

Verotoxigenic *Escherichia coli* transmission in Ireland: a review of notified outbreaks, 2004–2012

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SUMMARY

Verotoxigenic *Escherichia coli* (VTEC) are significant for their low infectious dose, their potential clinical severity and the frequency with which they generate outbreaks. To describe the relative importance of different outbreak transmission routes for VTEC infection in Ireland, we reviewed outbreak notification data for the period 2004–2012, describing the burden and characteristics of foodborne, waterborne, animal contact and person-to-person outbreaks. Outbreaks where person-to-person spread was reported as the sole transmission route accounted for more than half of all outbreaks and outbreak cases, most notably in childcare facilities. The next most significant transmission route was waterborne spread from untreated or poorly treated private water supplies. The focus for reducing incidence of VTEC should be on reducing waterborne and person-to-person transmission, by publicizing Health Service Executive materials developed for consumers on private well management, and for childcare facility managers and public health professionals on prevention of person-to-person spread.

Key words: Epidemiology, Shiga-like toxin-producing *E. coli*, transmission.

INTRODUCTION

Verotoxigenic *Escherichia coli* (VTEC) have emerged to become one of the most important gastrointestinal pathogens globally in the last few decades [1]. They are significant for their low infectious dose, their potential clinical severity and the frequency with which they generate outbreaks. Data for the European Union indicate an overall crude incidence rate of 1.5 cases/100 000 population in 2012 [2]. Ireland has consistently reported one of the highest incidence

rates among EU Member States rising from 1.6 to 12.07/100 000 population between 2004 and 2012 [3].

Unlike *Campylobacter*, *Listeria* and *Salmonella*, all of which are primarily foodborne, VTEC have been shown to be efficiently transmitted by a variety of routes, including food [4–6], water [7, 8], contact with infected animals or the environment [9], and person-to-person (P-P) spread [10, 11].

Understanding the relative importance of different modes of spread at a national level is important for the development of country-specific control and prevention policies which could lead to a meaningful reduction in disease incidence. Outbreak surveillance systems which focus solely on foodborne and waterborne outbreaks can underestimate the role of P-P spread and animal contact in disease transmission.

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Similarly, sporadic case-control studies, which usually exclude secondary cases, focus on primary transmission routes and are not designed to measure the relative importance of secondary transmission.

Outbreak surveillance systems such as the Irish system which capture information on all outbreaks regardless of transmission route provide an alternative source of information for learning about the epidemiology of VTEC disease. In this paper, we review Irish VTEC outbreak data for the period 2004–12, describing the burden and characteristics of foodborne, waterborne, animal contact and P-P outbreaks.

MATERIALS AND METHODS

In Ireland, since 2004 all outbreaks of infectious disease are notifiable under Infectious Disease Regulation SI707 (2003). This includes both family and general outbreaks. The system is considered very sensitive, particularly for the detection of VTEC family outbreaks, as there is active public health investigation of notified VTEC cases which frequently results in the discovery of additional VTEC cases either in household contacts or close contacts. Reported outbreaks must have at least one laboratory-confirmed VTEC case, with additional laboratory-confirmed cases and/or epidemiologically linked clinical cases.

The information collected on outbreaks includes number of cases and number hospitalized, suspected transmission route, location of outbreak, causative organism, source, evidence implicating source, and factors contributing to the outbreak. These data are maintained in the Computerized Infectious Disease Reporting (CIDR) System, a central data repository for all notifiable infectious disease data in Ireland.

Multiple transmission routes can be reported for a single outbreak. For simplicity in this report, outbreaks reported as ‘waterborne’ or ‘waterborne and P-P’ spread, for example, are grouped under the category waterborne \pm P-P, etc., on the assumption that P-P spread was secondary to the other specified mode of transmission. Outbreak locations were grouped as follows: outbreaks confined to one household or outbreaks including more than one household but where the cases were closely related were included in the same category; outbreaks where the common point of exposure was a premises which included a commercial activity, e.g. hotel or other food service establishment were grouped; and outbreaks described as associated with a childcare facility or where the

outbreak involved families and their childcare arrangements were grouped as childcare.

