

## Effect of precipitation on seasonal variability in cryptosporidiosis recorded by the North West England surveillance system in 1990–1999

Elena N. Naumova, John Christodouleas, Paul R. Hunter and Qutub Syed

### ABSTRACT

The goal of this study was to examine temporal and spatial variability of reported cryptosporidiosis in 15 health authorities in the North West of England using regression modelling. We also examined the role of precipitation as a driving factor for seasonal variation. We separated the time series of the reported cryptosporidiosis into two processes: an endemic process and an epidemic process, and examined the spatial variability of each of these processes. In the North West region of England we observed a strong seasonal pattern that consists of two waves, spring and autumn, during which the weekly rates exceeded the endemic level 3.5 and 3 times, respectively. Health authorities with the high endemic cryptosporidiosis incidence and well-pronounced seasonal patterns exhibited a significant increase in rates of cryptosporidiosis associated with increased precipitation. The endemic level and the magnitude of epidemic peaks were inversely related, which might be indicative of multiple exposures to the pathogen in these localities and the development of some partial immunity.

**Key words** | cryptosporidiosis, geographical distribution, North West of England, precipitation, seasonality, waterborne disease

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### INTRODUCTION

*Cryptosporidium parvum* is known to cause substantial illness via waterborne transmission in both developed and developing countries (Rose 1997; Clark 1999). Worldwide, it is responsible for 2–6% of all diarrhoeal disease in immunocompetent people, and 14–24% of diarrhoeal disease in patients with HIV (Guerrant 1997). Though the illness is self-limiting in immunocompetent people, it can be a life-threatening disease in patients with HIV infection, AIDS and certain other immunosuppressed individuals (Hunter & Nichols 2002). Cryptosporidiosis typically manifests itself through a low endemic level and well-pronounced seasonal outbursts (Hunter 1997). In the United States, *Cryptosporidium* was responsible for the single largest known outbreak of waterborne disease, which was estimated as affecting over 400,000 people (MacKenzie *et al.* 1994). Despite the considerable health burden of cryptosporidiosis, countries have only recently recognized its

importance and begun collecting human cryptosporidiosis surveillance data.

Numerous previous studies have reported temporal variation of cryptosporidiosis in humans and animals (Skeels *et al.* 1990; Public Health Laboratory Service Study Group 1990; Garber *et al.* 1994; Clavel *et al.* 1996; Chai *et al.* 2001). Most of these studies have found a seasonal pattern to cryptosporidiosis, although their reported seasonal peaks are in different times of the year. Data published worldwide document a higher prevalence during the warmer and wetter months (Casemore *et al.* 1997). In the tropical climates the highest prevalence was seen with hot and humid weather. Studies in India, Bangladesh and Guatemala showed that the highest number of cryptosporidiosis cases occurred during the rainy season (Shahid *et al.* 1987; Nath *et al.* 1999; Bern *et al.* 2000). Two studies, which were done in West Africa, showed that the highest prevalence was seen in the hot and humid

months just preceding the months with the highest rainfall (Molbak *et al.* 1990; Perch *et al.* 2001). In both studies the number of cases gradually decreased throughout the rainy season and very few cases were seen in the remainder of the year. In two studies from Brazil, the relationship between rainfall and prevalence of cryptosporidiosis was not as obvious; however, there was a slight increase in disease with increased rainfall (Newman *et al.* 1999; Pereira *et al.* 2002).

In temperate climates the incidence of cryptosporidiosis has been shown to peak in late summer to early autumn. In the United Kingdom, researchers have reported either seasonal peaks in spring and early autumn or no seasonal association (Baxby & Hart 1986; Thompson *et al.* 1987; Public Health Laboratory Service Study Group 1990; Hunter *et al.* 2001). In Northern American studies the highest reported prevalence has been seen in the summer and the early autumn (Wolfson *et al.* 1985; Sorvillo *et al.* 1998; Naumova *et al.* 2000; Dietz *et al.* 2000; Majowicz *et al.* 2001). This agrees with the finding of the Centers for Disease Control (CDC) on outbreaks of waterborne diseases. Several years of surveillance data from the CDC has shown that an increased number of waterborne disease outbreaks occur in the summer and early autumn (Moore *et al.* 1993; Kramer *et al.* 1996; Levy *et al.* 1998; Barwick *et al.* 2000).

