



Public Health
England

Protecting and improving the nation's health

Legionnaires' disease in England and Wales – 2015

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Executive summary

In 2015, 388 cases of Legionellosis (confirmed and presumptive) were reported to the National Surveillance Scheme for Legionnaires' disease in residents of England and Wales.

Of the 382 confirmed cases of Legionnaires' disease reported with onset of symptoms in 2015, 287 (75.1%) were male and 95 (24.9%) were female, giving a male to female ratio of 3.0.

In excess of 80% of the 382 confirmed cases of Legionnaires' disease, (313 cases), were reported in individuals aged 50 years and over.

Over the three-year period 2013 to 2015, the incidence rate in England and Wales reached a mean of 5.8 cases per million population (pmp). Peak incidence was reported in the areas covered by the East Midlands (7.6 pmp) and West Midlands (7.4 pmp) PHE centres.

Of the 382 confirmed cases of Legionnaires' disease, 191 (50.0%) cases were considered to have been exposed to the infecting organism in the community, 177 (46.3%) cases were associated with travel abroad and 14 (3.7%) were considered to have links to a healthcare facility (nosocomial).

At least one underlying condition/risk factor was found in 284 (74.3%) confirmed cases of Legionnaires' disease; with heart conditions and smoking being the most frequently reported risk factors.

The crude case fatality rate in 2015 was 6.8%, which is even lower than the case fatality rate for 2014.

The number of cases microbiologically confirmed by polymerase chain reaction (PCR) increased from 2014 from 25.7% to 30.1% of cases tested by PCR during 2015.

The two most common *L. pneumophila* serogroup 1 subtypes identified in clinical isolates continue to be ST1 and ST47.

A total of 35 clusters/outbreaks were identified in 2015 compared to 26 observed in 2014. The highest increase was seen in the number of community clusters/outbreaks where four clusters/outbreaks were identified in 2014 compared to 12 clusters/outbreaks in 2015.

The number of travel associated cases of Legionnaires' disease increased from 139 to 177 cases in cases associated with travel abroad and from 25 to 45 cases associated with UK travel between 2014 and 2015.

Spain remains the destination most frequently travelled to by cases of Legionnaires' disease during 2015. However, the countries with the highest incidence rates were Thailand followed by United Arab Emirates with 41.7 and 41.0 cases per million visits, respectively.

Introduction

Legionella pneumophila was identified as the organism responsible for an outbreak of severe respiratory illness among a group of men attending a American Legion convention in Philadelphia, USA in 1976 (1). The outbreak resulted in 182 cases of a flu-like-illness with symptoms including a productive cough, fever, headache, rigor and diarrhoea leading onto confusion, sepsis, organ failure and death; 29 of the 182 cases died (2). The infecting organism has since been classified as a gram negative bacterium of genus *Legionella* of which there are now in excess of 60 different species (3) with at least 30 documented as being pathogenic to humans (4).

Legionella spp. are ubiquitous and have been isolated from soil but primarily inhabit naturally warm, stagnant water systems such as ponds, lakes and rivers (4). However, the creation of artificial man-made water systems has provided an alternative habitat that mimics the natural environment, thereby conducive to the growth of *Legionella spp.* Many artificial water systems such as cooling towers, evaporative condensers and spa pools provide the organism with a potential means of dispersal to distances of up to 10km from cooling towers (5-7).

Inhalation of aerosols dispersed from water systems colonised with *Legionella* is the primary route of infection but in rare instances can also be attributed to aspiration (8). Person to person spread is generally not considered to be a significant route of transmission.

Legionella pneumophila is responsible for 90% of human infection, 85% of which are identified as *L. pneumophila* serogroup 1 (4). Infection by the organism can cause one of two recognised syndromes; Legionnaires' disease (1), a severe, potentially fatal, form of pneumonia and Pontiac fever (9), a self-limiting, non-fatal, mild influenza-like illness. A third atypical form of the disease also exists and is characterised by symptoms similar to those of Legionnaires' disease but with the absence of pneumonia and is termed non-pneumonic Legionellosis.

Enhanced surveillance has been undertaken on every reported case of Legionnaires' disease in residents of England and Wales since 1980. The primary purpose of the National Enhanced Legionnaires' disease Surveillance Scheme (NELSS) is to identify clusters and prevent or minimise the impact of potential outbreaks.

Prevention and control of Legionellosis

Methods for the prevention and control of Legionnaires' disease are distinct compared to other infectious diseases. There are no vaccines to protect against the organism and antimicrobial prophylaxis in those exposed has not been shown to work (8). The focus for the control and prevention of Legionnaires' disease therefore lies in the implementation of stringent regulations on the management and maintenance of man-made water systems.

In the United Kingdom those in charge of premises with man-made water systems are obliged to adhere to statutory regulations including the Health and Safety and Work Act 1974 (10), the Management of Health and Safety at Work Regulations (11) and the Control of Substances Hazardous to Health Regulations 2002 (COSHH) (12). These collectively create a framework of actions aimed to ensure water systems are designed and maintained to standards that avoid the creation of an environment conducive to the colonisation of the system with Legionella.

It is the failure to implement and adhere to the necessary legislation that leads to the colonisation of water systems which have the potential to become the source of major outbreaks of Legionnaires' disease. It then falls upon the health protection agencies to identify and investigate such incidents and partner organisations such as environmental health to investigate potential environmental sources of legionella.

The national enhanced Legionnaires' disease surveillance scheme

Public health surveillance is one of the most effective ways in which to monitor and evaluate public health practices and can act as an early warning system for public health emergencies. Based on this school of thought by 1980 the National Enhanced Legionnaires' disease Surveillance Scheme (NELSS) was established to collect enhanced surveillance data on all cases of Legionnaires' disease in residents of England and Wales.

The scheme is managed by the Legionella Section, Respiratory Diseases Department, National Infections Service, Colindale. The primary aim of NELSS is to identify clusters to prevent potential outbreaks and where they occur, to support the management and control of the incident. The functions of NELSS include:

- issue notifications and alerts to Health Protection Teams (HPTs) related to clusters

- implement the European guidelines for travel associated cases of Legionnaires' disease, as a collaborating member of ELDSNet
- report travel associated cases of Legionnaires' disease to the European Legionnaires' Disease Surveillance Network (ELDSNet)
- issue alerts on possible travel-associated clusters in other countries
- validate and assure the quality of the data submitted to the scheme
- monitor risk groups and trends over time
- collaborate with international counterparts to follow up cases associated with accommodation sites in England and Wales

Other formal responsibilities of the national surveillance scheme include the composition and provision of the following outputs:

- local and regional datasets to support investigations, outbreaks, and research
- monthly *Legionella* reports
- annual official statistics dataset for Legionnaires' disease
- annual statistics for the World Health Organization
- annual dataset for ELDSNet operated by the European Centre for Disease Prevention and Control (ECDC)

Methodology

The data presented in this report is extracted from the NELSS database, which holds data on confirmed and suspected cases of Legionellosis in residents of England and Wales. The majority of cases were reported by HPTs and some were reported by the national Legionella reference laboratory, Respiratory and Vaccine Preventable Bacterial Reference Unit (RVPBRU), at Public Health England (PHE), Colindale.

Data is collated and verified by the national surveillance scheme for Legionnaires' disease, managed at the National Infections Service (NIS), PHE, Colindale.

Cases thought to have Legionnaires' disease were reported to NELSS through the completion of the national surveillance form that requests enhanced surveillance data to:

- establish whether an individual meets the case definition for Legionnaires' disease or one of the other syndromes listed below
- identify risk factors
- determine the likely category of exposure
- identify potential sources of infection

Case Definitions

Legionellosis is the collective term used to describe infection caused by the Legionella bacteria. The organism can cause one of three syndromes:

- **Pontiac fever** – a non-fatal, non-pneumonic, mild, self-limiting influenza-like illness usually resolving within 24 to 48 hours
- **Legionnaires' disease** – severe, potentially fatal, atypical form of pneumonia
- **Non-pneumonic legionellosis** – a urinary antigen positive case, indicating infection by *Legionella spp* with symptoms that do not fit those for Pontiac fever and with no evidence of pneumonia

Cases of Legionnaires' disease are defined as confirmed or presumptive based on their microbiology. The definitions are as follows:

Confirmed case of Legionnaires' disease

- A clinical and/or radiological diagnosis of pneumonia with microbiological evidence of one or more of the following:
 - isolation (culture) of *Legionella* spp. from clinical specimens
 - the presence of *L. pneumophila* urinary antigen determined using validated reagents/kits

Presumptive case of Legionnaires' diseases

- A clinical and/or radiological diagnosis of pneumonia with microbiological evidence of one or more of the following:
 - detection of *Legionella* spp. nucleic acid (e.g. PCR) in a clinical specimen
 - a positive direct fluorescence (DFA) on a clinical specimen using validated *L. pneumophila* monoclonal antibodies (also referred to as a positive result by direct immunofluorescence (DIF))

Epidemiological Analysis

Age and Gender

The proportion of males and females were studied to determine the male to female ratio. Analysis was also carried out for gender by age group, with cases categorised into four groups; under 50 years, 50 to 59 years, 60 to 69 years, and 70 years and over.

Seasonality

Seasonality was studied through analysis of the number of confirmed cases of Legionnaires' disease by reported month of onset of symptoms.

