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Epidemiology of anthroponotic and zoonotic human cryptosporidiosis in England and Wales, 2004–2006

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SUMMARY

In order to monitor epidemiological trends, *Cryptosporidium*-positive samples ($n=4509$) from diarrhoeic patients were typed. Compared to the previous 4 years, the proportion of *Cryptosporidium hominis* cases in 2004–2006 increased to 57·3%, while 38·5% were *C. parvum*. The remaining 4·2% cases included mixed *C. parvum* and *C. hominis* infections, *C. meleagridis*, *C. felis*, *C. ubiquitum* and a novel genotype. When the typing results were combined with enhanced surveillance data to monitor risk exposures, *C. hominis* was linked to urban dwelling, previous diarrhoea in the household, any travel especially abroad, and using a swimming or paddling pool. *C. parvum* was linked to having a private water supply, contact with surface water, visiting or living on a farm, and contact with farm animal faeces. The proportion of laboratory-confirmed indigenous cases acquired from direct contact with farm animals was estimated to be 25% for *C. parvum* and 10% of all reported *Cryptosporidium* cases.

Key words: *Cryptosporidium*, epidemiology, human cases, risk factors, zoonoses.

INTRODUCTION

The protozoan parasite *Cryptosporidium* is a common cause of acute human gastroenteritis. In England and Wales, an annual mean of 4189 laboratory-confirmed cases of cryptosporidiosis were reported to national surveillance (range 3010–5863) in the 10 years to the end of 2008 [1], an annual incidence of around 8 cases/100 000 population. Infecting species are not identified in routine diagnosis but specialist testing of a representative proportion of cases has shown that *Cryptosporidium parvum* and *Cryptosporidium hominis* account for over 96% of the cases typed to the species level [2]. Between 2000 and 2004 these occurred in approximately equal proportions nationally but with seasonal and geographic variation. Spring peaks were due to *C. parvum*, and *C. hominis* was more prevalent in the late summer and early autumn [2]. *C. parvum* predominated in Wales and the South West of England and *C. hominis* in more eastern regions [2]. Sources of infection and risk factors vary according to infecting species; for *C. hominis* these are anthroponotic and for *C. parvum* both anthroponotic and zoonotic [3, 4]. Genetic linkage between

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C. parvum isolates from some of the sporadic human cases described here and their suspected farm animal sources has been investigated by sequencing part of the 60-kDa glycoprotein (*GP60*) gene [5]. A high proportion of isolates at both the farm level and individual case/animal contact level were indistinguishable at this locus [5].

Recognized outbreaks, which account for about 10% of all cases routinely reported to national surveillance, are often linked to settings such as open farms and contact with young ruminants in particular [6]. However, the proportion of sporadic cases, which account for the vast majority of human cryptosporidiosis, that can be attributed to animal sources and zoonotic transmission is not known. Although prevention of acquisition and spread will have some commonality between *C. parvum* and *C. hominis*, such as personal hygiene, targeting of interventions will be different for zoonotic and anthroponotic transmission.

To investigate the ongoing distribution of *C. parvum* and *C. hominis*, we typed isolates from cases submitted between 2004 and 2006 to the species level in the first instance. To investigate exposures to known risk factors, we further investigated a subset of cases by establishing an enhanced surveillance scheme in three regions, and linking infecting species identification with analysis of case exposure data. To estimate the burden of zoonotically acquired cryptosporidiosis from farmed animals, we applied the proportion shown by analysis at the *GP60* gene to be linked to this source [5] to the national data.

METHODS

National typing for epidemiological purposes

National typing of *Cryptosporidium*-positive faecal samples from publicly funded primary diagnostic laboratories in England and Wales was undertaken as described previously [2]. In addition, between January 2004 and December 2006, all 28 publicly funded primary diagnostic laboratories serving the population defined by 41 local authorities (LAs) in three study areas within the Government Office Regions of Wales, the South West of England and the East of England, were asked to send all *Cryptosporidium*-positive faecal samples for typing. A minimum dataset was systematically collected for all samples on a structured submission form, including the patient demographics, clinical details, specimen date, history of recent foreign travel and whether the case was considered to be part of a family or household cluster or a general outbreak [7].

Methods to identify *Cryptosporidium* spp. were as described previously [2]. Briefly, oocysts were separated by flotation from faecal debris, disrupted by incubation at 100 °C for 60 min and DNA extracted by proteinase K digestion and spin-column filtration (QiAMP DNA mini kit, Qiagen, UK). *Cryptosporidium* spp. were identified by PCR–RFLP of the *Cryptosporidium* oocyst wall protein (*COWP*) gene [8] in the first instance. Isolates where no amplicons were obtained or equivocal results generated using the *COWP* PCR were further tested by nested PCR–RFLP of the *SSU rRNA* gene [9]. To obtain quality assurance of typing results, a subset of PCR products was analysed by bi-directional DNA sequence analysis (Geneservice, UK). The results were compared to sequences published in the National Institutes of Health's National Center for Biotechnology Information GenBank database using the Basic Local Alignment Search Too1 [10].