While seasonal variation in waterborne disease incidence is well known, the reasons for such seasonal heterogeneity are poorly understood. Recent studies have shown that individual extreme precipitation events, and high water turbidity, correlate with individual epidemics of waterborne disease, and elevated pathogens in water at the local level. In the USA, heavy rainfall has been shown to be associated with sharp spikes in *Cryptosporidium parvum* concentration (Atherholt *et al.* 1998) and waterborne outbreaks of cryptosporidiosis (Curriero *et al.* 2001). Climate variability might be manifest by a change in frequency and intensity of extreme weather events, such as unusually heavy precipitation, flooding, droughts, changing snow and snowmelt patterns, depleted late spring and summer snowmelt water flows and higher water temperatures. These extreme events have the potential to overwhelm drinking water or wastewater treatment systems, overload sewer capacity, lead to watershed discharges of untreated human waste, and flush animal wastes from the

land to surface waters; as a result, pathogens can appear in drinking water. If the surface waters serve as a source of drinking water and these water supplies receive both agricultural run-off and treated wastewater, then both sources of contamination will frequently contain pathogens, particularly *Cryptosporidium parvum*, which is found in manure and sewage and is resistant to chlorine.

The goal of this study was to examine temporal and spatial variability of reported cryptosporidiosis in 15 health authorities (HA) of the North West of England (NWE) using regression modelling adapted to time series data. In particular, in this study we modelled temporal fluctuations using reported weekly rates and assessed how temporal patterns in reported cryptosporidiosis vary geographically. We separated the time series of the reported cryptosporidiosis rates into two processes, an endemic process and an epidemic process, examined the variability of each of these processes spatially, and examined the potential impact of precipitation on temporal and spatial variations in the reported rates of cryptosporidiosis.

## METHODS

### Description of the data

The data set consists of 8,094 cases of laboratory-confirmed cryptosporidiosis recorded by 15 health authorities (HA) in the North West of England (NWE). Data from one HA was not included in the analysis as most years there was not a single case reported despite the detection of a *Cryptosporidium* waterborne outbreak during the study period. Each case of cryptosporidiosis was assigned to the week in which the reporting microbiology laboratory confirmed the pathogen's presence. A week was defined as seven consecutive days from Monday to Sunday irrespective of whether the weeks overlapped two calendar years. The first week began on Monday 1 January 1990 and the last week ended on Sunday 2 January 2000, for a total of 522 weeks. For each week in each of the 15 HA, and for all NWE, the number of reported cases was calculated, and a set of 16 time series of weekly counts over the 10-year period was formed. Each year in the time series was made up of 52 weeks, except for 1992 and 1998, which had 53 weeks. To standardize the year, cryptospor-

idiosis cases in the 53rd weeks of those years were added to the cryptosporidiosis cases in the 52nd week. The 53rd weeks were then deleted from the time series, leaving 520 weeks for each HA. Finally, we calculated the weekly rates using the estimated annual population for each HA over the 10-year period (UK Census data for 1990 and 2000, Office of National Statistics, Population Estimates Units). These annual population averages were used to convert time series of counts into time series of rates, expressed as number of cases per week per 1 million people.

The monthly precipitation totals for England and Wales over the 10-year period were downloaded from the UK Climatic Centre's website ([www.cru.uea.ac.uk/~mikeh/datasets/uk/engwales.htm](http://www.cru.uea.ac.uk/~mikeh/datasets/uk/engwales.htm)). The monthly precipitation totals were derived from measurements at 35 gauges across the region, providing best data coverage for the region. The data compiling procedure was discussed in detail elsewhere (Wigley *et al.* 1985; Jones & Conway 1997). To incorporate the available data in a model of weekly rates we disaggregated monthly levels of precipitation into weekly weighted averages and used these synthetically created values in the analysis.

### Exploratory analysis and descriptive statistics

For each HA we examined a distribution of weekly rates and estimated a set of descriptive statistics including mean,

median, maximum, standard deviation and coefficient of skewness. Then, the relations between estimated statistics were analysed in order to assess how well the observed distribution can be approximated by a Poisson distribution and how well pronounced the temporal variations were. We displayed time series using time series plots to reflect temporal variations over the entire 520-week period and using a scatter-plot of superimposed 10-year periods to reveal a seasonal pattern and variation in weekly means (see Figure 1).

### Analysis of temporal variations

To examine the temporal pattern in the weekly time series for the entire NWE region, and for each HA, we developed a set of regression models that assess the relative importance of temporal fluctuations in a given week. We developed a regression model for the time series of weekly rates for the entire NWE region by considering all 15 HA in one model and by including indicators for weeks, years and locations. Using the results of the model we separated the time series into endemic periods (weeks with low rates) and epidemic periods (weeks with high rates) for each HA and for the entire NWE region. Finally, we explored the effect of precipitation on cryptosporidiosis rate for each HA and for the entire NWE region. Below we provide the description of