Geographical spread

The geographical spread of cases was analysed by dividing cases into the nine PHE centres and Wales according to their place of residence. The average annual rates were calculated using population data from the Office for National Statistics mid-2014 population estimates.

Category of Exposure

Cases were categorised into one of three groups based on the most likely 'category of exposure'. The cases were divided in accordance with the following definitions:

- **Community acquired**
Cases with no history of overnight stays outside the UK (travel abroad) or hospital admission or association with a health care facility during the incubation period prior to onset of illness are deemed to be community acquired
- **Travel associated**
Cases that spent one or more night in holiday or business accommodation abroad in the 2 to 10 days before onset of symptoms. Overnight stays include accommodation in hotels, camp sites, ships, rented holiday apartments or other tourist facilities
- **Nosocomial** (hospital/healthcare facility acquired)
Cases of Legionnaires' disease who were in a hospital or other healthcare facility during the incubation period. These include cases who stayed or spent time (eg as an outpatient or healthcare worker) in a hospital or other healthcare facility for part of the incubation period and where there may or may not have been previous cases of Legionnaires' disease

Risk factors

The medical history of each case was reviewed by the reporter and any underlying conditions noted on the national surveillance form. The underlying conditions were analysed by separating the individual ailments/conditions into one of eight groups:

- Diabetes
- Heart conditions – includes all cardiovascular conditions, stroke, blood disorders, hypertension
- Liver conditions
- Neoplasms – past and current cancers of all types, blood cancers
- Renal disorders – includes various kidney conditions, dialysis, transplants
- Respiratory conditions – includes full range of respiratory disorders from asthma, chronic obstructive pulmonary disorder, lung transplants, tuberculosis
- Smoking – past and current smoking
- Immunosuppression – any other condition not included in the above seven groups that cause immunosuppression, including arthritis, HIV, prescribed use of steroids, systemic lupus erythematosus

Mortality

NELSS is informed of the outcome of cases by the investigating HPT and, where available, through the ONS deaths data for cases where the cause of death has been registered as Legionnaires' disease, with an ICD code A481. These figures were used to calculate the case fatality rate by year of onset of symptoms, by category of exposure and by age group. Statistical analysis of mortality was undertaken using the statistical package, STATA 13.

Microbiology

Confirmed cases of Legionnaires' disease must have positive microbiology carried out by local hospital laboratories and preferably sent to the national Legionella reference laboratory for confirmation. Urine samples were tested for the presence of antigens and respiratory samples were cultured and examined by polymerase chain reaction (PCR). PCR enables respiratory samples to be analysed further to deduce the sequence-based type in order to identify the strain of organism infecting the case. The most prevalent strains were identified from cases where respiratory samples were tested and PCR successfully produced a full genetic profile.

Clusters/outbreaks

Every reported case undergoes detailed analysis by the national surveillance team in order to check for association with any other recently reported case(s) in terms of geography, time, travel or any other possible links. Cases that met the following definitions formed a cluster or outbreak:

- **Cluster** - Two or more cases that initially appear to be linked by area of residence or work, including a healthcare or other type of community setting and which have sufficient proximity in dates of onset of illness (within six months) to warrant further investigation
- **Outbreak** - An outbreak is defined as two or more cases where the onset of illness is closely linked in time (weeks rather than months) and where there is epidemiological evidence of a common source of infection, with or without microbiological evidence

Travel cases

Travel associated cases were analysed to determine the rate of infection associated with each country of travel. These were calculated using travel statistics obtained from the Office for National Statistics 2014 travel trends for 'UK residents visits abroad'.

This report presents the epidemiological data collated by the NELSS based on reported cases of Legionnaires' disease among residents of England and Wales who experienced the onset of symptoms during 2015. Data from previous years have been included, where appropriate, for comparison.

Descriptive epidemiology

Legionellosis

NELSS received reports on 491 potential cases of Legionellosis in residents of England and Wales experiencing onset of symptoms during 2015. Of these reports, 74 were proven to be negative for Legionella infection, nine reports were lost to follow up and 20 reports were associated with residents from outside of England and Wales. The remaining 388 reports were classified as confirmed or presumptive cases of Legionellosis in residents of England and Wales (Table 1).

388 reports were for individuals with onset of symptoms during 2015 and of these 387 were microbiologically confirmed to have Legionella infection whilst one individual was 'presumed' to have Legionella infection based solely on a positive PCR result. Overall, 383 of the 388 infected cases of Legionellosis were diagnosed with pneumonia and met the definition for Legionnaires' disease outlined previously (382 confirmed cases and one presumptive case). Five individuals were reported to have had no clinical or radiological evidence of pneumonia and therefore classified as cases of non-pneumonic Legionellosis.

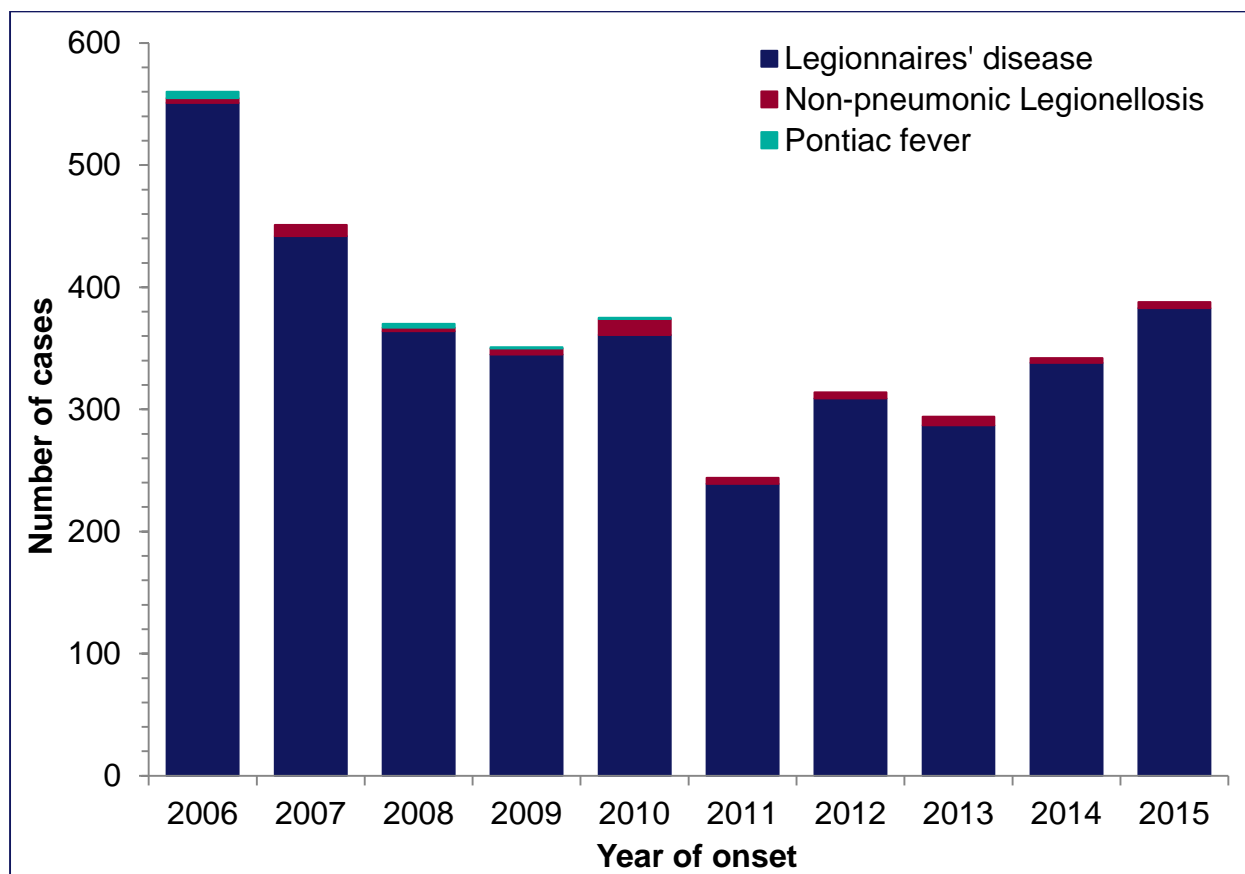
Table 1: Number of cases of Legionellosis (including presumptive) by disease type and year of symptoms onset 2013 to 2015.

	Number of confirmed (presumptive) cases		
	2013	2014	2015
Legionnaires' disease	285 (2)	331 (7)	382 (1)
Non-pneumonic Legionellosis	7	4	5
Pontiac Fever	-	-	-
Total	294 (292 confirmed, 2 presumptive)	342 (335 confirmed, 7 presumptive)	388 (387 confirmed, 1 presumptive)

() additional presumptive cases (ie cases with a serological diagnosis (a single high titre) or PCR result.

Figure 1 indicates that the number of cases of Legionellosis with onset of symptoms during 2015 continues the general upward trend in case numbers observed since 2011. Since 2011 the number of cases of Legionellosis has increased by 59.0% but the number of cases of non-pneumonic Legionellosis remains at a mean of 5.0 cases per year.

Figure 1: Number of cases of Legionellosis (including presumptive) by year of onset of symptoms 2005 to 2014.



The total number of microbiologically confirmed, pneumonic cases of Legionella infection (ie cases of Legionnaires' disease), reported to NELSS with onset of symptoms during 2015 was 382 among residents of England and Wales. The remainder of this report will describe, analyse and interpret confirmed Legionnaires' disease cases only.