To describe the national trends in the epidemiology of *C. parvum* and *C. hominis* cases, data were analysed in Epi Info, version 6 (Centres for Disease Control and Prevention, USA). To investigate representativeness of submission of typing, comparison was made with national reports collected via CoSurv, a set of interconnected database modules for communicable disease reporting [11].

Enhanced surveillance in 41 LAs in three study areas, November 2004–2006

Confirmed cryptosporidiosis cases are routinely reported by the laboratory to the relevant LA Environmental Health Department (EHD) for follow-up using a structured questionnaire [12]. For the duration of this study, a modified exposure questionnaire was used, with additional questions relating to direct and indirect (environmental) animal contact.

Prior to analysis, the data were error-checked for outliers and impossible values and a random selection of 10% cases validated, by cross-checking the forms. For the purpose of categorical analyses, patients' age was allocated to 10-year categories. Key words were used to extract data from free-text fields (e.g. other symptoms). Occupation information was grouped according to risks of transmission; those that worked

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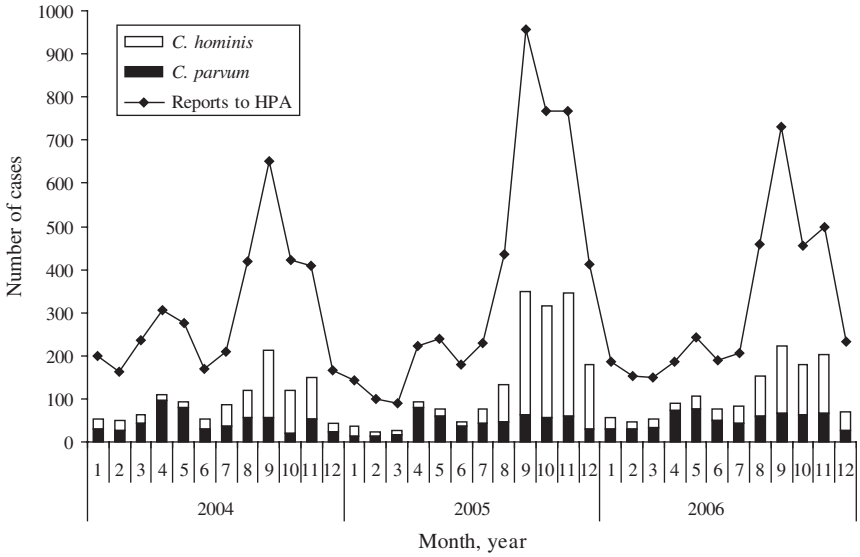

Fig. 1. Temporal distribution of *Cryptosporidium* in England and Wales, 2004–2006 (Cryptosporidium Reference Unit and Health Protection Agency data).

on a farm, with food, with children (e.g. carers at home, nursery staff, school staff), or had close contact with other people (e.g. care workers, hospital). Other occupations were coded as 'no risk'.

Descriptive analysis was completed using MS Excel. The number of cases from different areas was compared against population figures from the 2001 census [13]. To compare the *Cryptosporidium* spp. distribution by urban classification, an urban index was used. The settlement types (urban, town and fringe, village, hamlet, isolated dwellings) in each region were combined with population density classification (sparse or less sparse) to give eight indices [14]. The indices for each region were ordered and replaced by a numeric ID and the mode of the ordinal urban index data was used for each LA. To compare the species-specific risk contacts for *C. parvum* and *C. hominis*, χ^2 analysis was completed using the Yates corrected version for 2×2 tables and linear trend for age groups and month in Epi Info 6. Missing values or answers stated as 'don't know' were omitted from the cross-tabulations.

To estimate the proportion of sporadic zoonotic cryptosporidiosis in laboratory-confirmed and reported cases acquired directly from farmed animals, non-outbreak (i.e. apparently sporadic) *C. parvum* cases were studied. The proportion reporting contact with farm animals was multiplied by 71·4% which was the proportion of cases found by analysis of the *GP60* gene to have isolates indistinguishable from suspected farm animal sources [5]. This estimate was then applied to national surveillance data.