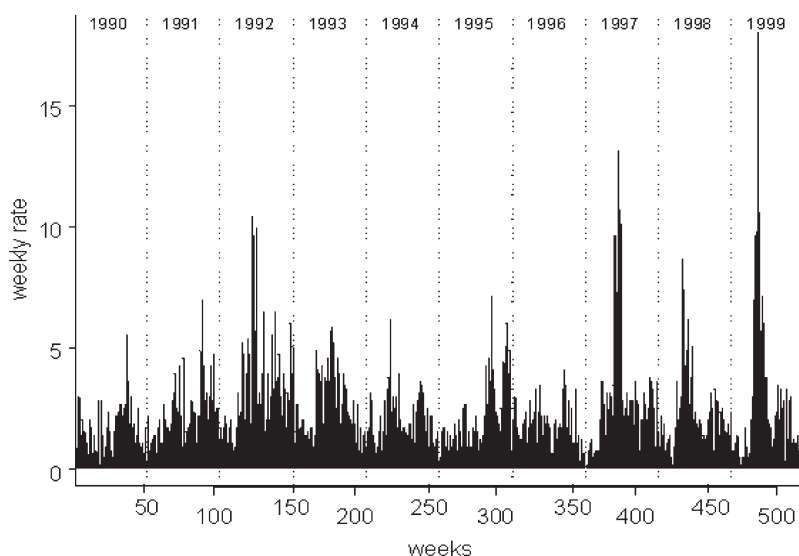


Figure 1 | Ten-year time series of weekly rates of cryptosporidiosis in North West England, 1990–1999.

the modelling procedures. All analyses were performed using S-plus statistical software.

To evaluate the temporal patterns in the NWE region as a whole, as well as in each HA separately, we applied a generalized linear model (GLM) that adapts the Poisson distribution as an outcome's distributional assumption (McCullagh & Nelder 1989), and includes a set of dummy variables for 52 weeks, 10 years and 15 locations:

$$\log(E[Y]) = \beta_0 + \beta_i X_i + \epsilon,$$

where  $Y = \{y_1, y_2, \dots, y_N\}$ , is a time series of weekly rates for 520 weeks for all 15 HA ( $N = 7,800$ ),  $X$  is a matrix of indicator variables,  $\beta_0$  is an intercept,  $\beta_i$  are slopes for a corresponding indicator of week (for  $i = 2, \dots, 52$ ), year (for  $i = 53, 54, \dots, 61$ ) and location (for  $i = 62, 63, \dots, 74$ ), and  $\epsilon$  is an error term. Based on regression parameters, we estimated a predicted weekly rate for a given week: for example,  $Y_0^* = \exp\{\beta_0\}$  is an estimate for a weekly rate at week 1;  $Y_i^* = \exp\{\beta_0 + \beta_i\}$  is an estimate for a weekly rate at week  $i$ . For each estimate, we calculated a corresponding 95%-confidence interval,  $CI_{95} = \exp\{\beta_0 + \beta_i \pm 1.96(S_{\beta_0} + S_{\beta_i})/2\}$ , where  $S_{\beta_i}$  is a standard error of a regression parameter  $\beta_i$ . The first week, the year 1990 and Bury & Rochdale HA were arbitrarily chosen as the reference categories. By fitting these 75 parameters on this dataset of 7,800 values of weekly rates, the model allows us to evaluate the relative impact of seasonal, annual and spatial variations and to estimate an adjusted predicted weekly rate.

### Separating endemic and epidemic periods

The results of the model, expressed as a time series of predicted weekly rates for 52 weeks, were separated into two fragments. We viewed such partitioning as a tool to separate a time series into endemic periods (weeks with low rates) and epidemic periods (weeks with high rates). We performed the separation in the following way: if the predicted rate for week  $i$ ,  $R_i$ , ( $i = 1-52$ ), had a value less than a pre-specified cut point,  $R_c$ , then we assigned this week to an endemic period. Conversely, if  $R_i$  was greater than or equal to  $R_c$ , then we assigned this week to an epidemic period. The cut point was chosen as the 65th percentile of a predicted rate distribution to better reflect the seasonal increase.

### Analysis of a precipitation effect

To assess the impact of precipitation on the cryptosporidiosis rates, we incorporated synthetically disaggregated weighted weekly precipitation averages into the model as a separate term. We examined the lag structure between weekly precipitation and the outcome and selected a variable that reflects weekly rainfall with the lag of 1 week based on the Akaike Information Criterion (AIC), information criterion. The relative impact of precipitation, seasonal, annual and spatial variations in the time series of weekly rates was assessed using the percentage of variance explained by the model. Using Arc/View GIS we produced maps of predicted endemic and epidemic rates with the indication of HA, which reflects significant association with precipitation.