Age and gender distribution

In 2015, 287 (75.1%) cases were reported in males and 95 (24.9%) in females, (Table 2a) creating a male to female ratio similar to that observed in 2013 at 3.0 males: 1.0 female. The higher proportion of males infected with Legionella is well documented and a unique characteristic of Legionnaires' disease (13).

Table 2a: Number and proportion (%) of confirmed cases of Legionnaires' disease by gender and age group 2013 to 2015.

	2013		2014		2015		Total	
	Females	Males	Females	Males	Females	Males	Females	Males
< 50 years	13 (26.0)	37 (74.0)	11 (22.0)	39 (78.0)	13 (18.8)	56 (81.2)	37 (21.9)	132 (78.1)
50-59 years	15 (26.3)	42 (73.7)	27 (32.5)	56 (67.5)	25 (25.5)	73 (74.5)	67 (28.2)	171 (71.8)
60-69 years	23 (24.2)	72 (75.8)	31 (31.3)	68 (68.7)	32 (29.4)	77 (70.6)	86 (28.4)	217 (71.6)
70+ years	21 (25.3)	62 (74.7)	32 (32.3)	67 (67.7)	25 (23.6)	81 (76.4)	78 (27.1)	210 (72.9)
All Ages	72 (25.3)	213 (74.7)	101 (30.5)	230 (69.5)	95 (24.9)	287 (75.1)	268 (26.9)	730 (73.1)

The age distribution of cases had remained fairly constant between 2013 and 2015, Table 2b. The lowest proportion of cases were in those aged below 50 years, 18.1% in 2015, with the proportion increasing with age until 69 years. After which, the proportion decreases somewhat from 28.5% in the 60 to 69 years to 27.7% in those aged 70 years and over. Across the three years, 2013 to 2015, both genders follow this pattern, with case numbers increasing with age, up to the 60 to 69 years age group, Table 2a. Variability in proportions of genders was observed during this period in the 70+ age group.

Table 2b: Number and proportion (%) of confirmed cases of Legionnaires' disease by year of symptom onset and age group 2013 to 2015.

	2013 (%)	2014 (%)	2015 (%)	Total (%)
< 50 yrs.	50 (17.5)	50 (15.1)	69 (18.1)	169 (16.9)
50-59 yrs.	57 (20.0)	83 (25.1)	98 (25.7)	238 (23.8)
60-69 yrs.	95 (33.3)	99 (29.9)	109 (28.5)	303 (30.4)
70+ yrs.	83 (29.1)	99 (29.9)	106 (27.7)	288 (28.6)

Seasonality

Historically case numbers usually peak at any time between the months of July and October in England and Wales. Figure 2 shows that the highest number of cases experienced onset of symptoms in September 2015, a month later than the peak observed in August 2013 and a month before the highest number of cases in reported in 2014. Of note is the fact that over a third (38.5%) of cases reported with onset of symptoms during 2015 experienced onset of symptoms in the third quarter of the year, between July to September, which is in line with trends observed in previous years.

Figure 2: Number of confirmed cases of Legionnaires' disease by month and year of onset of symptoms 2013 to 2015.

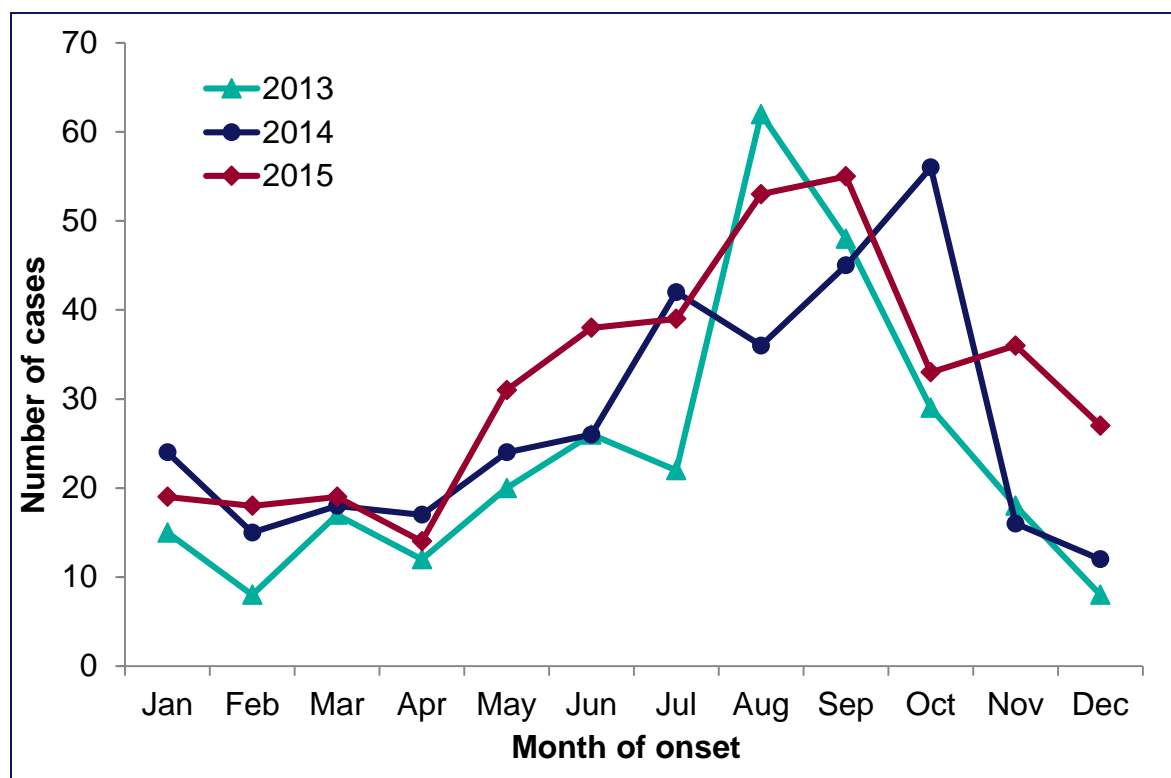
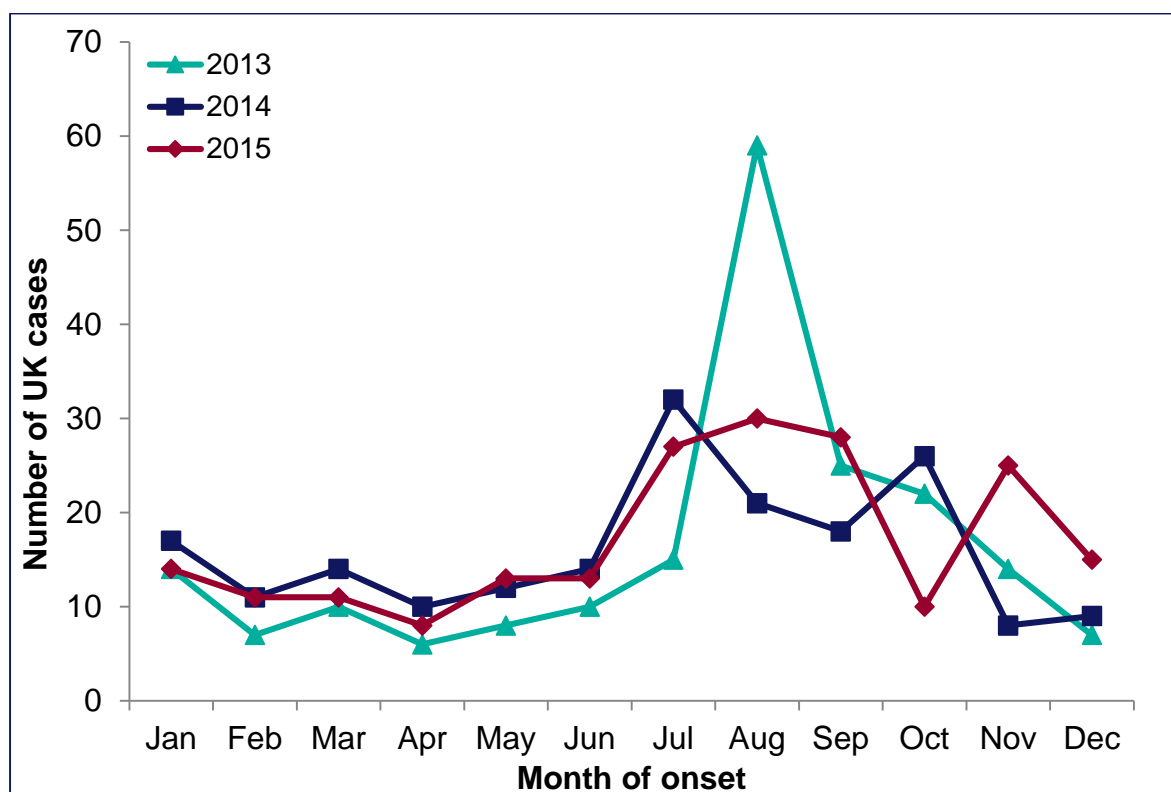