Population data from the Central Statistics Office Census 2006 Report was used as the population denominator for outbreak incidence rates per 100 000 population [12]. The Kruskal–Wallis test was used to test for the difference in medians, and the χ^2 test or Fisher’s exact test to test the difference in proportions as appropriate. For the variable ‘Health Service Executive area’ (the Irish public health administrative districts), a comparison was made between the transmission route distribution for each individual area against that for all the other areas combined. Stata v. 11.2 (StataCorp, USA) was used for all statistical calculations.

RESULTS

Burden of illness in outbreaks of VTEC infection

Between 2004 and 2012, 355 VTEC outbreaks were notified, an average of 39 per year (range 8–97), including 1035 cases (mean 3.0 per outbreak). Family outbreaks accounted for 83% (296/616) of all outbreaks, but accounted for only 59.5% (616/1035) of outbreak cases (Table 1). The majority (89%) of family outbreaks were reported in private homes or in extended families; in general outbreaks, the most common setting was childcare (55.9%).

Table 2 shows a statistically significant difference in percentage of cases hospitalized by outbreak location. The lower hospitalization rates for childcare (12.2%) and commercial setting (4.5%) outbreaks are likely to reflect more active case finding that is possible within closed setting outbreaks. There was also a statistically significant difference in the number of persons laboratory investigated, laboratory confirmed, and the proportion of samples positive (yield) by outbreak location. Notably, the yield was lower for outbreaks in childcare facilities (10.5%) with 9.5 persons investigated on average per laboratory-confirmed case, reflecting to some extent the testing for clearance exclusion policy recommended during outbreaks in these settings.

Organism

Sixty-six per cent of outbreaks were associated with VTEC O157, 25% with VTEC O26, with the remainder being due to other VTEC strains or a mixture of VTEC strains (Fig. 1). In tandem with increasing use of VTEC diagnostic methods which detect a broader range of VTEC serogroups (e.g. polymerase chain

Table 1. VTEC outbreaks by location and type, Ireland 2004–2012

Location	Family outbreak		General outbreak		All	
	No. of outbreaks	Total no. ill	No. of outbreaks	Total no. ill	No. of outbreaks	Total no. ill
Childcare	5	14	33	193	38	207
Commercial premises	2	4	6	108	8	112
Community outbreak			9	82	9	82
Other or travel	3	8	1	2	4	10
Private house or extended family	275	577	8	30	283	607
Unknown or not specified	11	13	2	4	13	17
Total	296	616	59	419	355	1035

reaction, chromogenic agars, etc.), the number of outbreaks associated with non-O157 infections has increased over the study period. In 2004, all reported VTEC outbreaks were associated with serogroup O157, while in 2012, just under half of all reported outbreaks were associated with VTEC O157.

Transmission routes

P-P spread accounted for 56% of outbreaks (123/219), waterborne transmission for 25%, foodborne for 10%, and animal contact/environmental exposure for 9% (Table 3). Waterborne outbreaks, however, were responsible for a higher proportion of outbreak cases at 34% ($P = 0.043$). P-P spread was the most common transmission route reported both in childcare (84%) and private house (59%) outbreaks. Waterborne and foodborne transmission were reported more frequently in community outbreaks and in outbreaks associated with commercial premises.

The overall 9-year outbreak incidence rate (number of outbreaks per 100 000 population) was 8.4 (95% confidence interval 7.5–9.2), being highest in the Health Service Executive-Midlands (HSE-M) and lowest in the largely urban HSE-East (HSE-E). This is consistent with national case-based VTEC notification data. Although the overall VTEC outbreak incidence was much lower than in all other HSE areas, foodborne transmission was the most common route reported in the HSE-E, whereas waterborne transmission was responsible for the highest proportion of outbreaks in the HSE-M.