## RESULTS AND DISCUSSION

### Exploratory analysis and descriptive statistics

Table 1 shows the total number of cases recorded over the 10 year period, average population and descriptive statistics including mean, median, maximum, standard deviation and skewness coefficient of weekly rates, estimated on 520 weeks for every HA and the entire NWE region. The mean weekly rates varied substantially, almost 30-fold, from as low as  $0.23 \pm 0.9$  cases per week per 1 million people in St Helens & Knowsley to  $7.67 \pm 12.0$  cases per week per 1 million people in North-West Lancashire. For all HA, the median of weekly rates was less than the mean, the maximum values substantially exceeded five standard deviations from the mean, and the coefficient of skewness was always large and positive. These properties indicate that for every HA the distribution of weekly rates was highly skewed to the right, which is typical for Poisson-like distributed data. The magnitude of skewness (measured by the ratio of the weekly maximum to the weekly mean rates) varied greatly from the lowest in Bury & Rochdale and South Cheshire (~10-fold increase) to the highest in Liverpool and South Lancashire (~40-fold increase). Furthermore, we observed a negative correlation of  $-0.5$  ( $p < 0.05$ ) between this measure of skewness and the mean along with a positive correlation of  $0.66$  ( $p < 0.05$ ) between mean and maximum weekly rates. This indicates

**Table 1** | Descriptive statistics: mean, median, maximum, standard deviation and skewness of weekly rates of reported cryptosporidiosis per 1,000,000 population, estimated for 520 weeks for every health authority, 1990–1999

	Health authority	Average population	Total cases	Mean rate $\pm$ SD	Median rate	Maximum rate	Skewness coefficient
1	Bury & Rochdale	387,628	832	4.13 $\pm$ 4.70	2.58	33.54	2.26
2	East Lancashire	512,615	853	3.20 $\pm$ 4.00	1.95	33.16	2.79
3	Liverpool	473,272	108	0.44 $\pm$ 1.41	0.00	16.91	5.47
4	Manchester	433,133	1,028	4.56 $\pm$ 6.26	2.31	46.18	2.41
5	Morecambe Bay	306,889	544	3.41 $\pm$ 5.23	3.26	55.39	4.31
6	North Cheshire	463,154	242	1.01 $\pm$ 2.59	0.00	36.71	3.53
7	NW Lancashire	310,724	1,239	7.67 $\pm$ 12.02	3.22	93.33	4.25
8	Salford & Trafford	447,514	754	3.24 $\pm$ 5.84	2.24	51.39	4.15
9	Sefton	292,271	156	1.03 $\pm$ 2.37	0.00	17.12	3.05
10	South Cheshire	663,075	402	1.17 $\pm$ 1.81	0.00	10.56	2.04
11	South Lancashire	309,702	382	2.37 $\pm$ 6.91	0.00	109.78	10.21
12	St Helens & Knowsley	445,050	54	0.23 $\pm$ 0.89	0.00	6.74	4.71
13	Stockport	180,109	104	1.11 $\pm$ 3.49	0.00	27.76	4.17
14	West Pennine	528,792	394	1.43 $\pm$ 2.69	0.00	22.69	3.02
15	Wigan & Bolton	575,198	1,002	3.35 $\pm$ 4.50	1.74	45.20	3.37
	The entire NWE	6,329,127	8,094	2.46 $\pm$ 1.91	2.05	18.01	2.46

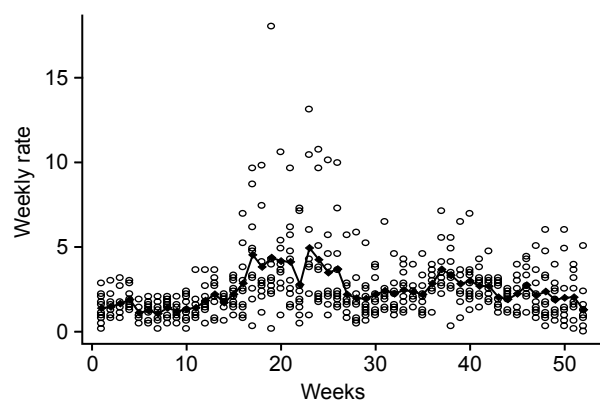
that HA with low weekly rates exhibited a higher degree of skewness than the HA with high weekly rates. Such skewness is probably due to the presence of strong temporal variations with well-pronounced increases in weekly rates over short periods of time and low rates most of the time.

### Analysis of temporal variations

To reflect temporal patterns in weekly rates we graphically displayed the 520-week time series using a straightforward time series plot with weeks on the horizontal axis and weekly rates on the vertical axis. The time series of weekly rates for the NWE region as a whole is shown in [Figure 1](#).

To better visualize a seasonal pattern, each year of data (52 weeks) was superimposed on the others. The superimposed time series for the NWE region as a whole is shown in [Figure 2](#). The scatter-plot reflects consistency in seasonal variations over the 10-year time period. The solid line represents fluctuations in the weekly mean. Two waves in the temporal pattern were observed: one with a peak in the spring (around week 20) and another with a peak in the autumn (around week 40).