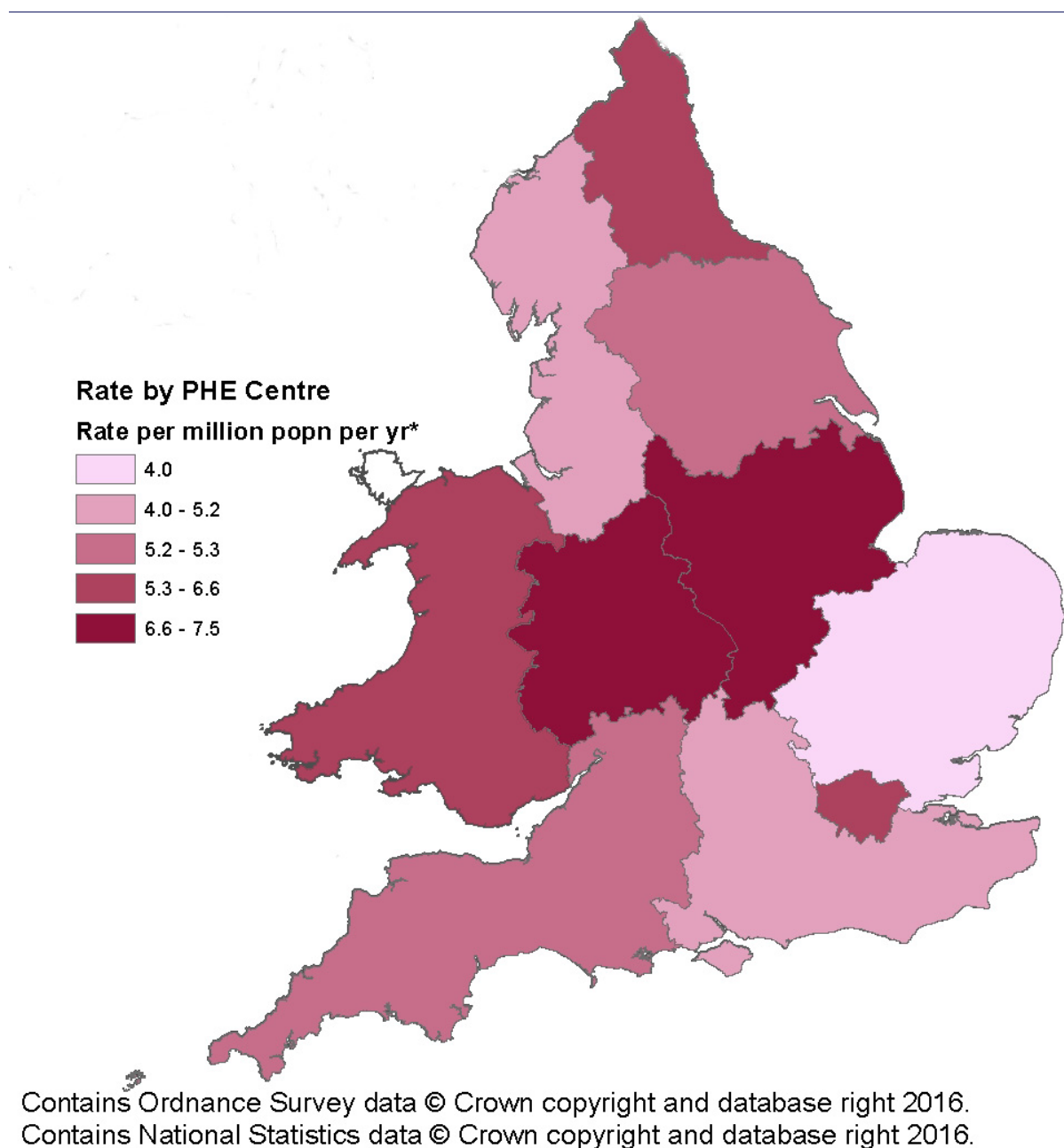
Figure 3: Number of confirmed cases of Legionnaires' disease excluding all travel abroad cases, by month of onset of symptoms 2013 to 2015.



Geographic distribution

Enhanced surveillance is carried out on every case of Legionnaires' disease reported to NELSS by the local HPT in which the case resides. Thus, cases of Legionnaires' disease are managed across England by the HPTs in nine local PHE centres and Wales.

Figure 4: Incidence rate per million population[†] of confirmed Legionnaires' disease cases by PHE centre of residence (and Wales) and year of onset 2013 to 2015.



[†] Population denominators based on mid - 2014 population estimates from office of national statistics.

The number of cases with onset of symptoms reported by PHE centres and Wales with onset of symptoms during 2015 ranged from 18 cases from Wales to 57 cases from London. Average case numbers across the three years, 2013 to 2015 showed London to report the highest number of cases with an average of 54 cases per year followed by the South East PHE centre which reported an average of 46 cases per year and West Midlands with 42 cases per year.

Table 3: Mean rate (million population[†]) of confirmed cases of Legionnaires' disease for PHE centres (and Wales) by year of symptom onset, 2013 to 2015.

Public Health England centres and Wales	2013	2014	2015	Total	Mean rate per million popⁿ per year.[†]
East Midlands	26	46	33	105	7.6
East of England	33	14	26	73	4.0
London	58	48	57	163	6.4
North East	10	15	27	52	6.6
North West	23	41	45	109	5.1
South East	38	46	54	138	5.2
South West	15	34	38	87	5.4
Wales	15	25	18	58	6.3
West Midlands	44	39	43	126	7.4
Yorkshire and Humber	23	22	40	85	5.3
Other	-	1	1	2	-
Total	285	331	382	998	17.4

[†] Population denominators based on mid - 2014 population estimates from office of national statistics.

Case numbers, however, do not reflect an accurate picture of the distribution of Legionnaires' disease cases across England and Wales. Taking into

account the population covered by the different PHE centres shows that the highest mean incidence rate for 2013 to 2015 was 7.6 cases per million population in East Midlands, followed by 7.4 cases per million population in residents of West Midlands (Figure 4, Table 3). The centre with the third highest incident rate at 6.6 cases per million population was the North East PHE centre which reported the lowest mean number of cases between 2012 to 2015.

Source of exposure

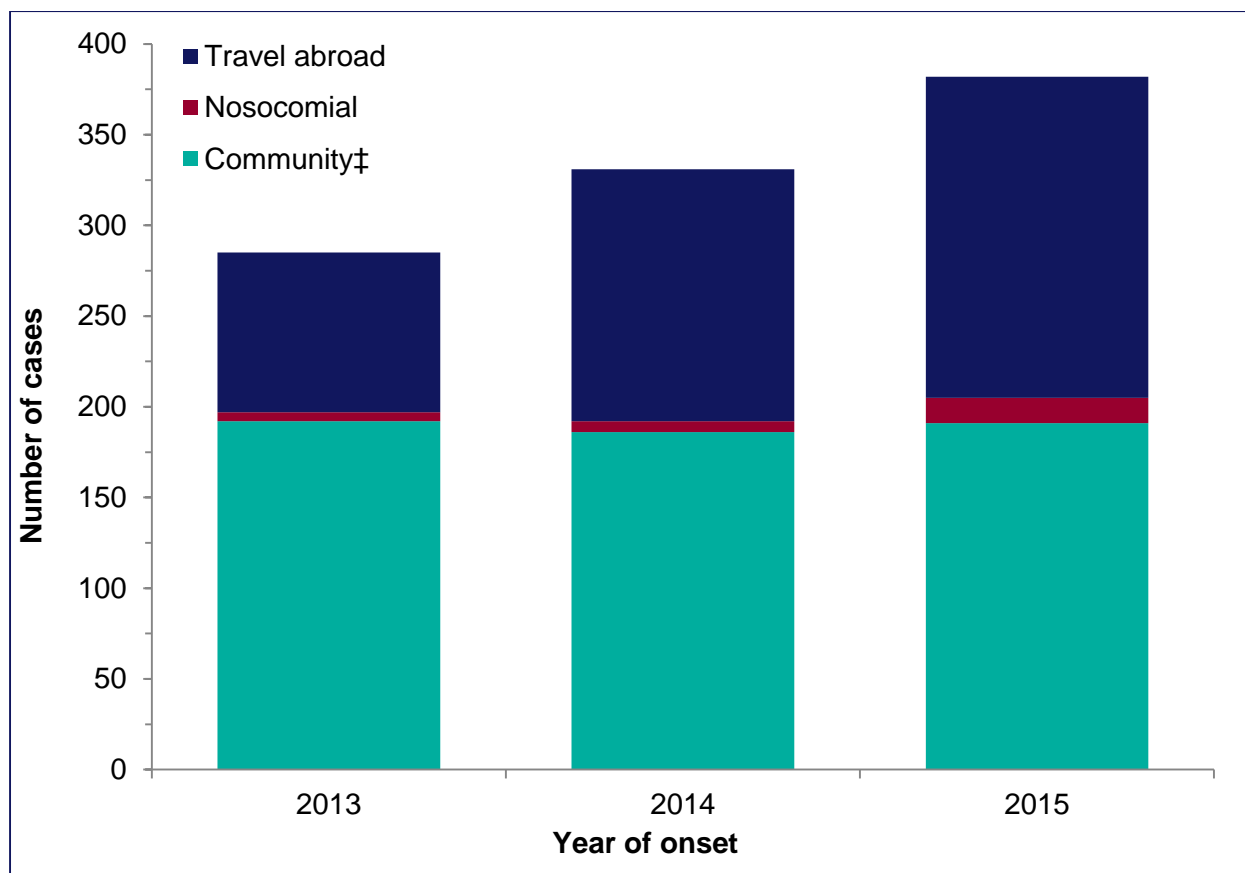
Half of all cases reported with onset of symptoms during 2015 were thought to have been exposed to the source of infection from within the community (Figure 5). This is a 6.2% fall in the proportion of community - acquired cases compared to 2014 and a 17.4% fall compared to 2013. The proportion of travel associated cases on the other hand increased from 42.0% in 2014 to 46.3% in 2015. However, of note is the change in the number of cases of Legionnaires' disease associated with healthcare facilities; case numbers increased from six cases in 2014 to 14 in 2015 (Table 4).