RESULTS

National trends in *C. parvum* and *C. hominis*

A total of 4509 samples were submitted for typing from England and Wales, representing 38·1% of the 11 830 reports to national surveillance over the 3 years (Fig. 1). Submission numbers reflected reports to national surveillance (Fig. 1) although some regions were better represented than others (Table 1). Of these samples, 130 were either not confirmed as *Cryptosporidium* ($n=87$) or were repeat samples ($n=43$). A total of 4379 were initial samples from confirmed cases; 1686 (38·5%) were *C. parvum*, 2509 (57·3%) were *C. hominis* and 184 (4·2%) other or unidentified species or genotypes. These were 33 *C. meleagridis*, 26 *C. felis*, seven co-infections of *C. parvum* and *C. hominis*, two *C. ubiquitum* (synonymous with cervine genotype), one novel genotype (Genbank accession numbers HM191264 and HM191258) and 115 were not typable as no PCR amplicons were produced or the reaction was too weak to identify.

The distribution of *C. parvum* and *C. hominis* varied annually: in 2004 and 2006 there were 1·1 and 1·2 *C. hominis* cases for each *C. parvum* case, respectively, while in 2005 the ratio was 2·3; there were two large drinking waterborne outbreaks of *C. hominis* in 2005 (Table 2). *C. parvum* cases peaked in April or May each year and *C. hominis* in September, although numbers generally were elevated from August to the end of the year (Fig. 1). Compared with the North West where the species distribution was equal (Table 1), Wales and the South West consistently had

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Table 1. *Annual distribution by region of* Cryptosporidium *laboratory reports to national surveillance, samples submitted for typing and confirmed* C. parvum *and* C. hominis *cases in England and Wales, 2004–2006*

	Government Office Region										
	East of England	East Midlands	London	North East	North West	South East	South West	West Midlands	Yorkshire & the Humber	Wales	Total
2004											
Submitted for typing/reports to HPA (%)	327/692 (47·3%)	176/280 (62·9%)	0/260 (0%)	4/123 (3·3%)	155/456 (34·0%)	105/362 (29·0%)	126/504 (25·0%)	98/336 (29·2%)	54/418 (12·9%)	207/183 (113·1%)*	1252/3614 (34·6%)
C. parvum	87	73	0	1	72	45	70	56	11	135	550
C. hominis	230	78	0	1	69	49	50	31	38	59	605
2005											
Submitted for typing/reports to HPA (%)	169/463 (36·5%)	205/307 (66·8%)	21/364 (5·8%)	37/199 (18·6%)	118/565 (20·9%)	348/779 (44·7%)	197/559 (35·2%)	101/411 (24·6%)	115/428 (26·9%)	497/454 (109·5%)*	1808/4529 (39·9%)
C. parvum	68	43	2	26	41	40	100	50	27	122	519
C. hominis	87	146	18	6	69	293	88	48	81	345	1181
2006											
Submitted for typing/reports to HPA (%)	158/445 (35·5%)	219/199 (110·0%)*	11/226 (4·9%)	11/250 (4·4%)	188/572 (32·9%)	132/447 (29·5%)	176/472 (37·3%)	134/432 (31·0%)	168/433 (38·8%)	252/202 (124·8%)*	1449/3678 (39·4%)
C. parvum	72	70	1	7	97	40	100	62	42	126	617
C. hominis	73	134	5	4	70	85	70	62	110	110	723
Three year distribution (2004–2006)											
C. parvum	227	186	3	34	210	125	270	168	80	383	1686
C. hominis	390	358	23	11	208	427	208	141	229	514	2509

HPA, Health Protection Agency.

* More cases were typed than reported because more samples were submitted for typing than cases reported via CoSurv.

Table 2. Cryptosporidium *spp. where identified in outbreaks of cryptosporidiosis in England and Wales January 2000 to December 2003 (UK Cryptosporidium Reference Unit, Health Protection Agency and Public Health Wales data)*

