

Legionnaires' disease in Europe, 2009-2010

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The surveillance of Legionnaires' disease (LD) in Europe is carried out by the European Legionnaires' Disease Surveillance Network (ELDSNet) and coordinated by the European Centre for Disease Prevention and Control (ECDC). All cases reported in 2009 and 2010 and meeting the European case definition were electronically transmitted to The European Surveillance System (TESSy) database. A total of 5,551 and 6,305 cases were reported by 29 European countries in 2009 and 2010, respectively. The age-standardised rate of all cases was 1.20 per 100,000 inhabitants in 2010, 12% higher than in 2009, which was consistent with the increasing trend observed since 2005. Most of this increase consisted of community-acquired cases reported by France, Germany and the Netherlands with dates of onset in August–September. The exceptionally hot summer of 2010 in some parts of Europe may have played a role in this increase.

Background

Legionnaires' disease (LD) is the severe and sometimes fatal form of an infection with *Legionella* spp. LD is classically described as a severe pneumonia that may be accompanied by systemic symptoms such as fever, diarrhoea, myalgia, impaired renal and liver functions, and delirium. These gram-negative bacteria are found in freshwater environments worldwide and tend to contaminate man-made water systems [1]. Humans are infected by inhalation of aerosols containing legionellae. One species of *Legionella*, *L. pneumophila* is the aetiological agent of approximately 90% of all LD cases. Among the 16 identified serogroups of *L. pneumophila*, *L. pneumophila* serogroup 1 is the most commonly involved (approximately 85% of all LD cases) [1,2]. The surveillance of LD at European level started in 1996 and LD surveillance reports were published every other year from 2000 onwards [3-6]. Since 2010, the surveillance of LD in Europe has been carried out by the European Legionnaires' Disease Surveillance Network (ELDSNet) and coordinated by the European Centre for Disease Prevention and Control (ECDC) in Stockholm, Sweden.

Following a period of steady increase of annually reported cases after implementing surveillance at

European level, the number of reported cases of LD seemed to reach a plateau of between 5,500 and 6,000 cases from 2005 to 2009 [7]. Here we present cases reported in the European Union (EU) as well as Iceland and Norway for 2009 and 2010, with a focus on the increase observed in 2010. To put this increase into perspective, the trend observed since 2005 was also analysed.

Methods

ELDSNet comprises all 27 EU Member States, Iceland and Norway. One of the key objectives of the network is the annual collection, analysis, interpretation and communicating of surveillance data on all LD cases reported at national level during the previous year. Each year, nominated ELDSNet members in each of the participating countries are asked to electronically transmit their data to The European Surveillance System (TESSy) database hosted by ECDC. In 2010, when the first data call was made, ELDSNet members were also asked to upload respective historical data since 2005. All cases reported in 2009 and 2010, meeting the EU case definition of confirmed and probable cases, were included in the main analysis [8]. Cases reported since 2005 were included in the trend analysis.

Cases were to be reported as part of a cluster if they had been exposed to the same source as at least one other case with dates of disease onset no more than two years apart. Information retrieved from TESSy included age, sex, date of disease onset, probable setting of infection, laboratory methods used for diagnosis, and clinical outcome. Possible settings of infection were, among others, community-acquired, travel-related and healthcare-associated. Population denominator data for calculating rates were obtained from the Statistical Office of the European Union (Eurostat) [9].

Continuous variables were compared across strata by the Mann-Whitney U test. Categorical variables were compared using the Chi-square or Fisher exact tests. Age-standardised rates (ASR) were calculated using the direct method and the average age structure of the EU population for the period 2000 to 2010.

TABLE 1

Number, crude and age standardised (ASR) rates of reported confirmed and probable cases of Legionnaires' disease by reporting country, European Union, Iceland and Norway, 2009-2010