To quantify the seasonal pattern in NWE as a whole, we estimated the predicted weekly rates along with the 95%CI using a regression model ([Table 2](#)). The highest increase in cryptosporidiosis rates was observed at week 23: the predicted weekly rate was 4.95 cases per week per 1 million



**Figure 2** | The scatter-plot of weekly rates for ten annual superimposed 52-week periods with their mean weekly rates in North West England, 1990–1999.

population, 95%CI = (2.73, 8.97). The shaded areas in the table reflect weeks 16–26, 36–41 and 46, when substantial increases in weekly rates (above the 65th percentile, that was 2.69 cases per week per 1 million population) were observed. To examine the relative contribution of the two waves to the overall temporal pattern, we estimated adjusted median weekly rates during each wave and during the endemic period. The endemic period, which was made up of weeks 1–15, 27–35, 42–45 and 47–52, had a rate of  $1.90 \pm 0.44$  cases per week. The early summer wave included weeks 16–26 (May and June) and had the highest predicted rate of  $4.15 \pm 0.73$  cases per week. The autumn wave (September and October), which was made up of weeks 36–41, had a rate of  $3.09 \pm 0.47$  cases per week per 1 million population.

### Analysis of temporal variations in a spatial context

To quantify the seasonal patterns for each HA, we examined temporal patterns in individual HAs. Then we separated each predicted time series of weekly rates into three periods according to a pattern observed in the entire NWE region. We estimated the average predicted rates for the endemic period, the spring wave and the autumn wave for each HA, which are shown in Table 3. The results demonstrate substantial spatial variation in the seasonal patterns across the region. Eight HA (East Lancashire, North West Lancashire, South Lancashire, Morecambe Bay, Wigan & Bolton, Salford & Trafford, Bury & Rochdale and

**Table 2** | The results of generalized linear model (GLM) for the entire NW England: estimates of the predicted weekly rates and two corresponding boundaries for the 95% confidence interval. The values in italics represent weeks with rates above the 65th percentile

Week	Rate	LCI *	UCI *	Week	Rate	LCI	UCI
1	1.390	0.822	2.352	27	2.196	1.122	4.299
2	1.469	0.706	3.059	28	1.975	0.995	3.922
3	1.659	0.814	3.383	29	1.943	0.976	3.868
4	1.896	0.949	3.788	30	2.196	1.122	4.299
5	1.122	0.511	2.463	31	2.417	1.250	4.676
6	1.248	0.581	2.680	32	2.244	1.149	4.380
7	1.074	0.485	2.382	33	2.465	1.277	4.756
8	1.406	0.670	2.951	34	2.354	1.213	4.568
9	1.201	0.555	2.599	35	2.196	1.122	4.299
10	1.343	0.634	2.843	36	<i>2.844</i>	<i>1.498</i>	<i>5.401</i>
11	1.406	0.670	2.951	37	<i>3.681</i>	<i>1.986</i>	<i>6.823</i>
12	1.833	0.913	3.680	38	<i>3.334</i>	<i>1.783</i>	<i>6.233</i>
13	2.212	1.131	4.326	39	<i>2.828</i>	<i>1.488</i>	<i>5.374</i>
14	1.722	0.850	3.491	40	<i>3.002</i>	<i>1.590</i>	<i>5.669</i>
15	2.212	1.131	4.326	41	<i>2.702</i>	<i>1.415</i>	<i>5.159</i>
16	<i>2.860</i>	<i>1.507</i>	<i>5.428</i>	42	2.686	1.406	5.132
17	<i>4.535</i>	<i>2.487</i>	<i>8.269</i>	43	2.038	1.031	4.030
18	<i>3.824</i>	<i>2.070</i>	<i>7.064</i>	44	1.912	0.958	3.815
19	<i>4.377</i>	<i>2.394</i>	<i>8.000</i>	45	2.244	1.149	4.380
20	<i>4.171</i>	<i>2.273</i>	<i>7.653</i>	46	<i>2.749</i>	<i>1.442</i>	<i>5.240</i>
21	<i>4.124</i>	<i>2.246</i>	<i>7.573</i>	47	2.149	1.095	4.218
22	<i>2.781</i>	<i>1.461</i>	<i>5.293</i>	48	2.370	1.222	4.595
23	<i>4.945</i>	<i>2.728</i>	<i>8.965</i>	49	1.880	0.940	3.761
24	<i>4.250</i>	<i>2.320</i>	<i>7.787</i>	50	2.007	1.013	3.975
25	<i>3.492</i>	<i>1.876</i>	<i>6.501</i>	51	2.038	1.031	4.030
26	<i>3.697</i>	<i>1.996</i>	<i>6.849</i>	52	1.296	0.608	2.759

\*LCI, lower confidence interval; UCI, upper confidence interval.