Year	Month	HPA outbreak database no.	Government Office Region	Type of supply; source or contact	Cases ill (laboratory confirmed)	Isolates submitted for typing	*Cryptosporidium* spp.			Reference
							C. parvum	*C. hominis*	Other	
Drinking water										
2005	Sept. to Nov.	05/552	South East	Mains water supply	140 (76)	76	0	76	0	[15]
2005	Oct. to Jan. 2006	05/790	Wales	Mains water supply	231 (231)	223	3	218	2 NT	[16, 17]
Swimming pools										
2004	Mar.	—	North West	Public swimming pool	4 (4)	3	0	3	0	Unpublished data
2004	May/June	04/186	Yorkshire & the Humber	Public swimming pool	7 (7)	4	0	3	1 NT	[18]
2004	Oct.	04/371	Yorkshire & the Humber	Public swimming pool	10 (9)	9	0	9	0	[18]
2005	Sept./Oct.	05/554	South East	Public swimming pools	>88 (88)	86	7	76	3 NT	[19]
2005	Aug. to Dec.	05/623	London	Public swimming pools and community spread	>129 (129)	12	0	12	0	[19, 20]
2006	Jan.	06/36	North West	Holiday complex swimming pool	16 (16)	6	0	6	0	[21]
2006	Jan.	—	West Midlands	Club swimming pool	4 (4)	2	0	2	0	Unpublished data
2006	June	06/481	North West	Public swimming pool	5 (4)	4	4	0	0	Unpublished data
2006	June/July	06/739	East Midlands	Hotel swimming pool	13 (13)	7	0	7	0	Unpublished data
2006	July	—	South East	Swimming and splash pool	10 (10)	9	1	7	0	Unpublished data
2006	Sept.	—	Wales	Public swimming pool	9 (5)	5	0	5	0	Unpublished data
2006	Oct.	—	Wales	Club swimming pool	13 (7)	6	0	6	0	Unpublished data
2006	Oct.	06/741	South West	Hotel swimming pool	4 (4)	4	0	4	0	Unpublished data
2006	Nov.	06/607	Yorkshire & the Humber	Club swimming pool	14 (14)	2	0	2	0	Unpublished data
2006	Nov.	06/668	East Midlands	Holiday complex swimming pool	53 (27)	6	0	6	0	Unpublished data
2006	Nov.	06/670	North West	Public swimming pool	5 (4)	4	0	4	0	Unpublished data
Farm or animal contact										
2004	May	—	East Midlands	Open farm	9 (8)	8	8	0	0	Unpublished data
2004	July	04/241	South West	Residential farm centre	20 (9)	7	6	0	1 NT	[6]
2004	Nov.	04/484	Wales	Residential farm centre	3 (2)	2	2	0	0	[6]
2005	Jan.	05/076	South West	Open farm	2 (2)	2	2	0	0	[6]
2005	Apr.	—	North East	Open farm	8 (8)	5	5	0	0	[22]
2005	May	05/409	South West	Farm campsite	2 (2)	1	1	0	0	[6]
2006	Mar.	06/350	South West	Open Farm	3 (3)	1	1	0	0	[6]
2006	Apr.	—	South East	Open farm	3 (3)	3	3	0	0	Unpublished data
2006	May	—	North East	Working farm	3 (3)	1	1	0	0	Unpublished data

Table 2 (*cont.*)

Year	Month	HPA outbreak database no.	Government Office Region	Type of supply; source or contact	Cases ill (laboratory confirmed)	Isolates submitted for typing	*Cryptosporidium* spp.			Reference
							C. parvum	*C. hominis*	Other	
Institutions										
2005	Jan.	05/208	Wales	Residential outdoor activity centre	2 (2)	2	2	0	0	[6]
2006	May	06/502	South West	Residential outdoor activity centre	20 (4)	4	4	0	0	[6, 23]
2006	Oct.	06/579*	North West	Childminders	7 (2)	2	0	2	0	Unpublished data
2006	Oct.	06/664	East of England	Day care nursery	8 (2)	1	0	1	0	Unpublished data
International										
2004	Sept.	—	Greece	Wedding party	>20 (6)	3	3	0	0	Unpublished data
2005	Aug./Sept.	—	Turkey	Hotel pool	>2 (2)	2	2	0	0	Unpublished data
2006	Sept.	—	Cyprus Welsh cases	Wedding party	14 (2)	2	0	2	0	Unpublished data

HPA, Health Protection Agency; NT, not typable.
* Concurrent viral and *Giardia* outbreak.

more *C. parvum* than *C. hominis* cases although this was only significant in Wales ($\chi^2=6{\cdot}25$, D.F. $=1$, $P=0{\cdot}12$). More *C. hominis* than *C. parvum* was found in the East Midlands ($\chi^2=24{\cdot}48$, D.F. $=1$, $P=0{\cdot}001$), Yorkshire & the Humber ($\chi^2=42{\cdot}92$, D.F. $=1$, $P<0{\cdot}001$), the South East ($\chi^2=78{\cdot}90$, D.F. $=1$, $P<0{\cdot}0001$) (Table 1) and the East of England ($\chi^2=17{\cdot}93$, D.F. $=1$, $P<0{\cdot}001$). In the East of England the high proportion of *C. hominis* cases in 2004 was not observed in 2005 or 2006. The distribution in the West Midlands was similar to the North West ($\chi^2=1{\cdot}05$, D.F. $=1$, $P=0{\cdot}305$). In London and the North East the number of samples submitted was small (Table 1).

Cases were mainly children aged <10 years (Fig. 2). *C. hominis* was more common than *C. parvum* in all age groups, with a significant linear trend for 10-year age bands ($\chi^2=64{\cdot}55$, D.F. $=8$, $P<0{\cdot}001$), and particularly in the <10 and 20–39 years age groups and especially in females in their thirties (Fig. 2).

