008)			Week 26: incident week (23–29 June 2008)			Week 27 (30 June – 6 July 2008)			
	Number of cases	GP consultation rate[b]	SIR[c] (95% CI)	Number of cases	GP consultation rate[b]	SIR[c] (95% CI)	QSurveillance denominator population[d]	Number of cases	GP consultation rate[b]	SIR[c] (95% CI)
East Midlands	1,068	57.5	112.7 (106.0–119.7)	1033	58.8	112.3 (105.6–119.4)	1,922,622	1,147	59.6	112.7 (106.3–119.4)
Trent SHA	482	54.4	106.6 (97.4–116.6)	451	53.8	102.8 (93.6–112.8)	930,841	471	50.5	95.6 (87.2–104.7)
Leicestershire, Northamptonshire and Rutland SHA	586	60.3	118.2 (108.9–128.2)	582	63.4	121.0 (111.4–131.3)	991,821	676	68.1	128.7 (119.3–138.9)
Daventry and South Northants PCT	57	90.9	178.0 (135.7–231.9)	71	113.2	216.1 (169.6–273.7)	62,698	65	103.7	195.9 (152.0–250.8)
Northamptonshire Heartlands PCT	101	53.5	104.8 (85.7–127.8)	146	69.2	132.1 (111.8–155.7)	189,101	138	73.0	137.9 (116.1–163.3)
Northampton PCT	40	46.8	91.6 (66.1–125.7)	58	84.3	160.9 (123.0–209.1)	94,964	94	99.0	187.0 (151.7 - 229.6)
United Kingdom	**10,593**	**51.0**	**100.0**	**10,836**	**52.4**	**100.0**	**22,015,291**	**3,276**	**52.9**	**100.0**

CI: confidence interval; GP: general practitioner; PCT: primary care trust; SHA: strategic health authority; SIR: standardised incidence ratio.

[a] Data are presented using the region/SHA/PCT boundaries that were in place before October 2006.

[b] Per 100,000 practice population.

[c] Calculated using the United Kingdom as the standard population. If both the upper and lower limits of the 95% confidence interval are above 100, the SIR is considered to be significantly high. In the shaded cells, the standardised incidence ratio is significantly above that of the United Kingdom.

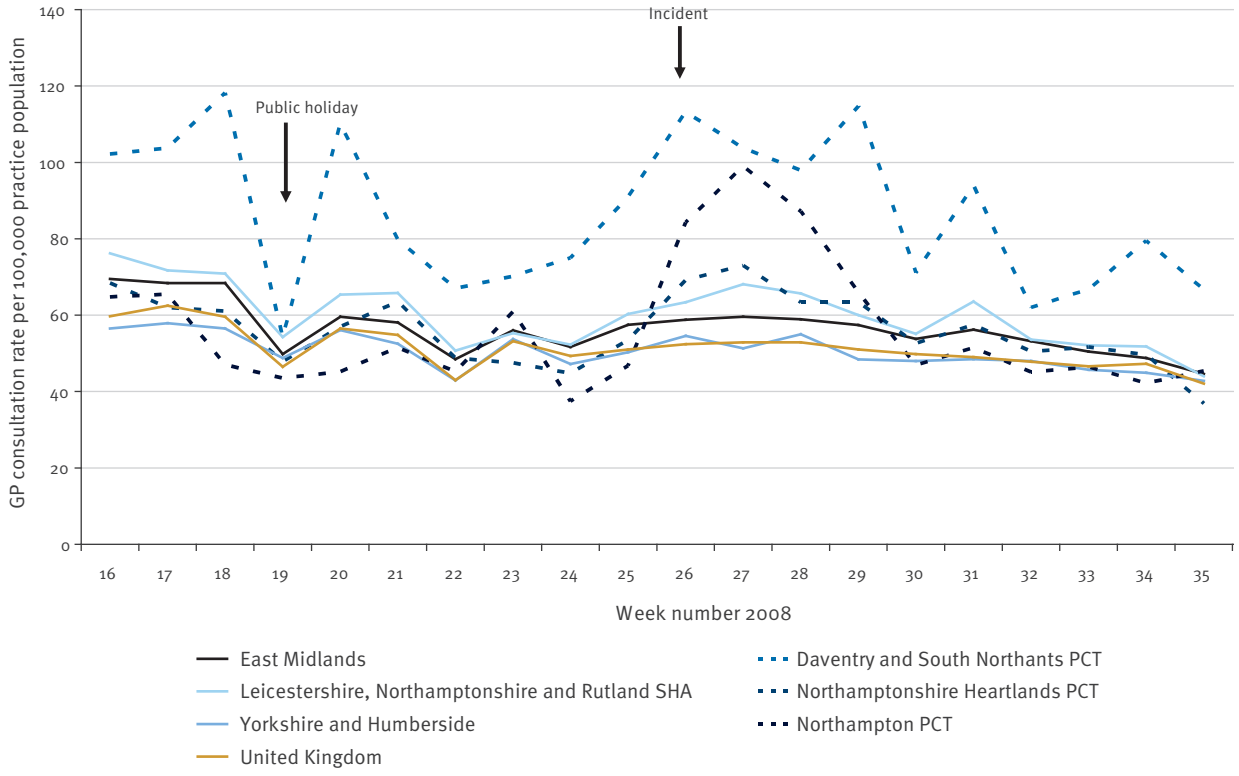
[d] The patient population of GP practices reporting to QSurveillance during week 27.