**Table 3** | The predicted weekly rate during the endemic period, early summer wave, and autumn wave, and excess weekly rates associated with 1-week lagged precipitation at 75th percentile of 22mm. The values in italics indicate health authorities with the well-defined temporal pattern

	Health authority	Endemic period	Summer wave	Autumn wave	Rate associated with precipitations
1	<i>Bury &amp; Rochdale</i>	<i>3.39 ± 1.16</i>	<i>5.56 ± 1.98</i>	<i>5.23 ± 1.69</i>	1.71 *
2	<i>East Lancashire</i>	<i>2.63 ± 0.96</i>	<i>4.59 ± 1.45</i>	<i>3.48 ± 1.31</i>	1.58 *
3	Liverpool	0.36 ± 0.29	0.38 ± 0.36	0.63 ± 0.55	0.27
4	<i>Manchester</i>	<i>3.18 ± 1.33</i>	<i>7.41 ± 2.91</i>	<i>6.70 ± 1.80</i>	1.23 *
5	<i>Morecambe Bay</i>	<i>2.43 ± 1.22</i>	<i>6.37 ± 2.78</i>	<i>3.49 ± 1.33</i>	0.81 *
6	North Cheshire	0.96 ± 0.81	0.98 ± 0.66	1.33 ± 0.77	0.81
7	<i>NW Lancashire</i>	<i>5.28 ± 2.38</i>	<i>14.36 ± 5.22</i>	<i>8.23 ± 1.77</i>	1.43 *
8	<i>Salford &amp; Trafford</i>	<i>2.17 ± 1.06</i>	<i>6.07 ± 1.83</i>	<i>3.93 ± 1.10</i>	1.88 *
9	Sefton	0.97 ± 0.76	0.68 ± 0.49	1.66 ± 0.64	0.50
10	South Cheshire	1.10 ± 0.61	1.10 ± 0.55	1.59 ± 0.52	0.21
11	<i>South Lancashire</i>	<i>1.51 ± 0.84</i>	<i>4.64 ± 3.17</i>	<i>2.91 ± 1.20</i>	1.39 *
12	St Helens & Knowsley	0.24 ± 0.27	0.20 ± 0.35	0.19 ± 0.42	0.32
13	Stockport	0.81 ± 0.75	1.97 ± 1.15	1.03 ± 1.58	0.56
14	West Pennine	1.03 ± 0.73	2.03 ± 0.89	2.51 ± 0.91	0.53
15	<i>Wigan &amp; Bolton</i>	<i>2.46 ± 1.03</i>	<i>5.89 ± 1.79</i>	<i>3.45 ± 1.05</i>	1.12 *

\*p-value &lt; 0.05.

Manchester) exhibited a well-defined seasonal pattern (shaded in grey in Table 3), while other HA did not.

### Effects of precipitation on rate of cryptosporidiosis

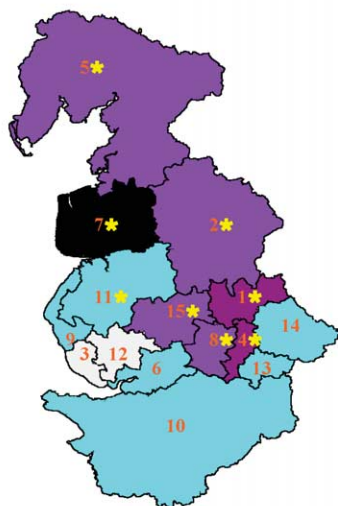
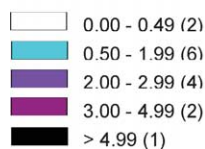
By incorporating rainfall data in the model, we estimated that the overall weekly rate of cryptosporidiosis in the NWE region increases by 27%, 95%CI = (21%, 33%) if the cumulative rainfall for the prior week was at the 75th percentile, or 22 mm. The excess weekly rates associated with precipitation of 22 mm, estimated for each HA are shown in Table 3. Eight HA exhibited a significant increase in weekly cryptosporidiosis rates associated with the increased precipitation ( $p < 0.05$ ). All of these HA also exhibited the well-define seasonal pattern. For the entire

NWE region, the model explains 30% of the variability in the weekly rates of cryptosporidiosis: 21% by spatial terms, 6% by terms of seasonal fluctuations and 3% by annual variation and precipitation effect. At the level of individual HA, temporal variations together with the precipitation effects explain 21–59% of the variability in the rates of reported cryptosporidiosis. The variability in the overall seasonal pattern in NWE and its association with precipitation is demonstrated in Figure 3: the map of the predicted endemic rates indicates the HA that exhibited a significant association with precipitation.