Table 4: Number of confirmed cases of Legionnaires' disease by exposure category and year of onset 2013 to 2015.

Category	Community [‡] (%)	Nosocomial (%)	Travel abroad (%)
2013	192 (67.4)	5 (1.8)	88 (30.9)
2014	186 (56.2)	6 (1.8)	139 (42.0)
2015	191 (50.0)	14 (3.7)	177 (46.3)

[‡] includes travel UK cases

Figure 5: Number of confirmed Legionnaires' disease cases by year of onset and category of exposure 2013 to 2015.



‡ includes travel UK cases

Risk factors

Immunocompromised individuals have been shown to have a high risk of Legionella infection. Therefore, it is unsurprising that almost three quarter (74.3%) of cases with onset of symptoms during 2015 reported one or more underlying medical conditions which is in line with proportions observed in 2013 and 2014 when 73.4%, and 74.7% of cases, reported one or more underlying conditions, respectively (Table 5).

The three most prevalent conditions reported by cases with onset of symptoms during 2015 remain the same as in the previous two years. In 2015 the most frequently reported underlying medical conditions were associated with the heart, reported by 31.7% of cases. This was followed by current or past history of smoking and diabetes reported by 28.8% and 17.5% of cases respectively.

Table 5: Underlying medical conditions and risk factors reported in confirmed cases of Legionnaires' disease 2013 to 2015.

	2013 (%)	2014 (%)	2015 (%)
Any underlying condition	213 (74.7)	243 (73.4)	284 (74.3)
Diabetes	42 (14.7)	50 (15.1)	67 (17.5)
Heart conditions	89 (31.2)	96 (29.0)	121 (31.7)
Immunosuppression[^]	31 (10.9)	41 (12.4)	44 (11.5)
Liver conditions	14 (4.9)	12 (3.6)	15 (3.9)
Neoplasms	30 (13.0)	25 (7.6)	28 (7.3)
Renal disorders	9 (3.2)	9 (2.7)	19 (5.0)
Respiratory conditions	37 (13.0)	28 (8.5)	51 (13.4)
Smoking	78 (27.4)	110 (33.2)	110 (28.8)

[^] immunosuppression due to other conditions or clinical treatments.

NB: Individual cases may have reported more than one underlying condition.

Mortality

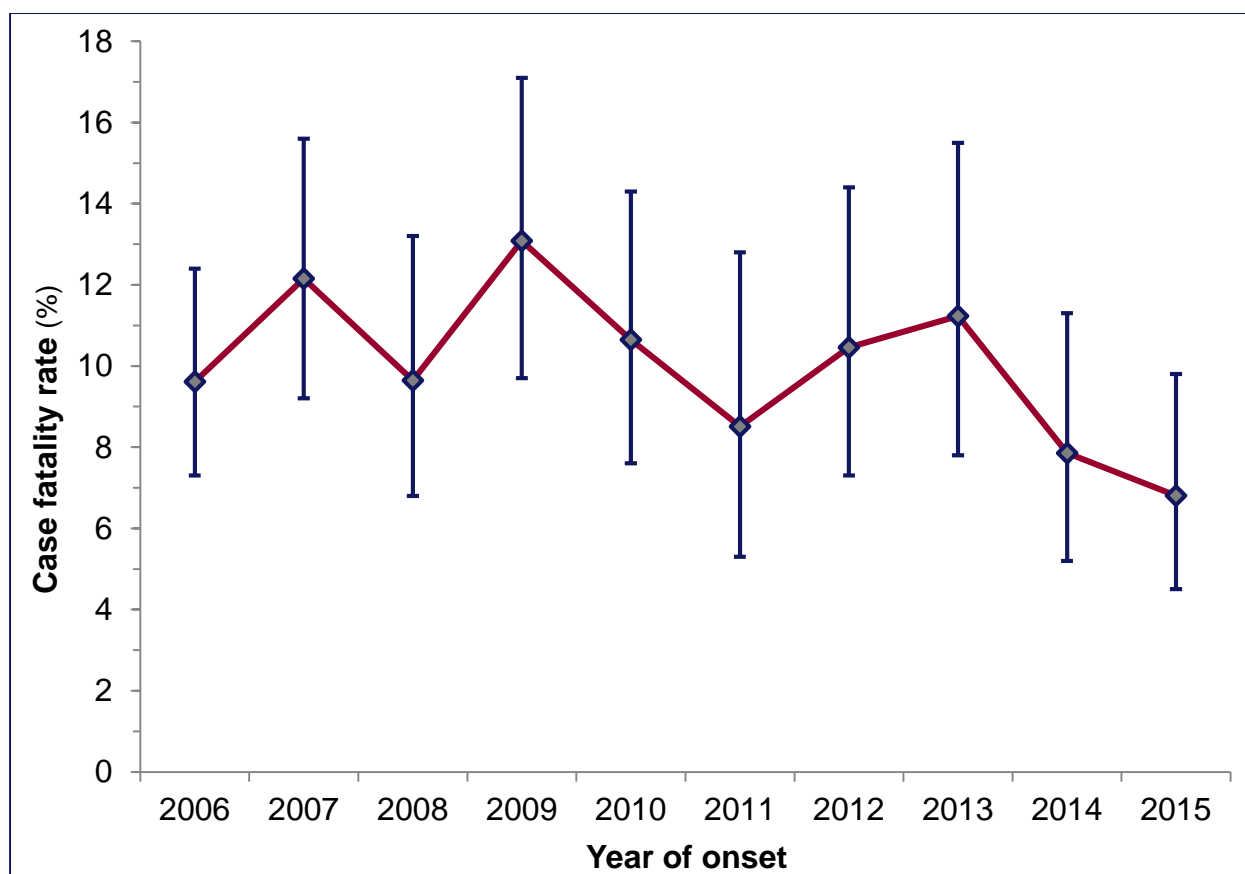
NELSS is informed of deaths in cases of Legionnaires' disease via the local HPT or from death certificates which have Legionnaires' disease recorded as a cause of death. Over the past decade, 2006 to 2015, the number of deaths reported among cases of Legionnaires' disease ranged from 20 deaths in 2011 to 53 in 2007 (Figure 6). The first half of the decade (2006 to 2010) experienced a much higher number of deaths with a mean of 45 deaths per year whilst more recent years, 2011 to 2015, experienced a mean of 27 deaths per year.

Analysis of the crude case fatality rate (CFR) for the same time period (2006 to 2015) ranged from 6.8% in 2015 to 13.1% in 2009. 2015 saw 26 deaths amongst the 382 reported cases of Legionnaires' disease. The CFR was 6.8% which continues the downward trend of the previous two years which saw the CFR fall from 11.2% to 7.9% in 2013 to 2014. The 2015 CFR of

6.8% is not only the lowest rate observed over the decade analysed here but is the lowest CFR recorded since records began in 1980.

Figure 6 shows that despite the peaks and troughs there appears to be an overall downward trend in CFR across the decade and chi-squared test for trend was performed to determine whether there is statistical evidence of a downward trend in mortality among cases of Legionnaires' disease in residents of England and Wales. At the 0.05 level of significance, statistically no evidence of a linear trend was observed between the year of onset of symptoms and a fatal outcome, (p-value; 0.1490, not significant), thereby suggesting that although year on year there has been a fall in CFR, overall since 2006 to 2015 there has been no significant improvement in the outcome of patients diagnosed with Legionnaires' disease in England and Wales.

Figure 6: Case fatality rates for Legionnaires' disease by year of symptoms onset 2006 to 2015.



There is a clear difference in the crude CFR when studying deaths by category of exposure (Table 6). The highest crude CFR between 2013 and 2015 was observed in nosocomial cases at a rate of 16.0%.

Community acquired cases showed a crude CFR of 11.5% whilst cases associated with travel abroad showed the lowest crude CFR at 3.5%. This is a significant difference in mortality between exposure groups (chi-squared test for association, p-value; <0.0001, significant).

Table 6: Case fatality rates for confirmed cases of Legionnaires' disease by category of exposure 2013 to 2015.