Source: Health Protection Agency/Nottingham University National Surveillance System weekly bulletins 188, 189 and 190.

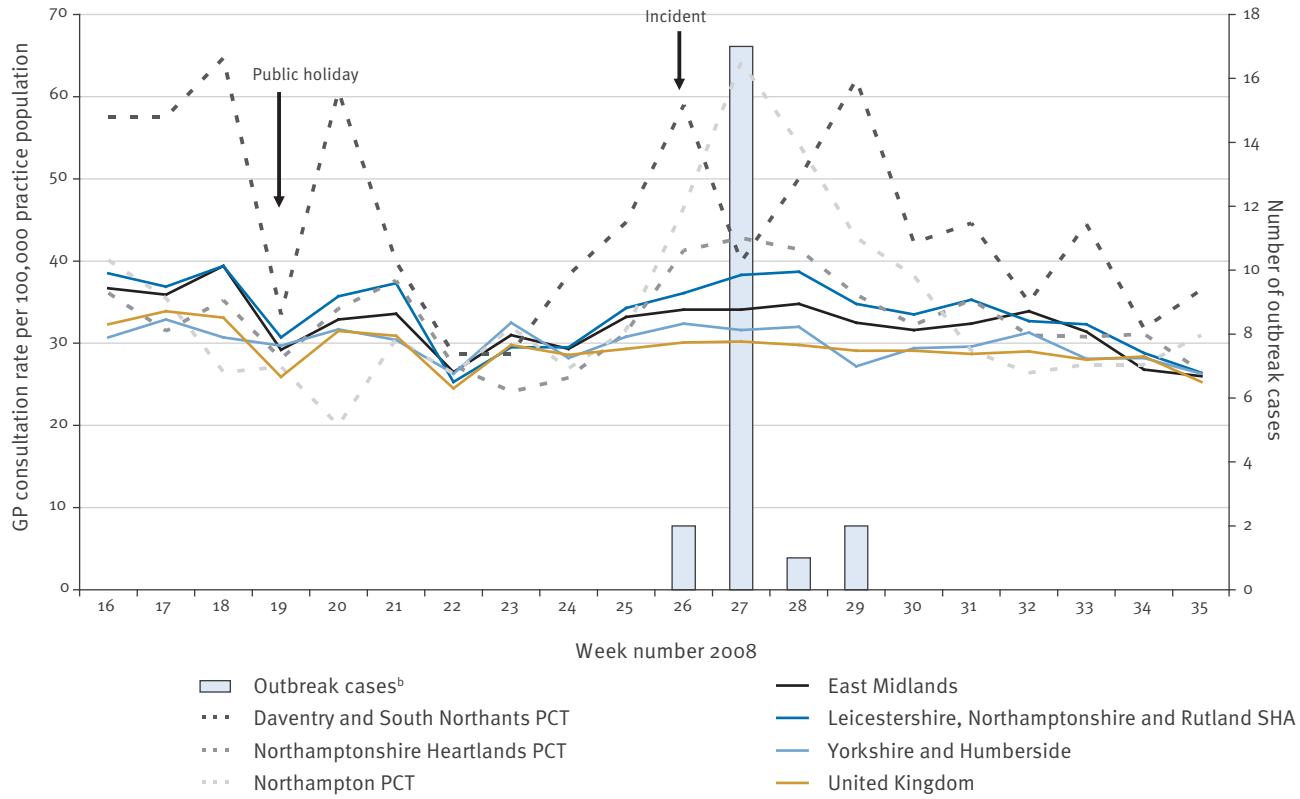
Figure 3

QSurveillance general practitioner consultation rates for (A) diarrhoea (and (B) gastroenteritis by region, strategic health authority and primary care trust (all ages), United Kingdom, weeks 16-35[a], 2008

A



B



Source: QSurveillance database version 1.