Waterborne (\pm P-P) outbreaks

In the 55 waterborne VTEC outbreaks notified, 234 persons were reported ill. Household/extended family

outbreaks predominated comprising 78% of waterborne outbreaks. Notably this was the most common reported transmission route for community outbreaks. Overall, the median number ill was 2 persons (range 1–42 persons).

Private wells were most commonly implicated (84%, $n = 46$ outbreaks). No waterborne outbreaks were identified which were associated with public water supplies. To assess the risk associated with home water supply, we have calculated the number of outbreak-associated illnesses associated with each supply type, and used this to estimate the risk of waterborne VTEC outbreak-associated disease by home drinking-water supply type. For this calculation, we have excluded one waterborne outbreak linked to a private well serving a commercial premises and an outbreak linked to exposure to a stream/river. The risk appears highest in private well users (Table 4).

There was definitive/strong microbiological evidence for water as the source of illness for 22 outbreaks [i.e. isolates indistinguishable by pulsed-field gel electrophoresis (PFGE)], analytical epidemiological evidence alone for one further outbreak [14], and both microbiological and analytical epidemiological evidence for one outbreak. In the remaining 31 (56%) outbreaks, descriptive epidemiological evidence alone was reported as implicating the water supply; in general with coliforms and/or *E. coli* detected, although in four of these outbreaks, VTEC was detected in the drinking water supply but the strain detected was not the same as that found in the human cases. While this did not provide definitive evidence implicating the drinking water source, it did provide circumstantial evidence that the water supply was either not adequately protected or treated against VTEC organisms.

Table 2. Number ill, hospitalized, laboratory-investigated and laboratory-confirmed by outbreak location, VTEC outbreaks Ireland 2004–2012

Location	No. of outbreaks	Total ill (n = 348)	Median no. ill (n = 348)	Total hosp. (n = 273)	Median no. hosp. (n = 273)	% hosp. (n = 272)	Total lab. invest. (n = 259)	Median no. lab. invest. (n = 259)	Total lab. confirmed (n = 319)	Median no. lab. confirmed (n = 319)	Yield (no. confirmed/ no. invest.) (n = 259)	No. invest. per lab. confirmed case (n = 259)
Childcare	38	207	3	20	1	12.1%	1384	35	212	4	10.5%	9.5
Commercial premises	8	112	3	3	0.5	4.5%	50	7	22	2.5	26.0%	3.8
Community outbreak	9	82	4	21	2	38.2%	62	14	68	4	41.9%	2.4
Other or travel	4	10	2.5	4	1	40.0%	75	7	8	2	10.7%	9.4
Private house or extended family	283	607	2	140	1	28.7%	1702	5	680	2	34.5%	2.9
P values	–	–	0.0002	–	0.0282	<0.0001	–	0.0015	–	0.0001	<0.0001	
Unknown or not specified	13	17	1	3	0	27.3%	72	3	23	2	13.9%	7.2
All	355	1035	2	191	1	24.0%	3345	5	1013	2	23.6%	4.2

Hosp., Hospitalized; lab., laboratory; invest., investigations. P values in bold denote significance at the 95% level

The suspected source of contamination of the water supply was recorded for only two outbreaks; in both instances, animal faeces were reported as the source of contamination. The highest number of waterborne outbreaks notified was in 2012. Clustering of waterborne incidents in 2008 coincided with a period of exceptionally high rainfall [15]. Also of note were four community waterborne VTEC outbreaks in HSE-M during the summers of 2011 and 2012 [16].