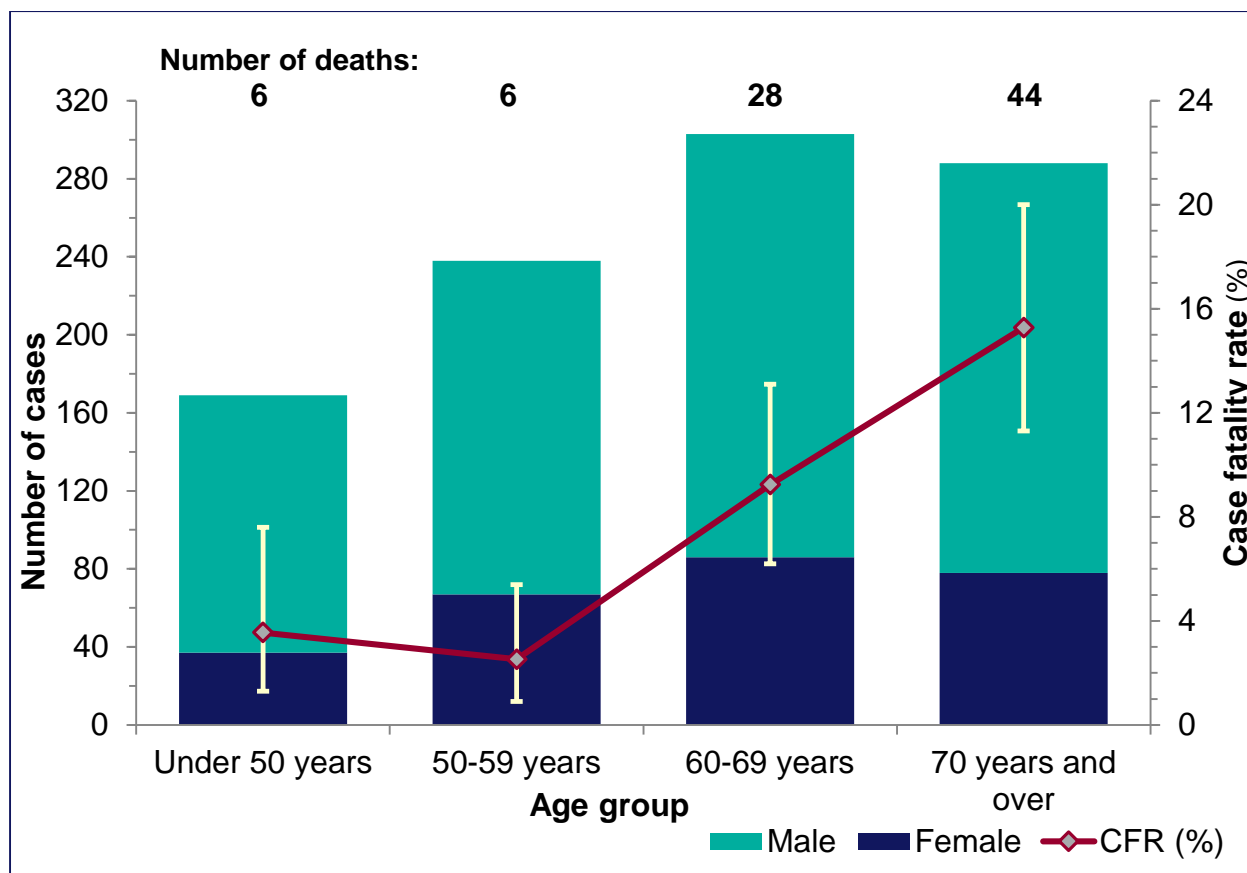
	Cases	Deaths	Case Fatality Rate (%) (95% CI)
Community[‡]	569	66	11.5 (9.1 - 15.9)
Nosocomial	25	4	16.0 (4.5 - 36.1)
Travel Abroad	404	14	3.5 (1.9 - 5.7)
Total	998	84	8.4 (6.8 - 10.3)

[‡] includes travel UK cases

Of the 26 deaths reported in cases with onset of symptoms during 2015, 21 were in males and five in females.

Table 2a showed a 3:1 male to female ratio in cases of Legionnaires' disease with onset between 2013 and 2015 but analysis of mortality among the same groups does not reflect such a pattern. In fact, the proportion of deaths amongst males ranged from 8.0 to 9.8% between 2013 to 2015 and 9.8 to 22.0% in females across the same time period. Although there appears to be a difference in mortality between the genders, this difference is not statistically significant (chi squared test for association, p-value; 0.071, not significant).

Figure 7: Number of confirmed cases of Legionnaires' disease by age and gender, with case fatality rate (%) and 95% CI, 2013 to 2015.



Despite the lack of significant evidence of an association between gender and mortality we were able to deduce from Table 2b that between 2013 and 2015 there was an increase in the proportion of cases from those under 50 years to the 60 to 69 years age group. Table 7 looks further into this observation to determine if the crude CFR also changes by age group. The CFR for the under 50 years age group was 3.6% gradually increasing with age to 15.3% in those aged 70 years and over. This is supported by the chi-squared test for trend at the 0.05 level of significance ($p < 0.001$), indicating a linear trend between age and mortality.

Table 7: Number of confirmed cases of Legionnaires' disease by age group with case fatality rate (%) and 95% CI, 2013 to 2015.

Age group	Cases	Deaths	Case Fatality Rate (%) (95% CI)
Under 50 years	169	6	3.6 (2.3 - 4.0)
50-59 years	238	6	2.5 (1.6 - 2.9)
60-69 years	303	28	9.2 (3.0 - 3.9)
70 years and over	288	44	15.3 (4.0 - 4.7)

Microbiology

In England and Wales since the introduction of the urinary antigen test for the diagnosis of Legionella infection in 1987, the urinary antigen test has become the main method of diagnosis for Legionella infection such that in 2010 100% of cases reported to NELSS were diagnosed by urinary antigen testing. Over the past decade, 2006 to 2015, a mean of 97.1% of reported cases of Legionnaires' disease were diagnosed by urinary antigen detection each year, with 2015 reporting 97.9% of cases diagnosed by this method, Table 8. The success of this method of diagnosis is not only its high sensitivity but also its low cost, simplicity and rapid speed of diagnosis (14).

Commercially available urinary antigen kits are generally marketed as being *L. pneumophila* serogroup 1 specific but non-serogroup 1 cases have been previously reported to be detected by these kits (15). With this in mind the national surveillance scheme records all cases diagnosed by urinary antigen alone as being infected with *L.pneumophila* serogroup unknown, of which there were 255 cases in 2015. Only urinary antigen positive cases further tested by culture and/or PCR and identified as serogroup 1 were recorded as cases infected by *L.pneumophila* serogroup 1; of which there were 120 cases with onset in 2015.

Of the 382 cases of Legionnaires' disease reported in 2015 only nine cases were not positive by urinary antigen detection. Of these, four cases were tested by urinary antigen but found to be negative. These four cases included one *Legionella Longbeachae* case, *Legionella Longbeachae* is a species of Legionella often associated with potting soil and compost (16), and three urinary antigen cases infected by *L. pneumophila* non-serogroup 1 strains. The remaining five cases had no reported urinary antigen test result but were

tested by other methods. These included three individuals infected with *L. pneumophila* serogroup 1 and two were infected with non-serogroup 1 strains.

Table 8: Legionnaires' disease cases by diagnostic test and year of onset, 2013 to 2015.

Diagnostic test	2013 (%)	2014 (%)	2015 (%)
Culture	79 (27.7)	82 (24.8)	87 (22.8)
Urinary antigen	280 (98.2)	321 (97.0)	374 (97.9)
Four-fold rise - (serology)	-	-	-
Single High Titre - (serology)	-	-	-
Polymerise Chain Reaction ^o	105 (36.8)	85 (25.7)	115 (30.1)

^o includes positive tests with complete and partial sequence-based types deduced.

NB: Individual cases may have been tested using one or more of the methods of diagnosis. Culture and PCR are usually only undertaken where a patient has already been confirmed by urinary antigen testing.

For cases with onset of symptoms during 2015, 39% had a lower respiratory tract sample tested by culture; up by 4.0% compared to 2014 but below the 45.0% of cases tested by culture in 2013. However, although the proportion of cases tested by culture increased, there was a continued decrease in the proportion of culture confirmed cases from 27.7% to 24.8% in 2013 to 2014, down to 22.8% in 2015, Table 8.

The 2015 trend observed for PCR as a method of diagnosis is similar to those for culture. Of the 382 cases of Legionnaires' disease, 33.5% were tested by PCR, between the 30.2% tested by PCR in 2014 and the 41.1% of cases in 2013. 30% of cases in 2015 were positive by PCR compared to the 36.8 and 25.7% in 2013 and 2014 respectively.

Apart from the ability of culture to be able to identify infections caused by *L.pneumophila* non-serogroup 1 and non-pneumophila species of Legionella, another advantage of culture and PCR is the ability to determine the sequence-based type (SBT) of the infecting strain (17). In 2015, of the 382 cases of Legionnaires' disease reported to NELSS, 116 (30.4%) cases had a complete or partial SBT identified which is the same as the proportion of

cases with complete or partial SBT's observed in 2013 and higher than the 26.6% of cases in 2014.

Table 9: Ten most prevalent strains/sequence types of *L. pneumophila* identified in clinical isolates from confirmed cases of Legionnaires' disease 2013 to 2015.

Sequence Type (ST)	Number of cases with isolates			
	2013 (%)	2014 (%)	2015 (%)	Total (%)
47	14 (4.9)	13 (3.9)	13 (3.4)	40 (4.0)
42	4 (1.4)	9 (2.7)	15 (3.9)	28 (2.8)
1	6 (2.1)	5 (1.5)	9 (2.4)	20 (2.0)
23	3 (1.1)	2 (0.6)	6 (1.6)	11 (1.1)
62	4 (1.4)	4 (1.2)	3 (0.8)	11 (1.1)
74	4 (1.4)	3 (0.9)	3 (0.8)	10 (1.0)
46	7 (2.5)	2 (0.6)	-	9 (0.9)
1554	5 (1.8)	3 (0.9)	1 (0.3)	9 (0.9)
37	-	2 (0.6)	5 (1.3)	7 (0.7)
616	1 (0.4)	5 (1.5)	1 (0.3)	7 (0.7)

In 2015, 20 (5.2%) cases had a partial SBT identified. Hence the clinical sample was unable to provide a definitive allele for one or more of the seven digit allelic profiles, thereby preventing identification of the infecting strain. Of the 96 cases in 2015 with a complete SBT, the three most frequently identified sequence types were the same as those in 2014, but with ST42 most prevalent in 2015 in 3.9% of cases compared to ST47 which was most frequently identified in 2013 and 2014, Table 9. The second most frequently identified SBT in cases with onset of symptoms during 2015 was ST47, in 3.4% of cases compared to the second most prevalent SBT in 2014 which was ST42. ST1 was the third most frequently identified sequence type for all three years, 2013 to 2015.