GP: general practitioner; PCT: primary care trust; SHA: strategic health authority.

[a] Week commencing 14 April 2008 to week commencing 25 August 2008

[b] Only 22 cases are displayed as date of symptom onset is missing for one case.

describes the support provided by the team to the local incident management team during a local cryptosporidiosis outbreak and shows the use of syndromic surveillance in monitoring the extent of an outbreak using the HPA/NHS Direct and HPA/QSurveillance national surveillance systems.

Cryptosporidiosis

Cryptosporidium is a protozoan parasite that can cause an infection in people, cattle and sometimes other animals [22]. Cryptosporidiosis is most common in children aged between one and five years, but it can affect all ages. Those with impaired immune systems are likely to be most seriously affected. Symptoms usually appear between three and 12 days after initial exposure and include watery diarrhoea, stomach pains, dehydration and fever. In its transmissible form, called an oocyst, the parasite is protected by an outer shell, which allows it to survive in the environment for a long time. Transmission occurs most often via the faeco-oral route through person-to-person or animal-to-person contact, but people may also be infected by consuming contaminated water or food or by swimming in contaminated water. Although uncommon, the largest outbreaks have occurred following contamination of drinking water [23,24]. Normal chlorine disinfection procedures do not kill the oocysts, so they are removed by filtration and water companies carry out routine monitoring of treated water.

Description of the incident

On 25 June 2008 the local Health Protection Unit was informed by Anglian Water of an exceedence in the level of *Cryptosporidium* oocysts found in water supplied from the Pitsford Reservoir in Northamptonshire, United Kingdom, during 19 to 24 June 2008 [25]. The reservoir supplied a population of more than 250,000 in the Northampton area. A notice advising people in the affected areas to boil all drinking water was issued on 25 June 2008 and public health messages were circulated to local health services and to the general public via the media. Those members of the public who were concerned about health risks associated with the incident were asked to ring NHS Direct for clinical advice [26]. The HPA wrote to local GPs and hospitals asking them to monitor potential patients for signs and symptoms of *Cryptosporidium* infection and to submit faecal specimens to the local hospital diagnostic laboratory if patients presented with diarrhoea. Samples from 34 patients where *Cryptosporidium* infection was identified were sent to the UK *Cryptosporidium* reference unit for typing.

On 30 June 2008, the *Cryptosporidium* oocysts found in the reservoir water were confirmed as being of the rabbit genotype *Cryptosporidium* cuniculus [27]. Subsequently, a dead rabbit was found in a treated water tank at the water treatment works. The genotype of *Cryptosporidium* oocysts in the rabbit's large bowel was indistinguishable from that of the oocysts found in the water [27].

After remediation of the water supply and distribution, the 'boil water notice' was lifted on 4 July and the following day the first case of cryptosporidiosis linked to the incident was identified by the reference laboratory (this case was infected with *C. cuniculus*). During the course of the outbreak (24 June – 18 July 2008, the dates of symptom onset in the first and last case, respectively), 23 cases of cryptosporidiosis were confirmed as being infected with *C. cuniculus*; one of the 23 was a secondary case.

The HPA Real-time Syndromic Surveillance Team provided data in order to aid the response to this incident and the first syndromic surveillance report was circulated to the incident management team and other relevant people in the HPA on 27 June 2008. Data from the HPA/NHS Direct and HPA/QSurveillance systems were provided in a series of regular reports, initially daily and eventually weekly, until the final report on 21 August 2008. Each report included a summary

Table 3

HPA/QSurveillance national surveillance system: estimated number of excess cases of diarrhoea by week (extrapolated to primary care trust population), Northamptonshire, United Kingdom, 16 June – 27 July 2008 (n=422)

Week 2008	Estimated number of excess diarrhoea cases			
	Daventry and South Northants PCT	Northamptonshire Heartlands PCT	Northampton PCT	Total[a]
25	6	2	9	17
26[b]	22	30	40	92
27	1	34	77	113
28	12	30	56	98
29	25	15	32	72
30	4	5	22	31
Total[a]	**69**	**117**	**237**	**422**

PCT: primary care trust.