P-P outbreaks

The most common outbreak transmission route reported was P-P spread, with this being reported as the sole suspected transmission route for 55% of outbreaks. Eighty-two percent of P-P outbreaks occurred in private households, with a further 17% being associated with childcare – this was the most common reported transmission route for childcare outbreaks. Forty-eight percent of P-P outbreaks cases were aged <5 years, similar to the percentage for animal contact outbreaks, but higher than the percentage in waterborne outbreaks (38.9%), although this difference was not statistically significant (Table 3).

During the study period, there were 1925 laboratory-confirmed cases reported to the VTEC case notification system [3]. The number of laboratory-confirmed cases within 107 P-P outbreaks where this information was available was 389, suggesting that at a minimum, 389–107 = 282 of the laboratory-confirmed cases within these outbreaks were due to secondary transmission, or 14.6% (282/1925) of all laboratory-confirmed cases in Ireland. As many of the outbreaks where the primary route was reported as waterborne, foodborne or animal contact also had cases of secondary spread, this represents the minimum proportion of cases due to secondary transmission. The minimum number of laboratory-confirmed presumed primary cases which had secondary cases associated with them was 107/(1925–282) = 6.5%, and there were 2.6 secondary cases (282/107) for each primary case in P-P outbreaks.

P-P spread is particularly important in childcare outbreaks. Childcare outbreaks make up over half (56%) of all general VTEC outbreaks, and almost half (47%) of all general outbreak-associated cases. P-P spread was reported as the sole transmission route for 84% of childcare outbreaks and was responsible for 88% of all childcare outbreak cases. There were 5.8 secondary cases [(143–21)/21] for each of the primary cases in P-P childcare outbreaks.

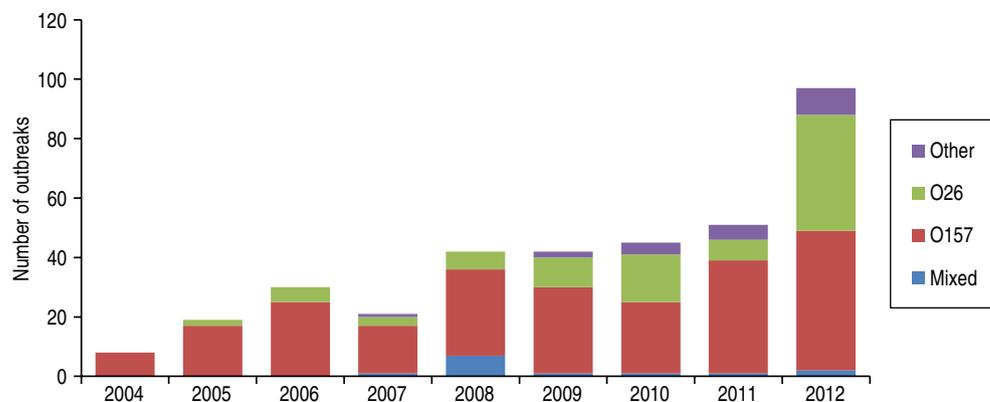


Fig. 1. Annual number of VTEC outbreaks by organism, Ireland 2004–2012.

Animal contact (\pm P-P) outbreaks

Between 2004 and 2012, animal contact or environmental exposure was reported as the suspected route of transmission for 9% of VTEC outbreaks, and just 7% of outbreak cases. The location was reported as private households for all outbreaks, with no pet farms or commercial animal venues implicated. The data collection on these outbreaks did not at the time systematically include information on the animal species or type of contact which was believed to have contributed to infection.

Foodborne (\pm P-P) outbreaks

Food was reported as a suspected transmission route for 10% of outbreaks, ranging in size from 1 to 7 persons ill (median 2 persons ill). Most (87%) were associated with private homes. No microbiological or analytical epidemiological evidence was reported implicating specific food items in any of these outbreaks. Suspected foods based on descriptive epidemiological evidence were reported for only four household outbreaks (minced beef for two outbreaks, and goat and lamb meat each for one outbreak), while a meal eaten out was suspected for one small travel-associated outbreak.