Foreign travel was reported by 421 (9·6%) cases, mainly to Spain ($n=54$), India ($n=42$), Pakistan ($n=39$) and Turkey ($n=28$). Of the cases reporting foreign travel, 67·0% were *C. hominis*, significantly more than *C. parvum* ($\chi^2=31{\cdot}03$, D.F. $=1$, $P=0{\cdot}000$). Foreign travel peaked in August and September, reported by 79 and 141 cases, respectively, accounting for 52·2% of all travel-related cases. Between eight and 31 cases reported foreign travel during each of the other 10 months of the year.

A total of 508 (11·6%) cases belonged to locally or nationally recognized outbreaks (Table 2). Two outbreaks were linked to mains drinking water, one in Wales and one in South East England, and both were caused by *C. hominis*. Sixteen outbreaks were linked to swimming pools, only one of which was *C. parvum* with the remaining outbreaks solely or mainly *C. hominis*. All of the nine farm-setting or animal contact-related outbreaks were caused by *C. parvum*. Of the four institutional outbreaks, two were *C. parvum* (both set at outdoor/activity centres) and two were *C. hominis* (both in childcare settings). Of the three international outbreaks, two were *C. parvum* and one was *C. hominis*, although the cause of these outbreaks is not known.

Enhanced surveillance and risk exposures in three study areas

A total of 883 questionnaires were collected, of which 790 were not linked to an outbreak and were analysed

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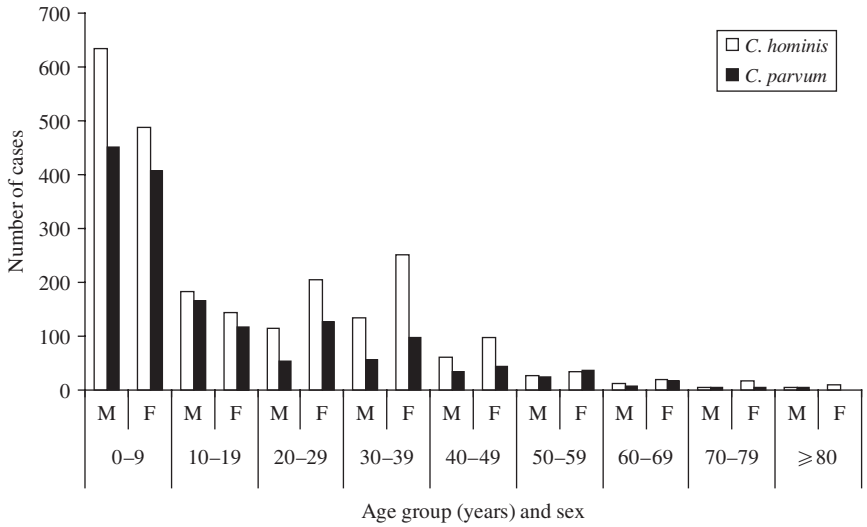

Fig. 2. Age and sex distribution of *C. parvum* and *C. hominis* cases in England and Wales, 2004–2006. M, Male; F, female.

for demographics (Table 3) and risk contacts (Table 4). A subset of 635 case isolates was submitted for typing, themselves forming a subset of the national dataset. Of these, 544 were non-outbreak cases, comprising 255 (46·8%) *C. hominis*, 252 (46·5%) *C. parvum*, two co-infections with *C. hominis* and *C. parvum*, five *C. meleagridis*, three *C. felis* and 27 untypable isolates. Species-linked demographics and risk factors were analysed for the individual *C. parvum* and *C. hominis* cases only (Tables 3 and 4, showing χ^2 and P values).

Although more cases were from Wales (Table 3), the population-based submission rate was similar across the three study areas, with an annual mean of 7/100 000 population, although Taunton Deane LA in South West England had the highest incidence (annual mean 25/100 000 population). *C. hominis* cases were more likely than *C. parvum* cases to be from less sparsely populated LAs ($P<0·001$) (Table 3). Cases peaked overall in the autumn with over half of the cases (58·9%) with onset dates between August and November (Table 3). These were mostly *C. hominis* cases. *C. parvum* cases peaked in April.

There was no difference in the proportion of male and female cases, and although *C. hominis* was most common in females, this was not significant ($P=0·512$) (Table 3). The peak age group of the cases was children aged <10 years, with a significant linear trend for 10-year age bands ($P<0·001$) (Table 3).

The main symptoms reported were diarrhoea (93·3%) and abdominal pain (73·9%), sometimes accompanied by vomiting (54·2%) and/or nausea (45·1%); these were not linked to infecting species. 'Other symptoms' reported by 30·6% cases included fatigue ($n=48$) and fever ($n=89$) and were more commonly reported by *C. hominis* cases ($P=0·01$). There were 8·9% of cases admitted to hospital, for a median of 1 day (range <1–21 days). One fifth of cases (20·9%) reported other household members with diarrhoea in the 2 weeks before illness, and these were significantly more likely to have *C. hominis* ($P=0·002$). Cases that had travelled abroad (17·5%) had mainly visited Spain ($n=46$), France ($n=17$) or Turkey ($n=11$), and were significantly more likely to be *C. hominis* ($P<0·001$).