[a] Figures may not add up due to rounding.

[b] Cryptosporidium exceedance in water from the Pitsford Reservoir was reported by Anglian Water in week 26.

Source: QSurveillance database version 1.

interpretation and more detailed data on diarrhoea, gastroenteritis and vomiting indicators.

Methods

Surveillance systems

HPA/NHS Direct surveillance system

NHS Direct is a 24-hour nurse-led telephone helpline that provides health information and advice to the general public. Nurses use a computerised clinical decision support system – the NHS Clinical Assessment System (NHS CAS) – to handle calls. This assessment system uses approximately 200 computerised symptom-based clinical algorithms. Nurses assign the call to the most appropriate algorithm and the patient's symptoms determine the questions asked and the action to be taken following the call (call outcome), which could be guidance on self-care or they could be referred to their GP or advised to attend a hospital emergency department. No attempt is made to provide a formal diagnosis.

Daily NHS Direct data are received by the Real-time Syndromic Surveillance Team, where the number and type of calls received during the previous day are analysed and interpreted. Call proportions are calculated by age group and algorithm against the total number of calls received.

HPA/QSurveillance system

The HPA/QSurveillance national surveillance system was set up by the University of Nottingham, United Kingdom, and Egton Medical Information Systems (EMIS), a supplier of general practice computer systems, in collaboration with the HPA. It comprises a network of more than 3,500 general practices throughout the UK, covering more than 22 million patients (about 38% of the population [28]). Aggregated data on GP consultations for a range of indicators are automatically uploaded daily from GP practice systems to a central database. Data are routinely reported on a weekly basis; however, daily reporting is possible for specific incidents. Reports are provided at national or regional level (strategic health authority, SHA) and by local health district (primary care trust, PCT).

Analysis of surveillance data

NHS Direct call proportions for gastrointestinal syndromes (diarrhoea and vomiting) for the East Midlands region in England, where Northampton is situated, were examined during the outbreak (24 June – 18 July 2008) and compared with those for England and Wales. A series of control charts for diarrhoea calls are routinely used to monitor significant rises in the numbers of calls received. Control charts are calculated by assuming that calls follow a Poisson distribution with the total number of calls as an offset: a model is fitted to each region and symptom separately [29]. The model takes into account call variation caused by weekends, public holidays and the time of year – variables that can affect the number of calls received by NHS Direct. A value above the upper limit of the 99.5% confidence interval would be considered to be unusual. The seven-day moving average for diarrhoea calls was also monitored. The number and percentage of calls for diarrhoea in the East Midlands region were presented by call outcome and the number of calls in the Northampton (NN) postcode districts and in particular the number of calls in the NN11 and NN12 postcode districts, which were most affected by the incident.

QSurveillance national consultation rates per 100,000 population for diarrhoea (in the age groups under five years, five years and over, and all ages), gastroenteritis (all ages) and vomiting (all ages) were compared with rates for the same period in 2007 (data not presented). Consultation rates by region for 2008 for diarrhoea (all ages), gastroenteritis (all ages) and vomiting (all ages) were compared with those for the East Midlands region. The gastroenteritis indicator includes all cases of diarrhoea and/or vomiting.

Consultation rates and standardised incidence ratios (SIRs) – calculated using the UK as the standard population – for diarrhoea, gastroenteritis and vomiting were compared for the UK, Yorkshire and Humberside, East Midlands, Leicestershire, Northamptonshire and Rutland SHA, and Daventry and South Northants PCT, Northamptonshire Heartlands PCT and Northampton PCT. Yorkshire and Humberside was not an affected region but was included as a control. The area supplied by the Pitsford Reservoir included the three PCTs, which were all within the Leicestershire, Northamptonshire and Rutland SHA. The consultation rates and SIRs were compared for the period from week 16 to week 35 of 2008 in order to compare the rates before and after the *Cryptosporidium* exceedance, which took place in week 26.