DISCUSSION

This is the first formal study in Ireland describing the relative importance of different outbreak transmission routes for VTEC infection. The data indicate that P-P transmission is a crucially important means of spread, both in private households and childcare settings. Outbreaks where P-P spread was reported as the sole

transmission route accounted for more than half of all outbreaks and outbreak cases. When secondary transmission is ignored, the most significant primary transmission route was waterborne spread from untreated or poorly treated private water supplies.

This contrasts with the United States where foodborne transmission was reported as the most common means of spread for VTEC infection during outbreaks, with P-P spread as the second most common means of spread [17, 18]. In addition, foodborne outbreaks constituted about one-third of VTEC outbreaks in the UK [19]. These differences almost certainly relate to variation in surveillance systems as well as true differences in risk.

The strengths of this study include first, unlike many outbreak surveillance systems, outbreaks are legally notifiable in Ireland, with a broad definition which includes household and general outbreaks. Second, the system includes outbreaks due to any transmission route, not just those transmitted by food and water. Third, thorough active case finding by public health personnel of VTEC cases increases the sensitivity of outbreak detection. Fourth, since 2010, all human VTEC isolates in Ireland have been typed not only by serotyping and verotoxin typing, but also by PFGE, ensuring that clusters not recognized by epidemiological investigations alone also come to the attention of authorities.

Potential limitations of the study include that the reported transmission routes were not always supported by strong evidence, many with descriptive epidemiological evidence only; this is particularly true for small household outbreaks where establishing strong evidence is often not possible. Second, certain desirable data are missing. For example, details on the animal species suspected as sources of infection

Table 3. Burden and characteristics of VTEC outbreaks by transmission route, Ireland 2004–2012

Characteristic	P-P	Waterborne ± P-P	Foodborne ± P-P	Animal contact/env. ± P-P	P value	Not specified	Total no. [crude incidence rate (95% CI)]
Number of outbreaks, <i>n</i> (%)	123 (56)	55 (25)	21 (10)	20 (9)		136	355
Total number ill, <i>n</i> (%)	352 (52)	234 (34)	44 (6)	51 (7)		354	1035
Total number hospitalized, <i>n</i> (%)	92 (54.1)	42 (24.7)	19 (11.2)	17 (10.0)		103	273
Total number laboratory confirmed, <i>n</i> (%)	389 (56.0)	203 (29.2)	41 (5.9)	62 (8.9)		318	1013
Number of outbreaks by location, <i>n</i> (%)							
Private house or extended family	101 (59)	43 (25)	18 (11)	19 (11)		102	283
Childcare	21 (84)	4 (16)	0 (0)	0 (0)		13	38
Community outbreak	1 (20)	4 (80)	0 (0)	0 (0)	0.001	4	9
Commercial premises	0 (0)	1 (33)	2 (67)	0 (0)		5	8
Other or travel	0 (0)	1 (50)	1 (50)	0 (0)		2	4
Unknown or not specified	0 (0)	2 (67)	0 (0)	1 (33)		10	13
Number of outbreaks by quarter, <i>n</i> (%)							
Q1	15 (60)	6 (24)	1 (4)	3 (12)		10	35
Q2	32 (67)	7 (15)	5 (10)	4 (8)		30	78
Q3	48 (53)	30 (33)	9 (10)	3 (3)	0.071	61	151
Q4	28 (50)	12 (21)	6 (11)	10 (18)		35	91
Number of outbreaks by year, <i>n</i> (%)							
2004–2006	10 (31)	8 (25)	9 (28)	5 (16)		25	57
2007–2009	39 (56)	19 (27)	7 (10)	5 (7)	0.003	35	105
2010–2012	74 (63)	28 (24)	5 (4)	10 (9)		76	193
Number of outbreaks by HSE area, <i>n</i> (%)							
East	6 (26)	6 (26)	9 (39)	2 (9)	<0.001	24	47 [3.1 (2.2–4.0)]
Midlands	7 (18)	16 (42)	5 (13)	10 (26)	<0.001	19	57 [22.7 (16.8–28.6)]
Mid West	28 (74)	7 (18)	1 (3)	2 (5)	0.120	11	49 [13.6 (9.8–17.4)]
North East	13 (72)	4 (22)	1 (6)	0 (0)	0.472	14	32 [8.1 (5.3–10.9)]
North West	27 (96)	1 (4)	0 (0)	0 (0)	<0.001	9	37 [15.6 (10.6–20.6)]
South East	9 (64)	1 (7)	0 (0)	4 (29)	0.032	10	24 [5.2 (3.1–7.3)]
South	30 (59)	17 (33)	2 (4)	2 (4)	0.112	11	62 [10.0 (7.5–12.5)]
West	3 (33)	3 (33)	3 (33)	0 (0)	0.086	38	47 [8.1–14.6]]
Total	123 (56)	55 (25)	21 (10)	20 (9)		136	355 [8.4 (7.5–9.2)]
Type							
Number of family outbreaks, <i>n</i> (%)	100 (55)	45 (25)	19 (10)	19 (10)	0.426	113	296
Number of general outbreaks, <i>n</i> (%)	23 (64)	10 (28)	2 (6)	1 (3)		23	59
Age distribution							
Total ill aged <5 years	147 (48.5)	49 (38.9)	15 (42.9)	30 (49.2)	0.325	110	351 (44.7)
Total ill aged ≥5 years	156	77	20	31		150	434