Cases had diverse occupations but the highest proportion (8·1%) had contact with children (Table 4). There was no significant difference between the *Cryptosporidium* spp. detected in these cases and the species in those with other occupations (Table 4). Only three cases had an occupational farm contact risk (two were farmers and one was a veterinary student), all three were infected with *C. parvum*. Of 35 children whose parents/guardians were farmers 24 had typing results; 22 were infected with *C. parvum*, one with *C. meleagridis*, and one had a co-infection of *C. parvum* and *C. hominis*. Of a further 15 cases who lived on farm, 12 were typed and 11 were infected with *C. parvum* and one with *C. hominis*.

Over a quarter of all cases (26·1%) had visited a farm in the 2 weeks before illness, and were more likely to be positive for *C. parvum* ($P<0·001$) (Table 4). Of all these cases, 71·0% reported contact with farm animals, mostly sheep (59·2%) but also cattle (37·4%). Data on farmed animal contact have been published elsewhere [5]. Contact with animal

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Table 3. *Cryptosporidiosis,* C. parvum *and* C. hominis *non-outbreak case demographics and clinical symptoms in three study areas*

Variable	Outcome	All cases ($n=790$)*	Subset of cases with typing data ($n=544$)*			
		No. of cases (%)	*C. parvum* ($n=252$)	*C. hominis* ($n=255$)	χ^2	*P* value
Study area	Wales	445 (56·3%)	178	158	4·36	0·113
	South West England (Avon and North Somerset)	181 (22·9%)	23	28		
	East of England (Suffolk and North Essex)	164 (20·8%)	51	69		
Urban index analysis†	Less sparse	660 (83·5%)	180	217	13·15	<0·001
	Sparse	130 (16·4%)	72	38		
Sex	Male	366 (46·3%)	113	114	0·43	0·512
	Female	373 (47·2%)	114	132		
Age (yr)	0–9	324 (41·0%)	109	90	12·21	<0·001
	10–19	112 (14·2%)	37	33		
	20–29	65 (8·2%)	19	27		
	30–39	62 (7·8%)	16	29		
	40–49	33 (4·2%)	4	14		
	50–59	22 (2·8%)	7	8		
	60–69	14 (1·8%)	4	2		
	70–79	6 (0·8%)	0	4		
	⩾80	3 (0·4%)	0	1		
Onset	January	22 (2·8%)	10	6	100·86	<0·001
	February	21 (2·7%)	11	2		
	March	28 (3·5%)	17	1		
	April	86 (10·9)	50	6		
	May	49 (6·2%)	31	2		
	June	42 (5·3%)	18	5		
	July	45 (5·7%)	18	12		
	August	109 (13·8%)	25	47		
	September	167 (21·1%)	27	79		
	October	95 (12·0%)	20	41		
	November	94 (11·9%)	21	41		
	December	29 (3·7%)	4	12		
Symptoms						
Diarrhoea	Yes	737 (93·3%)	234	237	0·68	0·409
	No	18 (2·3%)	4	8		
Vomiting	Yes	428 (54·2%)	140	137	0·31	0·580
	No	327 (41·4%)	98	108		
Nausea	Yes	356 (45·1%)	103	126	2·90	0·089
	No	399 (50·5%)	135	119		
Abdominal pain	Yes	584 (73·9%)	194	192	0·56	0·454
	No	171 (21·6%)	44	53		
Blood in stools	Yes	43 (5·4%)	14	8	1·35	0·246
	No	712 (90·1%)	224	237		
Other symptoms	Yes	242 (30·6%)	66	96	6·60	0·010
	No	513 (64·9%)	172	149		
Admitted to hospital	Yes	78 (8·9%)	30	25	0·45	0·503
	No	682 (86·3%)	209	220		

* Missing values or answers stated as 'don't know' omitted from the cross tabulations.
† Mode of all wards within each Local Authority.