Estimates of excess numbers of cases of diarrhoea occurring during and following the *Cryptosporidium* outbreak were made by calculating the mean consultation rate over a period of five weeks before and after the incident (weeks 20–24 and weeks 31–35, respectively). For each of the three PCTs, the calculated mean rate was applied to the PCT population to estimate the number of cases that would be expected each week. The actual consultation rates for diarrhoea for weeks 25 to 30 were used to estimate the number of cases for the PCT population each week. The expected number of cases was subtracted from the estimated number of cases in the PCT population to give the estimated number of excess cases.

Results

HPA/NHS Direct surveillance system

A peak in the number of calls for diarrhoea in the East Midlands was recorded in 25–26 June 2008, the period that coincided with the contamination incident and the associated media coverage (Figure 1). The neighbouring areas of the West Midlands, Yorkshire and the Humber, and East of England showed no increase in the number of calls for diarrhoea.

The peak produced a control chart exceedance for calls for diarrhoea on 25 June 2008 (Figure 2), when the proportion of calls exceeded the upper limit of the 99.5% confidence interval. There were further confidence interval exceedances on 26 and 28 June (which were not control chart exceedances).

There was no peak in calls for vomiting or control chart exceedance for these calls in the East Midlands.

HPA/QSurveillance national surveillance system

The East Midlands region had significantly high consultation rates for diarrhoea and gastroenteritis in week 25 (16–22 June), week 26 (23–29 June 2008, when the contamination incident was reported) and in the following four weeks. Within this region. Leicestershire, Northamptonshire and Rutland SHA had slightly raised consultation rates and significant SIRs across weeks 25 to 30 that were not seen in the neighbouring Trent SHA. At PCT level, all three of the PCTs in the area affected by the incident showed increased consultation rates for diarrhoea (Table 1) and gastroenteritis (Table 2) with SIRs significantly above the UK rate in week 26. Daventry and South Northants PCT also had a raised SIR for both indicators in week 25, and although Northamptonshire Heartlands and Northampton PCTs did not have SIRs significantly above that of the UK in week 25, the rise in consultation rates for diarrhoea and gastroenteritis began during week 25.

In Northampton PCT, consultations for both diarrhoea and gastroenteritis peaked in the week following the contamination incident, week 27, returning to normal levels by week 30 (Figure 3A and 3B). A similar effect can be seen in Northampton Heartlands PCT. Daventry and South Northants PCT also showed an increase, but appeared to have consistently higher rates for both indicators. This was the area with the smallest population so the rates were more variable than in the other PCTs and we therefore interpreted these results with caution.

The consultation rates for vomiting during weeks 25 to 30 in the East Midlands were not unusual at SHA or PCT level (data not presented).

Discussion

We have demonstrated the sensitivity of syndromic surveillance in detecting this small *Cryptosporidium* outbreak and the value of the surveillance in being able to describe the extent of its spread. Both the HPA/NHS Direct and HPA/QSurveillance systems showed demonstrable increases in calls and consultations for diarrhoea that were linked to the outbreak. QSurveillance consultations appeared to increase across the PCTs immediately affected but not in the surrounding area. Both the HPA/NHS Direct and HPA/QSurveillance systems showed a clear signal at the time of the incident and we were able to describe the extent of the impact on pre-primary care and primary care services. The HPA/QSurveillance system showed a rise in consultation rates for gastrointestinal symptoms that began the week before the outbreak, consistent with the period when *Cryptosporidium* was present in the water leaving the Pitsford Reservoir (19–24 June 2008) and with the onset of symptoms in the first outbreak case on 24 June. Although only 33 cases were identified by the outbreak investigation team, of which 23 were confirmed as having the outbreak *Cryptosporidium* strain, our syndromic surveillance data detected this limited outbreak.

Data also suggested a more widespread increase in general gastrointestinal symptoms around the time of the outbreak, with an estimated 422 excess diarrhoea cases; these excess cases represented an increase of about 25% above normally expected levels. It is highly probable that a proportion of these excess cases may have resulted from the increased publicity surrounding the incident – for example, it is likely that media reports contributed to the large peak in calls detected by the HPA/NHS Direct surveillance system on the day the boil water notice was issued, and could also have impacted on the GP consultation rate. It has been previously shown that reporting of mumps cases is sensitive to media coverage, with a rise in clinically reported cases following newspaper reports [30]. A similar mechanism could account for some of the excess GP consultations as cases experiencing gastrointestinal symptoms may have been more likely to consult their GP, whereas in normal circumstances they would have cared for themselves at home. It is also possible that the surveillance shows outbreak-associated cases that did not come to the attention of the outbreak team, perhaps because symptoms were not sufficiently severe to warrant further investigation, or stool samples were not provided for testing.