There has been virtually no change in the overall proportion of cases with complete sequence types identified since 2013 when 25.6% of cases had a complete SBT recorded to 2015 when 25.1% of cases had a completed SBT, Table 10. Nosocomial cases are the exposure group with the greatest proportion of cases with a complete SBT deduced at 42.9% compared to 19.8% of travel abroad cases and 28.8% of community cases with completed SBT's.

Table 10: Number and proportion (%), of confirmed cases of Legionnaires' disease with complete sequence-based type (SBT) identified by category of exposure.

Category	2013 (%)	2014 (%)	2015 (%)
Community[‡]	54 (28.1)	53 (28.5)	55 (28.8)
Nosocomial	2 (40.0)	2 (33.3)	6 (42.9)
Travel abroad	17 (19.3)	29 (20.9)	35 (19.8)
Total cases with complete SBT	73 (25.6)	84 (25.4)	96 (25.1)

[‡] includes travel UK cases

SBT: sequence-based type

Whilst it is widely accepted that it can be difficult to obtain lower respiratory tract samples from patients, analysis of the PHE centres show some areas proving to be more successful than others. A mean of 39.8% of cases with onset of symptoms during 2015 successfully had a respiratory sample tested by culture and/or PCR, Table 11; London and the North East PHE centres proved most successful in their endeavours with a respiratory sample tested in 54.4 and 48.1% of cases respectively. Wales were only able to ascertain respiratory samples from fewer than half of cases (16.7%), residing in their area and the South West PHE centre had only 21.1% of cases with a respiratory sample tested by culture and/or PCR.

Table 11: Number and proportion (%), of confirmed cases of Legionnaires' disease with complete or partial sequence-based type (SBT) by PHE centre 2015.

Public Health England centres and Wales	Confirmed cases	Respiratory samples	Culture &/or PCR positive cases	Cases with complete or partial SBT
East Midlands	33	15 (45.5)	13 (86.7)	12 (92.3)
East of England	26	10 (38.5)	7 (70.0)	6 (85.7)
London	57	31 (54.4)	27 (87.1)	26 (96.3)
North East	27	13 (48.1)	11 (84.6)	10 (90.9)
North West	45	21 (46.7)	18 (85.7)	17 (94.4)
South East	54	19 (35.2)	18 (94.7)	15 (83.3)
South West	38	8 (21.1)	6 (75.0)	6 (100.0)
Wales	18	3 (16.7)	3 (100.0)	3 (100.0)
West Midlands	43	16 (37.2)	10 (62.5)	10 (100.0)
Yorkshire and Humber	40	16 (40.0)	14 (87.5)	12 (85.7)
Other	1	-	-	-
Total	382	152 (39.8)	127 (83.6)	117 (92.1)

Clusters and outbreaks

One of the principal aims of the national surveillance scheme is to identify clusters and outbreaks of Legionellosis and whilst the majority of reported cases are sporadic, some clusters and outbreaks are identified. The total number of clusters/outbreaks identified involving residents of England and Wales has increased to 35 incidents involving one or more cases of Legionnaires' disease with onset of symptoms during 2015, Table 12.

Table 12: Number of outbreaks/clusters involving cases of Legionnaires' disease in residents of England and Wales by category of exposure 2013 to 2015.

	2013		2014		2015	
	OB/CI	Cases	OB/CI	Cases	OB/CI	Cases
Community	4	22 (10)	4	25 (1)	12	54 (3)
Nosocomial	2	4 (2)	-	-	3	9 (2)
Travel Abroad	8	14 (5)	20	47 (11)	17	39 (7)
Travel UK	3	6 (2)	2	5 (1)	3	8 (1)
Total	17	46 (19)	26	77 (13)	35	110 (13)

() cases with onset of symptoms in other years that are included in the cluster/outbreak

In comparison with incidents from 2013 and 2014, the number of clusters/outbreaks associated with community exposures has increased (Table 12). Nosocomial clusters/outbreaks also increased compared to the two previous years. The number of incidents associated with travel within the UK was similar to 2013 and 2014. The number of clusters/outbreaks associated with travel abroad in 2015 was lower compared to 2014.

Overall, the proportion of cases identified as being associated with one or more other cases of Legionnaires' disease has increased year on year since 2013 when 10.2% of the 285 cases of Legionnaires' disease were linked to a cluster/outbreak. In 2014 this increased to 19.3% and by 2015, 25.4% of the 382 cases with onset of symptoms during 2015 were identified as forming a cluster/outbreak with one or more other confirmed cases of Legionellosis.

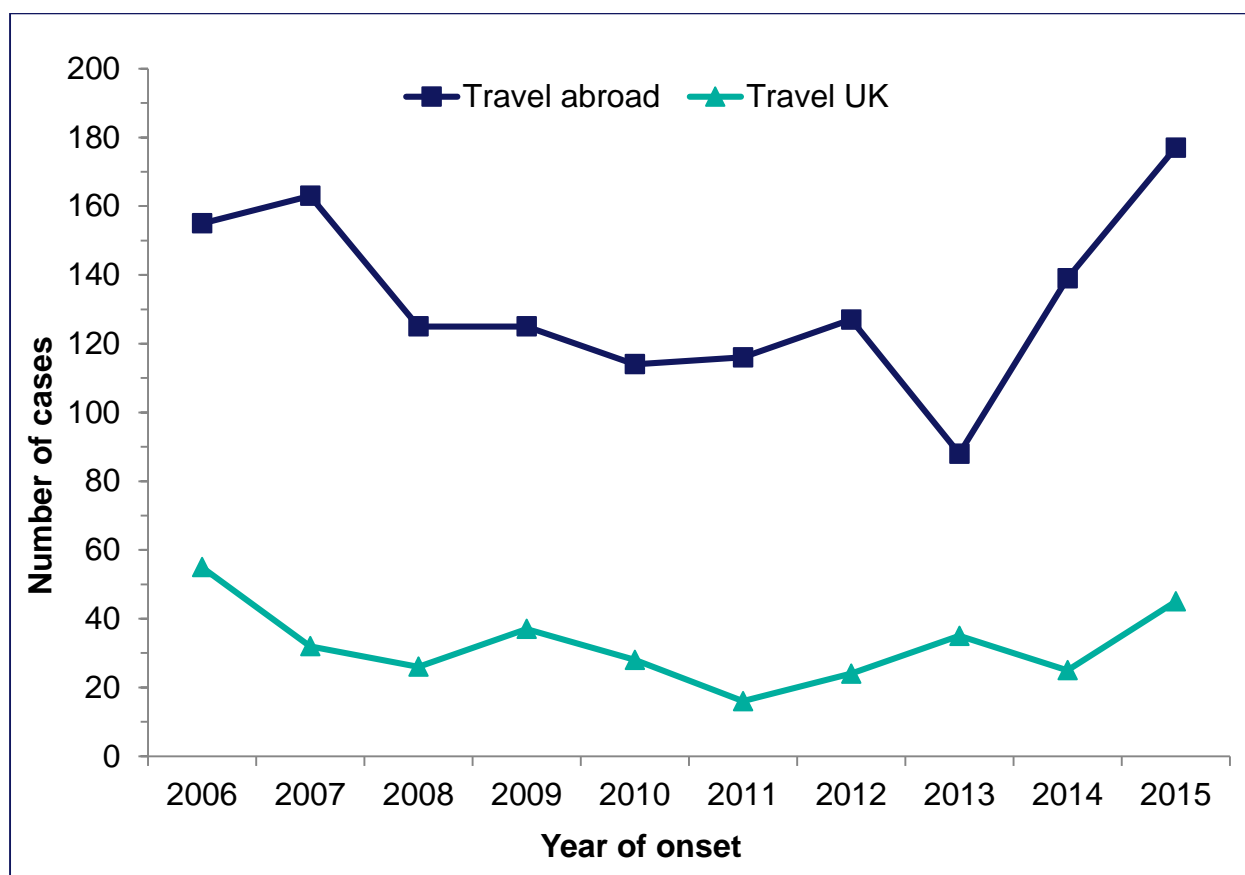
In 2015 a total of 35 incidents were identified eight of which involved between five and seven cases. Five incidents were in the community and two incidents involved residents of England and Wales who stayed overnight at accommodation sites abroad. Of the remaining 28 incidents identified in 2015 only two clusters/outbreaks had a source identified by an indistinguishable clinical and environmental strain.

Travel associated Legionnaires' disease (TALD)

The number of cases of travel associated Legionnaires' disease reported across the decade, 2006 to 2015, ranges from 88 cases in 2013 to 177 cases

in 2015 (IQR = 32.8). The number of cases associated with travel within the UK range from 16 to 55 cases (IQR = 11.2), Figure 8. Between 2008 and 2013 the number of travel associated cases was lower than the mean (133 cases) observed for the decade, 2006 to 2015.