Based on the estimated seasonal pattern in the rate of cryptosporidiosis, we divided the 15 HA into two groups. The first group represents eight HA (Bury & Rochdale, East Lancashire, Manchester, Morecambe Bay, North West

**Health Authorities:**

1. Bury and Rochdale\*
2. East Lancashire\*
3. Liverpool
4. Manchester\*
5. Morecambe Bay
6. North Cheshire
7. North-West Lancashire\*
8. Salford & Trafford\*
9. Sefton
10. South Cheshire
11. South Lancashire\*
12. St. Helens & Knowsley
13. Stockport
14. West Pennine
15. Wigan & Bolton\*



**Figure 3** | Map of estimated weekly endemic rates of reported cryptosporidiosis in North West England, 1990–1999. HA marked by the asterisk exhibited significant positive associations with precipitation.

Lancashire, Salford & Trafford, South Lancashire and Wigan & Bolton) with the pronounced spring increase and high overall rates of cryptosporidiosis. All eight HA exhibited relations with an increased precipitation level. The second group represents seven HA (Liverpool, North Cheshire, Sefton, South Cheshire, St Helens & Knowsley, Stockport and West Pennine) with a low overall rate of cryptosporidiosis, no spring increase and/or a slight increase in rates in the autumn. This analysis suggests that, despite substantial individual variability in the seasonal patterns, consistent temporal fluctuations were observed in the HAs with the highest endemic cryptosporidiosis incidence rates and the strongest associations with precipitation level.

The four main results of this study are the following: 1) the North West region of England exhibited a strong seasonal pattern that is most pronounced in eight health authorities; 2) the overall seasonal pattern consists of two waves, spring and autumn, during which the weekly rates exceeded the endemic level 3.5 and 3 times, respectively; 3) eight HA with this pronounced seasonal pattern exhibited a significant increase in rates of cryptosporidiosis associated with increased precipitation; and 4) the endemic level and the magnitude of epidemic peaks among all HA are inversely related.

In the United Kingdom, reports on seasonal peaks in cryptosporidiosis are inconsistent. Some studies reported seasonal peaks in the spring and early autumn (Baxby & Hart 1986; Thompson *et al.* 1987). Yet another group did not observe seasonal variations in cryptosporidiosis at all (Public Health Laboratory Services Study Group 1990). The observed seasonal pattern in the NWE differs from that reported in the USA. An analysis of reported cryptosporidiosis in the USA, based on the recently started non-mandatory nation-wide monitoring by the United States Environmental Protection Agency (EPA) and the CDC, found that during 1995–1998 the reported cryptosporidiosis was elevated from July through October (Dietz & Roberts 2000). In our recent study of temporal variations in the incidence of cryptosporidiosis in children and adults in Massachusetts, we observed a significant increase in laboratory-confirmed cases during three autumn months: September, October and November for both children and adults (Naumova *et al.* 2000). However, the systematic peak in the autumn observed in the reported cryptosporidiosis disagrees with parasitological investigations conducted in the USA, which show peak prevalence in spring (Amin 2002). These discrepancies probably relate to the substantial regional variability in the temporal pattern of cryptosporidiosis and potential biases in reporting practices.

This study demonstrates that, even within the NWE region, where there is a relatively uniform system of collection and reporting of cryptosporidiosis cases (Chalmers *et al.* 2002), there is substantial variability in the temporal patterns. Our analysis also shows that consistent temporal fluctuations do exist in locations that have a high cryptosporidiosis incidence and that are influenced by precipitation.

The observed overall seasonal pattern with two waves could result from a number of factors that affect oocyst concentrations in the environment, temporal and spatial changes in the host immunity and probability of exposure. A substantial fraction of reported outbreaks of cryptosporidiosis in the UK in 1990–1999 were associated with microbial contamination of drinking water (Furtado *et al.* 1998; Tillet *et al.* 1998). During the years 1997 to 1999, there were three major outbreaks of cryptosporidiosis in the NWE region all of which have been linked to varying degrees with a single water supply (Hunter *et al.* 2001). This water supply, which is a surface water reservoir in the

English Lake District, is chlorinated but unfiltered. Chlorination does not inactivate *Cryptosporidium*, and in the absence of filtration there is no effective barrier to its transmission. Six authorities were involved in the three outbreaks: Morecambe Bay, North West Lancashire, South Lancashire, Wigan & Bolton, Salford & Trafford and Manchester. These six authorities represent about a third of the population within the NWE region. Interestingly, not only do these six HA share the same water source, but they all had well-defined seasonal patterns and almost all exhibited significant associations with rainfall in our analysis.