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Table 4. *Reported risk factors for cryptosporidiosis,* C. parvum *and* C. hominis *non-outbreak cases in three study areas*

Variable	Outcome*	All cases ($n=790$)	Subset of cases with typing data ($n=544$)			
		No. of cases (%)	*C. parvum* ($n=252$)	*C. hominis* ($n=255$)	χ^2	*P* value
Household member with diarrhoea	Yes	165 (20·9%)	40	68	9·99	0·002
	No	572 (72·4%)	200	164		
All travel	Yes	318 (40·3%)	79	119	12·61	<0·001
	No	446 (56·5%)	166	127		
Foreign travel	Yes	140 (17·7%)	18	75	41·32	<0·001
	No	624 (79·0%)	227	171		
Occupation category for cases aged >15 years	Working with children	64 (8·1%)	21	25	5·91	0·206
	Agricultural	3 (0·4%)	—	—		
	Food industry	7 (0·9%)	1	4		
	Working with people (not specifically children)	29 (3·7%)	9	13		
	No risk occupation	149 (18·9%)	36	58		
Water supply at home	Mains	733 (92·8%)	229	240	8·48	0·037
	Private	16 (2·0%)	11	2		
	Both	9 (1·1%)	3	1		
	Other	6 (0·8%)	1	3		
Use of swimming/paddling pool	Yes	354 (44·8%)	90	137	15·99	<0·001
	No	395 (50·0%)	146	104		
Had contact with surface water	Yes	161 (20·4%)	65	39	9·65	0·002
	No	544 (68·9%)	154	192		
Contact with pets 2 weeks prior to illness	Yes	514 (65·1%)	172	155	2·35	0·125
	No	254 (32·2%)	73	90		
Visited or live on a farm	Yes	206 (26·1%)	112	29	65·29	<0·001
	No	548 (69·4%)	133	212		
Contact with farm animals	Yes	147 (18·6%)	87	17	2·01	0·156
	No	55 (7·0%)	24	10		
Contact with farm animal faeces	Yes	114 (14·4%)	59	20	22·67	<0·001
	No	632 (80·0%)	178	221		

* Missing values or answers stated as 'don't know' were omitted from the cross tabulations.

faeces was reported by 14% of all cases, and comprised farming activities such as mucking out and lambing, looking after pets, and indirect contact like picnicking and walking through fields. These cases were more likely to be *C. parvum* ($P<0·001$) (Table 4). Generally, cases that had farm animal or environmental (private or surface water or animal faeces) contact were significantly more likely to be *C. parvum* than the rest of the study population ($P<0·001$ and 0·035, respectively) (Table 4).

A total of 3·1% cases had a private water supply (either solely or as both private and mains supply), mainly from springs but also from boreholes and wells. These cases were more likely to be *C. parvum* ($P=0·037$) (Table 4). One fifth (20·4%) of cases had contact with surface water (e.g. swimming, working or playing in a river, stream, ditch, pond or water trough), and these cases were more likely to be *C. parvum* ($P=0·002$) (Table 4).

Almost half of the cases had swum in a swimming pool in the 2 weeks prior to illness, and were significantly more likely to be *C. hominis* ($P<0·001$) (Table 4). A number of cases reported swimming in the same swimming pools during a similar time period, and it is possible that some of these could have been unrecognized outbreaks.

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The majority (65%) of cases had contact with pets (Table 4), mainly with dogs, cats, or a combination of both. Data on pet contact from this study has been published elsewhere [24]. Only 4% of cases had contact with 'zoo' animals, mainly noted as 'various' animal types or horses. These cases had mainly visited the large zoos in each study area.

The proportion of *C. parvum* cases reporting contact with farmed animals was 34·5% (Table 4). We estimated that 71·4% of these (24·6%) *C. parvum* cases can be linked to direct contact with farm animals. National surveillance showed 11 830 *Cryptosporidium* reports during the 3-year study period, an annual mean of 3943. From our national typing estimate, 1518 (38·5%) cases are *C. parvum* and we estimated that around 373 (24·6%) reported cases of *C. parvum* were attributable to contact with farm animals per year.

DISCUSSION

We have described the national distribution and trends in human cryptosporidiosis caused by *C. parvum* and *C. hominis* in England and Wales during 2004–2006. Furthermore, these data have been augmented and analysed with risk exposure data in three areas of England and Wales, and the proportion of reported cases acquired directly from farmed animals during that period has been estimated. However, the number of cases fluctuates and so may the attributable fraction from different exposures [25].

The geographic and age-related trends are not dissimilar to those reported in previous years [2, 3], although data for some regions are more sparse than previously. *C. hominis* (57·3% of cases typed) was more prevalent than *C. parvum* (38·5%), which contrasts with previous data from 2000 to 2003 when the ratio nationally was closer to 1 [2]. Although large waterborne outbreaks of *C. hominis* in the autumn of 2005 may account for some of this increase [15, 17], the reasons are unclear. The autumnal increase is subsequent to peak foreign travel reports [2] and community spread through swimming pools may be involved [3, 20].

The small spring peaks were mainly attributable to *C. parvum* cases and since 2001 have been smaller than previously [2, 25]. The seasonality is similar to that seen in Scotland [26] but contrasts with data from Ireland which show no autumn peak in *Cryptosporidium* reports [27] and a clear predominance of *C. parvum* [28]. Calving, lambing and run-off are thought to contribute to zoonotic sources in the spring, but improvements in catchment protection and drinking water treatment have led to a reduction in cases in the UK [25, 29].