P-P, Person to person; env, environment; HSE, Health Service Executive; CI, confidence interval.
P values in bold denote significance at the 95% level

Table 4. Risk of waterborne VTEC outbreak-associated disease by home drinking-water supply type, Ireland 2004–2012

Home drinking-water supply type	No. of homes in Ireland served by supply type	Estimated no. of persons served by supply type*	No. of VTEC waterborne outbreak illnesses by supply type	Nine-year rate of VTEC waterborne outbreak illnesses by supply type per 100 000 population served
Public water supply	1 247 185	3 404 815	0	0
Group water schemes	190 202	519 251	57	10.98
Domestic private well and other private supply	161 532	440 982	133†	30.16

* Assumes an average of 2.73 per household – based on census 2011 [13].

† Includes private wells and the non-GWS private water scheme outbreak but excludes commercial premises outbreak (=148 + 27–42).

for animal contact outbreaks were not systematically collected at the time of the study, although changes have been made to ensure that this information is collected routinely in future. Third, although considerably improved since then, laboratory diagnostic practice for non-O157 VTEC was variable during the period of the study, particularly in earlier years, resulting in probable under-diagnosis of non-O157 infections. This is a common feature of VTEC surveillance internationally. Therefore, it is not necessarily valid to compare the regional or temporal incidence of the reported VTEC outbreaks. Caution should also be exercised in interpreting the relative importance of different transmission routes temporally or geographically as it is possible VTEC O157 and non-O157 have different reservoirs and/or transmission routes. Fourth, it is likely that many P-P outbreaks were originally seeded by non-human sources of infection, although the sole transmission route reported was P-P.

In this study, P-P spread was most commonly identified in private household and childcare outbreaks, the latter also being the most common location reported for P-P outbreaks in the United States [17]. P-P spread is well recognized as a transmission route for VTEC during outbreaks [20–23], and although known secondary cases are generally excluded from participation in most sporadic case-control study designs, contact with a person with diarrhoea was also recognized as a risk factor for VTEC infection and/or HUS in several risk factor studies [24–26].

At least 6.5% of VTEC cases resulted in onward transmission to others; this is slightly higher than the rate reported in a study by Parry *et al.* [24]. Our study does not examine the risk factors for secondary

transmission, but the latter authors did find secondary transmission to be higher in households where the index case was not hospitalized, while Werber *et al.* showed the risk of secondary transmission in a household increased when the index case was aged <5 years, or when there was at least one sibling in the household [10].