The results of genotyping *Cryptosporidium* spp. in fecal samples from humans and livestock animals demonstrate distinct geographical and temporal variations in the distribution of the genotypes (McLauchlin *et al.* 2000). In the spring, the bovine genotype was predominant in infected patients; however, during the late-summer-autumn peak the human genotype was significantly more common. These findings suggest that different environmental processes may underlie the temporal and spatial variations in microbial contamination of drinking water supply. The large spring wave, which we observed in the NWE region, may be related to lambing and calving that occurs in the late spring near the region's water supplies. The autumn peak is thought to be largely due to infections in people returning from foreign holidays (Tillet *et al.* 1998). Interestingly, the HA with a consistently high endemic level exhibited a relatively low magnitude of seasonal peaks, which might be indicative of multiple exposures to the pathogen in these localities and the development of some partial immunity.

The strength of this report relates to the wealth and quality of the surveillance data, which represent 10 years of weekly records of fairly uniformly reported laboratory-confirmed cryptosporidiosis across several HA (Chalmers *et al.* 2002). The analysed time series is substantially longer than the time series that have been previously explored by our group and by others (Dietz & Roberts 2000; Naumova *et al.* 2000).

Another important aspect of this report is the statistical approach employed. We chose not to aggregate the time series of health outcomes into monthly periods as our group and others had done in previous reports. By maintaining an aggregation level of 1-week periods, we did not lose details

associated with spikes in the incidence of cryptosporidiosis. In addition, instead of making individual statistical comparisons between one period of the year and another, we applied a regression model, which performed all necessary adjusted comparisons, both temporal and geographical, in one step. Unfortunately, data on precipitation available in the public domain for the 10-year period for the entire region were only monthly averages. We disaggregated monthly data into weighted weekly measurements and examined the validity of our approach using a limited dataset of daily precipitation measurements collected at 19 stations for 1994–1999. The correlation between our synthetic weekly data and the weekly measurements obtained from this smaller dataset by collapsing into the monthly data and then breaking down monthly data to the weighted weekly values was 0.68 ( $p < 0.05$ ). We analysed relations with the reported cryptosporidiosis using both measurements, and determined that the synthetic weekly measurements obtained from the full 10-year time series exhibited overall stronger relations with the outcome, than the weekly measurements obtained by collapsing daily measurements into weekly cumulative sums.

The results of this analysis suggest that the temporal link between reported cryptosporidiosis and precipitation in the studied region is of a seasonal nature. The North West England, the wettest region of the UK, is recently experiencing increases in total annual precipitations, numbers of wet days and heavy rainfalls (Osborn & Hulme 2002). Many precipitation records have been broken in recent years: the wettest 32-month sequence on record occurred between 1992 and 1994, 1999 and 2000 were much wetter than the long-term average, and 2000 was the wettest year in England and Wales for over a century. It is possible that a combination of such meteorological conditions together with the agricultural orientation of the region defines the observed dominant seasonal pattern.

The main difficulty in our analysis was the handling of autocorrelation and extreme values in the time series. The selected modelling procedure with indicator variables provides sufficiently good approximation for estimating seasonal variations, reliable independent assessment of a specific category vs. reference category, and an estimate of relative risk with straightforward epidemiological interpretation. The Poisson regression model is well suited for

non-negative right-skewed outcomes in general, the seasonal pattern was examined with and without three major outbreaks of cryptosporidiosis in the region, and the substantial fraction of variability (32–59%) was explained by a set of simple temporal and spatial variables; however, the model can be improved by using more sophisticated tools for handling extreme values. Until the nature of these extremes is better understood, the selection of such tools will still be arbitrary. In our case, approximation of the outcome by the Poisson distribution leads to the underestimation of predicted rates for weeks with very high rates, meaning that the actual degree of summer/autumn increase might be higher than predicted. Although our approach did not take into account the temporal dependency and treated each week as a separate independent category, we did not observe substantial autocorrelation in the residuals. To account for the potential effect of three major outbreaks on the seasonal pattern of cryptosporidiosis in the region, we examined temporality with and without these extreme data points. Neither the shape nor the strength of the seasonal patterns was different in these analyses.

## CONCLUSION

This communication is the first report of the detailed investigation of seasonal patterns that demonstrated characteristic features of a systematic component in the spatio-temporal variability of waterborne infections. These features suggest that environmental factors have a strong impact, potentially by their effect on water quality, on waterborne infection incidence. We found that seasonal precipitations can influence temporal fluctuations in cryptosporidiosis under both endemic and epidemic conditions. This report used a unique data set of reported laboratory-confirmed cryptosporidiosis, collected weekly over a 10-year period in 15 HA in NWE region by a thorough and uniform surveillance programme, and a modelling approach that is novel in this application and easy to implement for routine surveillance practice. Although there is a significant body of literature documenting the seasonal variations in cryptosporidiosis, as well as the relationship between heavy rainfall and cryptosporidiosis outbreaks, the underlying reasons for this are still poorly understood. Understanding

factors that contribute to the spatial-temporal variability in waterborne infections is a critical first step in designing preventive strategies and reducing a substantial financial burden on the healthcare system.

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