Reporting country	2009			2010		
	Cases	Rates ^a per 100 000 inhabitants		Cases	Rates ^b per 100 000 inhabitants	
		Crude rate	ASR		Crude rate	ASR
Austria	92	1.10	1.07	80	0.96	0.91
Belgium	80	0.70	0.68	89	0.82	0.79
Bulgaria	3	0.04	0.04	1	0.01	0.01
Cyprus	3	0.38	0.45	2	0.25	0.32
Czech Republic	18	0.17	0.18	38	0.36	0.35
Denmark	123	2.23	2.24	133	2.40	2.37
Estonia	6	0.45	0.44	0	0.00	0.00
Finland	22	0.41	0.40	24	0.45	0.42
France	1,206	1.87	1.88	1,540	2.38	2.37
Germany	503	0.61	0.55	688	0.84	0.75
Greece	15	0.13	0.13	9	0.08	0.07
Hungary	65	0.65	0.63	60	0.60	0.59
Ireland	7	0.16	0.19	11	0.25	0.31
Italy	1,207	2.01	1.80	1,238	2.05	1.83
Latvia	3	0.13	0.12	6	0.27	0.26
Lithuania	0	0.00	0.00	1	0.03	0.03
Luxembourg	5	1.01	1.08	10	1.99	2.02
Malta	5	1.21	1.25	6	1.45	1.33
the Netherlands	251	1.52	1.53	466	2.81	2.79
Poland	10	0.03	0.02	36	0.09	0.10
Portugal	96	0.89	0.86	128	1.19	1.15
Romania	3	0.01	0.01	1	0.00	0.00
Slovakia	2	0.04	0.04	4	0.07	0.07
Slovenia	66	3.25	3.11	58	2.83	2.68
Spain	1,231	2.68	2.66	1,150	2.48	2.45
Sweden	114	1.23	1.18	100	1.07	1.01
United Kingdom	374	0.61	0.61	376	0.61	0.61
EU 27	5,510	1.10	1.07	6,255	1.25	1.20
Iceland	7	2.20	2.83	2	0.63	0.87
Norway	34	0.70	0.73	48	0.99	1.02
Total	5,551	1.10	1.07	6,305	1.24	1.20

ASR: age standardised rates; EU: European Union.

^a Information on age available for 5,544 cases in 2009.

^b Information on age available for 6,293 cases in 2010.

To analyse the trend since 2005, we performed a time series analysis over the 2005 to 2010 period for the five largest reporting countries (France, Germany, Italy, Spain and the United Kingdom). The analysis was limited to these countries because they provided data for the whole period and accounted for a substantial proportion of all cases reported. Weeks of disease onset were analysed for trend (linear regression). Where the information on the exact day of disease onset was not available, it was assumed to be the first day of the month. It was assumed that the population in

these countries remained stable over the study period. Statistical analyses were performed using STATA version 11.2 (Statacorp, College Station, TX, USA).

Results

Case classification, notification rate and geographical distribution

Of the 11,856 cases notified over the 2009–10 period, 92% (n=10,960) were confirmed cases, with similar distribution in both years. Eight hundred and

TABLE 2

Distribution of reported cases of Legionnaires' disease by setting, European Union, Iceland and Norway, 2009-2010

Setting	2009 Cases (%)	2010 Cases (%)	2009-2010 difference (%)
Community-acquired	3,398 (68)	3,999 (71)	+18
Travel-associated	1,055 (21)	1,132 (20)	+7
Travel abroad	523 (10)	560 (10)	+7
Domestic travel	532 (11)	572 (10)	+8
Healthcare-associated	471 (9)	424 (8)	-10
Other settings	44 (1)	59 (1)	+34
Total	4,968 (100)	5,614 (100)	+13

ninety-six were probable cases with 24 defined on epidemiological grounds only. The ASR of confirmed and probable cases was 1.20 per 100,000 inhabitants in 2010, 12% higher than in 2009 (1.07 per 100,000) (Table 1). The ASR greatly varied across countries and was highest in Slovenia in 2009 (3.11 per 100,000) and in the Netherlands in 2010 (2.79 per 100,000). The six countries reporting the highest number of cases i.e. France, Germany, Italy, Netherlands, Spain and the United Kingdom, accounted for 86% (n=4,772) and 87% (n=5,458) of all cases reported in 2009 and 2010, respectively. The ASR increase was especially high in the Netherlands (+83%), Germany (+37%) and France (+26%).

Probable setting of infection

For 10,582 cases reported in 2009 and 2010, the probable setting of infection was known. Of these, 71% (n=7,397) were community-acquired, 20% (n=2,187) travel-associated, 8% (n=893) healthcare-related and 1% (n=103) were associated with other settings (Table 2). The distribution of probable settings of infection was similar in both years.

Clusters

Of 7,872 cases with known cluster status, 8% (n=662) were reported as part of a cluster. This proportion was higher in travel-associated cases 20% (284 of 1,399) and lower in community-acquired cases with 5% (259 of 5,015) reported as part of a cluster. This proportion was similar in both years.

Seasonality

Information for date of disease onset was available for 11,305 cases reported in 2009–10; 59% (n=6,702) fell ill between June and October (warm season). This proportion was identical in both years and the same seasonal pattern was observed as in previous years (Figure 1).