Figure 8: Number of confirmed cases of Legionnaires' disease associated with travel by year of onset of symptoms 2006 to 2015.



A total of 39 different countries were visited by one or more of the 177 cases of travel associated cases of Legionnaires' disease diagnosed in residents of England and Wales with onset of symptoms during 2015. Of the 177 cases that travelled abroad during their incubation period, 58.2% visited at least one of 15 European countries and 41.8% visited at least one of 24 non-European countries during their incubation period. As in previous years, the most popular destination was Spain which was the country of travel for 26 cases, whilst the most popular non-European travel destination was the United Arab Emirates. However, the countries with the highest rate of infection at 41.7 cases per million visits were Thailand closely followed by the United Arab Emirates at a rate of 41.0 cases per million visits. The European destination with the highest rate of infection was Italy at 10.3 cases per million visits.

Table 13: Ten most prevalent travel destinations visited by confirmed cases of Legionnaires' disease in residents of England and Wales with onset of symptoms in 2015.

Country	LD cases	Visits by UK residents	Rate [‡] of cases per million visits
Spain	26	10,850,000	2.4
Italy	21	2,031,000	10.3
Greece	17	1,737,000	9.8
United Arab Emirates	17	415,000	41.0
Thailand	13	312,000	41.7
United States of America	13	2,062,000	6.3
France	12	5,969,000	2.0
Turkey	8	1,099,000	7.3
Bulgaria	6	193,000	31.1
Portugal	6	1,809,000	3.3

‡ denominators based on 2014 travel trends of UK residents visits abroad, from office of national statistics.

Of the 39 countries visited by cases of Legionnaires' disease in residents of England and Wales who experienced onset of symptoms, 16 countries were determined by ELDSNet to have accommodation sites that formed a cluster with two or more cases of Legionnaires' disease, with at least one resident of England and Wales, and with onset within two years (18). A total of 43 clusters were identified involving one or more residents of England and Wales with onset of symptoms during 2015, Table 14. The countries associated with travel clusters involving one or more residents of England and Wales follow trends similar to those observed for countries of highest prevalence among travel associated cases. Hence Thailand and the United Arab Emirates had the highest number of these clusters in 2015.

Table 14: Destinations associated with clusters involving residents of England and Wales with onset of symptoms during 2015.

Country of Travel	No. clusters	No. EAW cases
Belgium	1	3
Bulgaria	1	5
Cruise (>1 European country)	1	1
Cyprus/Turkey	1	1
France	1	1
Greece	3	6
Italy	6	8
Kosovo	1	1
Mauritius	1	1
Portugal	1	2
Spain	5	5
Thailand	6	7
Turkey	4	4
United Arab Emirates	7	7
United Kingdom	1	2
United States of America	3	6

EAW: England and Wales

Discussion

NELSS has observed a 15.4% rise in the number of cases of Legionnaires' disease with onset of symptoms during 2015 compared to the number reported with onset in 2014, thereby continuing the upward trend in case numbers reported since 2012. Many of the trends and characteristics for Legionnaires' disease in England and Wales have remained constant in 2015 when compared to previous years including the higher prevalence of the disease in males, increased risk with age and increased risk in those with certain underlying clinical conditions. Analysis of the 2015 data does, however, raise a few interesting features to consider.

A palpable explanation for the increase in case numbers may be attributed to the changes observed by category of exposure; 2015 cases show an increase in the proportion of cases associated with exposures abroad and a decrease in community acquired exposures. Between 2008 and 2013 the number of travel associated cases was lower than the mean (133 cases) computed for the decade, 2006 to 2015. This may reflect the changes in travel among residents of the UK between 2008 and 2013 as cited by the Office of National Statistics travel trends data (19) which shows that in 2008 69.0 million UK residents travelled abroad.

However, following the recession in 2010, the number of UK travellers fell to a low of 55.6 million. This decline was then followed by a gradual annual rise with 2015 travel figures reaching a peak of 65.7 million UK travellers. There is also evidence from the Institute of Fiscal Studies (IFS) that since the recession there has been an increase of 7.0% in pensioners' income (the age group at higher risk of Legionella infection), compared to a decrease of 2.7% in working aged individuals' income (20). Therefore, the over 60 years age group may be more likely to have disposable income to potentially spend on travel. This may be one explanation for an increase in cases associated with travel abroad.

Seasonal changes in incidence of Legionnaires' disease are readily observed in temperate climates and studies have shown high temperatures and humidity to increase the risk of Legionnaires' disease (21, 22). It is, therefore, unsurprising to note that the number of cases of Legionnaires' disease reported in residents of England and Wales generally increases month on month between April through to August during the spring and the summer period in the UK.

Principally, the proportion of community acquired cases reported to NELSS in 2013 to 2015 followed a very similar trend month on month throughout the year. However, a discrepancy seen in October 2015 may in part provide an explanation for the fall in community acquired cases during 2015. Fewer than half the number of community acquired cases of Legionnaires' disease were reported to NELSS with onset of symptoms during October 2015 compared to the same month in the previous two years. October 2015 brought about both temperatures and rainfall that were unfavourable for the growth of Legionella. The mean temperature for October 2015 was 1.5 degrees lower than in the previous two years and rainfall considerably lower, with a decrease of 87.1mm and 51.4mm compared to 2013 and 2014 respectively (23).

Analysis of mean temperature, monthly rainfall and case numbers indicates that rainfall has a greater impact on case numbers than temperature, with higher rainfall increasing the risk of infection (21). Further studies and in-depth analysis need to be conducted to improve understanding of the relationships between meteorological factors and the risk of Legionella infection.

Despite the observed decline in the proportion of community acquired cases of Legionnaires' disease to 50.0 % in 2015, it still remains the largest single category of exposure in England and Wales and the potential for a community source to give rise to a large cluster or outbreak remains a risk.

Another area that has seen a noticeable change in 2015 when compared to 2013 and 2014 are the number of clusters/outbreaks involving residents of England and Wales. The overall number of incidents increased from 2013 to 2015 but there was no consistent relationship between the number of cases reported in the various exposure categories and the number of clusters/outbreaks identified. The greatest change in incident numbers was for those with a suspected exposure within the community. 2015 saw a significant rise in the number of incidents identified with a community exposure compared to 2013 and 2014.

This observation may reflect an increase in awareness among healthcare professionals to test for Legionnaires' disease. Alternatively, the increase in the number of clusters/outbreaks identified in 2015 may be due to improved ascertainment related to the 'active cluster detection' program that was introduced by the national surveillance team in 2012. This 'active cluster detection' program is a more pro-active approach to the detection of clusters of Legionella infection in which specific cases reported to NELSS are reviewed to determine any common geographical links with previous cases

with symptom onset dates within the previous six months. The local HPT(s) are notified of any such clustering to determine if further local investigation are warranted. Although it can take a number of years for the true impact of programmes such as this to be revealed, this programme may have raised awareness of the potential for community clusters. However, a formal evaluation would need to be conducted in the future to determine if this is a true impact of the programme.

Despite the year on year fall in the CFR since 2013 the overall change in the fatality rate since 2013 has been shown not to be statistically significant. There may be a number of reasons for this such as delays in diagnosis, thereby delaying treatment with the correct antibiotics. It may be beneficial to increase awareness of Legionnaires' disease among clinicians and improve testing of patients admitted to hospital with community acquired pneumonia (CAP) for Legionella infection.

The British Thoracic Society recommend testing all patients with severe CAP and related risk factors for Legionnaires' disease (24) and studies have shown that testing of all CAP patients for Legionella positively influences the treatment regime, thereby improving the patient survival (25). This is important as dual or combination antibiotic treatment, offered to moderate/severe pneumonia patients, is more likely to include antibiotics effective for Legionella infection, thereby increasing the chances of survival (26). The observed significantly increased mortality for nosocomial cases (at a rate of 16.0%); between 2013 and 2015 is not entirely unexpected considering the age and immunosuppression of the population at risk in healthcare settings (27).

It has been widely shown that males are at greater risk of Legionella infection than females but whether the same pattern is observed in the outcome of confirmed cases of Legionnaires' disease has not been studied in detail. Analysis of mortality in England and Wales shows that although almost two thirds of all deaths are in males, a higher proportion of females diagnosed with Legionnaires' disease will die from the disease. This difference is currently not statistically significant, but future trends will be monitored closely.

Recommendations

- The improvement in cluster detection across England and Wales highlights the need to improve the detection of sources to inform subsequent investigation. Comparison of strains from clinical and environmental specimens, using highly discriminatory microbiological techniques, helps to identify likely sources of infection. This itself relies on the typing of lower respiratory tract samples within the national reference laboratory. It is therefore important to reinforce the need for front line clinicians to collect respiratory samples from all confirmed and suspected cases of Legionnaires' disease
- The varied proportion of lower respiratory tract clinical samples collected from cases across England and Wales suggests that some health protection teams may have successful arrangements in place that support submission of lower respiratory tract samples from cases of Legionellosis. It may be beneficial for best practice to be shared between HPTs to improve submission of these specimens nationally.
- As evidence has shown that early diagnosis of LD is associated with improved outcomes, frontline clinicians are strongly encouraged to consider LD as a possible cause of community-acquired pneumonia, particularly among older persons

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