In our study, waterborne transmission of VTEC infection was the most significant mode of primary VTEC transmission, being associated with several untreated or poorly treated private water supplies. Ireland's location in the west of Europe ensures it has a wet, maritime climate, making agricultural land well-suited to livestock farming. Ireland has the third highest cattle density among EU Member States [2]. Moreover, in Ireland, 10% of private homes are served by domestic wells [13]; in many instances these are untreated, and are outside the scope of water regulation as they serve fewer than 50 persons or produce <10 m³/day, and do not serve a commercial activity. A further 12% of private homes are served by small private water schemes managed by trustees, private individuals or companies. Many of these schemes also fall outside the scope of water regulations for the same reason, although all water supplies which serve a commercial use fall within the scope of the water regulations regardless of supply type (including private wells) or size. Even for private water supplies that are covered by water regulations, the quality is reported to be generally inferior to that of public water supplies [27].

Water is a particularly effective medium for dissemination of gastrointestinal pathogens [7], and has the potential to infect large numbers of people. Untreated or poorly managed water supplies,

especially those drawing their source water from areas close to livestock farming, are likely to present significant risk. A combination of a high reliance on private domestic wells and a high cattle density is likely to have contributed to Ireland's high waterborne VTEC incidence.

Foodborne outbreaks were reported infrequently in the Irish dataset, but may be underestimated as evidence that an outbreak is foodborne can be difficult to establish. In addition to the 21 outbreaks suspected to be foodborne, there were at least four general VTEC outbreaks reported to be associated with commercial premises with unknown transmission route, and it is possible that some or all of these were foodborne although other transmission routes could not be ruled out by the outbreak investigation teams.

We acknowledge that the risk factors that lead to outbreaks may differ from sporadic cases. Food, in particular undercooked hamburger/minced beef and raw milk/milk products, were identified as key risk factors in case-control studies elsewhere [24, 26, 28–31]. Similarly, direct animal contact was a minor contributor to the burden of VTEC outbreaks in Ireland, although it is possible that it has a greater role in sporadic disease [24, 26, 28, 29].

Recommendations

In the first instance, the focus for reducing incidence should be on reducing waterborne and P-P transmission (particularly in childcare facilities). Active follow-up of childcare facilities attended by VTEC cases should remain a key public health intervention given the potential for transmission in these settings, because of the less developed hygiene skills of small children and the higher vulnerability of this group to more severe disease such as haemolytic uraemic syndrome (HUS) (historically 5–8% of VTEC cases in Ireland have been reported as HUS). In Ireland, 42% of families in the general population use non-parental childcare [32]. The Health Protection Surveillance Centre has published national guidance for crèche owners, and management in the prevention of infectious disease spread in childcare facilities [33], and for public health professionals on the management of VTEC cases and outbreaks in childcare facilities [34] in 2012 and 2013, respectively.

The evidence here suggests that private sources of water present a risk to public health when they have not been designed and managed appropriately, and those responsible should be mindful of the

requirements for their maintenance and protection. In 2013, the HSE published a leaflet for well owners outlining the infectious disease risks associated with drinking water from private wells, providing advice on actions that can be taken including: checking the supply, water testing and treatment, and what to do in the event the well water is found to be contaminated [35].

Efforts in Ireland should focus, initially, on publicizing these materials and ensuring that they are widely available. Given international evidence on the potential for outbreaks due to food and animal contact, advice should also continue to be provided to food businesses [36], open farms and farm families [37, 38, 45]. Longer term objectives could include strategies which reduce the VTEC prevalence in the farm animal population and in the environment, e.g. husbandry and hygiene practices proven to reduce carriage [39] or cattle vaccination [40], as it is likely that these serve as an important reservoir for VTEC infection in Ireland.

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DECLARATION OF INTEREST

None.

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