Adding additional exposure data to the model suggested that direct farm animal contact accounts for about one quarter of *C. parvum* cases or about 10% of all reported cryptosporidiosis cases. Other direct zoonotic sources may include contact with farm animal faeces, or contact with companion animals, although we have previously shown there is little evidence for pets as a risk to public health from *Cryptosporidium* [24]. Indirect zoonotic transmission is also a factor in cryptosporidiosis caused by *C. parvum* (e.g. through private water supplies or environmental contact) [26].

The distribution and descriptive epidemiology (person, time, place) of *C. parvum* and *C. hominis* in the enhanced surveillance was broadly as expected from the continuing national data [2, data from this study]. Although univariate exposures were analysed in our study, multiple potential risks were reported by 68·1% cases, with up to seven recorded per patient (mean 2·4). The most common combination was companion animal contact and use of swimming pools (8·6%). Nonetheless, the risk exposures were broadly similar to those identified in an earlier case-control study in Wales and the North West of England [3] and an environmental and socioeconomic factors study which also found that *C. hominis* was more prevalent in more densely populated areas [30].

There is potential bias in any laboratory-based surveillance system at all levels of the ascertainment pyramid [7]. Our studies relied on primary diagnostic laboratory referrals to the Cryptosporidium Reference Unit (CRU), comparison with CoSurv data, and for the enhanced surveillance, reporting to LAs as well as case responses to the questionnaires. Of 141 laboratories surveyed in England and Wales in 2006, 105 (74·5%) tested all community samples for *Cryptosporidium*, as did 21 of the 28 (75·0%) laboratories serving the enhanced surveillance study areas, while the others apply selection criteria for testing including patient's age or a report of farm animal contact (CRU, unpublished observations) which might have some small bias for our study. Although all 28 laboratories sent samples for typing, submission rates were variable nationally. Because not all laboratories report cases via CoSurv, and not all send samples for typing, there is a consequence on the estimates of percent of samples typed. A further bias that might

have affected the enhanced surveillance was that where human cases had contact with pets and farm animals, the questionnaire may have been more likely to have been submitted to the study by the EHD.

Foreign travel reports were more common in the enhanced surveillance than in the national data, probably because this was actively sought in the former. The destinations were also different; in the enhanced surveillance Spain, France and Turkey were the most common whereas in the national data these were Spain, India and Pakistan. This difference is probably due to the differing ethnicity of the populations in the three study areas compared to national data [13].

Symptoms described were similar to other case series captured in the same way, i.e. from patients seeking medical assistance, with a high proportion reporting abdominal pain, vomiting and nausea [3]. Here, we additionally identified other symptoms (fever, fatigue) more commonly reported by *C. hominis* cases than *C. parvum*. Acute clinical correlates appear to be more common and varied with *C. hominis* than *C. parvum* [31], especially with the *C. hominis GP60* subtype family Ib [32] which predominates in the UK [33]. It is thus possible that *C. hominis* cases may be more likely to present for medical attention, and that *C. parvum* cases are under-represented in this study design. The patients would not have known which species they were infected with when they completed the questionnaire.

Almost a quarter of the cases, especially those with *C. hominis*, noted other household members with diarrhoea in the 2 weeks prior to illness, indicating the importance of person-to-person spread. As most cases stated more than one risk contact it is difficult to quantify direct attribution to person-to-person contact, but further exploration is required as this indicates an important aspect of public health intervention. *C. hominis* also predominated in cases who used swimming pools which may be linked to the high prevalence in young children who are at risk in this setting [34].

The significant proportion of *C. parvum* cases living on a farm or having contact with farm animal faeces concurs with previous findings [3, 35], although regular exposure may lead to the development of acquired immunity resulting in milder disease [36].

It has been estimated that 1% of the population of England use private water supplies [37] but in the enhanced surveillance, 3·1% used private drinking-water supplies. The excess of cases may reflect geographical distribution of the study population or an increased risk. These cases were mainly *C. parvum* indicating contamination of private water supplies with animal faeces is common.

There is good evidence that the epidemiology of each of the two main *Cryptosporidium* spp. infecting the population of England and Wales is different, as are the risk factors for acquisition, and this needs to be recognized in national surveillance. Zoonotic spread of *C. parvum* from farmed animals contributes to the burden of illness. The autumn peak in infections, mainly caused by *C. hominis* is currently not controlled and the main drivers for this need to be identified so that interventions can be implemented. Person-to-person spread of both *C. parvum* and *C. hominis* has not been properly evaluated for sporadic cases and prevention through this route is likely to be an important control measure.

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DECLARATION OF INTEREST

None.

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