It is interesting to note that there was no demonstrable impact on the number of calls for vomiting (which is not a prominent clinical feature of cryptosporidiosis). Other common community-based pathogens such as norovirus and rotavirus were at low levels, as is normal for that time of year [31].

In this instance, public health authorities had already been alerted to a potential problem by the water company, although the extent of the outbreak was detected by syndromic surveillance. In 2003 the syndromic surveillance systems in the city of New York, United States, were able to detect an increase in diarrhoeal illness following a power outage when there was no other indication of citywide illness [32]. The New York system covers a population of nine million, but does not regularly detect localised outbreaks [33]. It has been shown previously that the HPA/NHS Direct surveillance system would be unlikely to detect a *Cryptosporidium* outbreak unless call volumes are high (72% chance of detection if nine-tenths of cases called NHS Direct) [29], although the value of syndromic surveillance for

such outbreaks has been recognised [34]. The system detected the East Midlands *Cryptosporidium* outbreak that affected a smaller population than that covered by the New York system. The three PCTs affected have a combined population of around 600,000, of which just over half use GP practices reporting to QSurveillance, yet this syndromic surveillance system was able to describe an increase in consultation rates for diarrhoea and gastroenteritis around the time of the outbreak.

Limitations of the data

There was extensive media reporting of the incident that may have affected both the HPA/NHS Direct and HPA/QSurveillance systems and contributed to the increase in reported gastrointestinal symptoms around the time of the contamination incident. However, the rise in consultation rates for diarrhoea began before the outbreak had been detected and therefore cannot be attributed to media coverage.

The HPA/NHS Direct and HPA/QSurveillance systems monitor general symptoms and so could only monitor the relevant symptoms of diarrhoea and vomiting. They are not able to detect *Cryptosporidium* cases, as this would require laboratory confirmation of diagnosis, so some of the estimated excess cases could be unconnected with this incident. This outbreak was discovered by other means but both the HPA/NHS Direct and HPA/QSurveillance systems were able to describe the extent of the disease in the general population and provide reassurance that there was no widespread impact.

Compared with other populations, older people and ethnic minorities are less likely to call NHS Direct [29], and although this should not prevent detection of gastrointestinal symptoms as a result of drinking water contamination as this would affect the whole population, this may reduce the signal from the system [35]. With such large surveillance systems, there will be 'background noise' in the data, so procedures must be in place to correctly interpret the data and set appropriate thresholds for action.

Conclusion

To our knowledge, this is the first time that PCT-level data from a syndromic surveillance system, the HPA/QSurveillance national surveillance system, have been able to show the extent of such a limited outbreak at a local level. QSurveillance, which covers about 38% of the UK population, is currently the only GP database that is able to provide PCT-level data and this *Cryptosporidium* contamination incident demonstrates the potential usefulness of this system.

Acknowledgements

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Report published on factors contributing to the spread of Campylobacter in the European Union

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The European Food Safety Authority (EFSA) recently published a report on factors that may contribute to the spread of *Campylobacter* in live chickens and chicken carcasses. The findings of the report [1], based on an European Union (EU)-wide survey [2] will provide the basis for further work by scientific experts to investigate further how *Campylobacter*-contaminated chicken meat affects the levels of human campylobacteriosis.

The report states that it is about 30 times more likely that a *Campylobacter*-colonised broiler batch produces findings of sampled carcasses being contaminated with *Campylobacter*, compared with a non-colonised batch. Risks for contamination increase with the age of the slaughtered broilers as well as during certain months of the year. The contamination of carcasses with *Campylobacter*, higher *Campylobacter* counts on carcasses and *Campylobacter* colonisation of batches vary between countries and between slaughterhouses within countries, even when taking into account associated factors [1].

Over the last five years, campylobacteriosis is the most commonly reported zoonosis in the EU followed by salmonellosis and yersiniosis. The annual trends on the occurrence of zoonoses are reported on an annual basis in the joint European Centre for Disease Prevention and Control (ECDC) and EFSA annual report on zoonoses and food-borne outbreaks [3].

It is estimated that the handling, preparation and consumption of broiler meat may directly account for 20 to 30% of human cases of campylobacteriosis in the EU [4].

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