Age and sex

Information on age was available for 11,836 cases, of which 43% (n=5,100) were 65 years old or older. Of

the 11,849 cases reported with known sex in 2009–10, 73% (n=8,611) were male. Sex ratio was similar in both years. The notification rate increased with age in both sexes and was below 0.1 per 100,000 inhabitants in those under 24 years of age, 0.5 in 25–44 year-olds, 1.9 in 45–64 year-olds and 2.9 in those 65 years of age and older.

Laboratory tests and pathogens

A total of 11,832 confirmed and probable cases were ascertained by 11,976 laboratory tests. Of these tests, 82% (n=9,780) were urinary antigen tests, 10% (n=1,185) were cultures, 5% (n=571) single high titre in specific serum antibody, 2% (n=303) polymerase chain reaction (PCR), 1% (n=141) fourfold titre rise and only 10 tests performed were direct immunofluorescence. The distribution of the tests was similar in both years. Of the 1,166 culture-confirmed cases for which the pathogen was reported, 85% (n=991) were due to *L. pneumophila* serogroup 1 and this proportion was similar in both years.

Outcome

The clinical outcome was known for 8,107 cases, 852 of them died, yielding a case fatality rate (CFR) of 11% which was similar in both years.

Increase of number of cases reported in 2010 compared to the 2008–09 average

Of the 995 excess cases reported in 2010 compared with the 2008–09 average, 67% (n=663) were reported by France, Germany and the Netherlands. Analysis by month of disease onset showed that the largest increases were observed in January (+52%, 148 cases) and August (+50%, 325 cases). Of the 775 excess cases reported in 2010 with known setting of infection, 89% (n=686) were community-acquired. When restricting the analysis to community-acquired cases reported by France, Germany and the Netherlands, the increase was concentrated on January, August and September with a two-fold increase compared to the 2008–09 average in these respective months (Figure 2).

FIGURE 1

Reported cases of Legionnaires' disease by month of onset, European Union, Iceland and Norway, 2010 and 2008-2009 average (n=16,549)

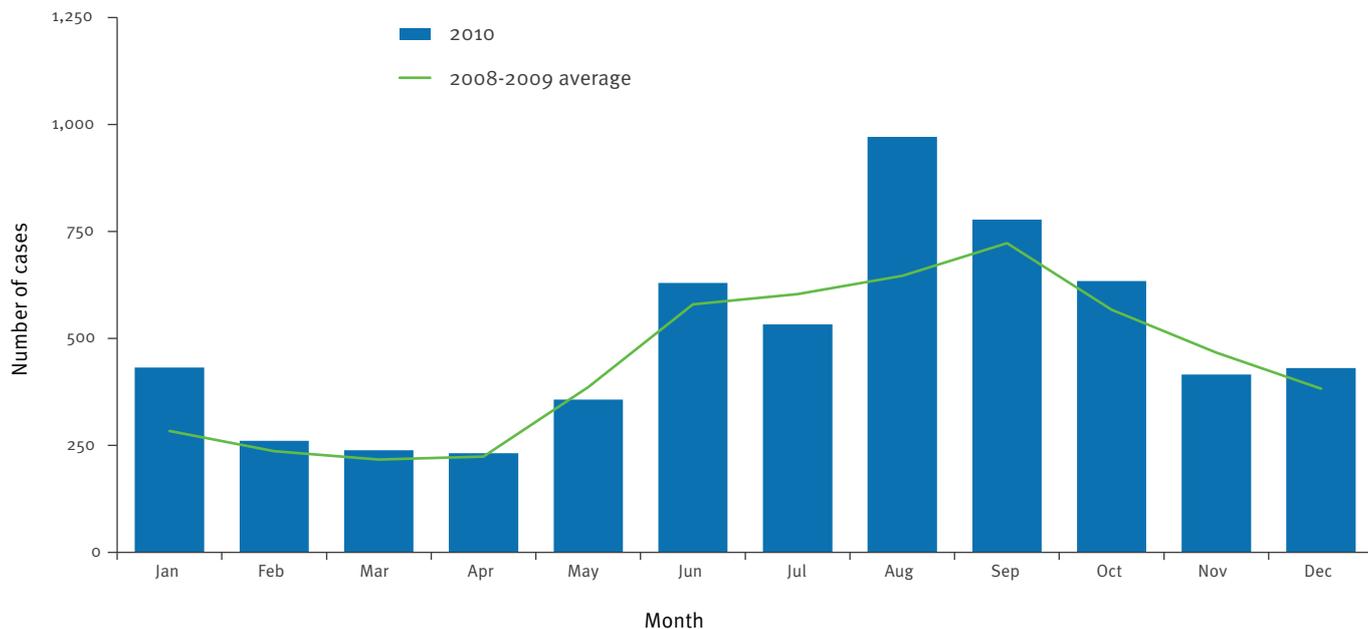


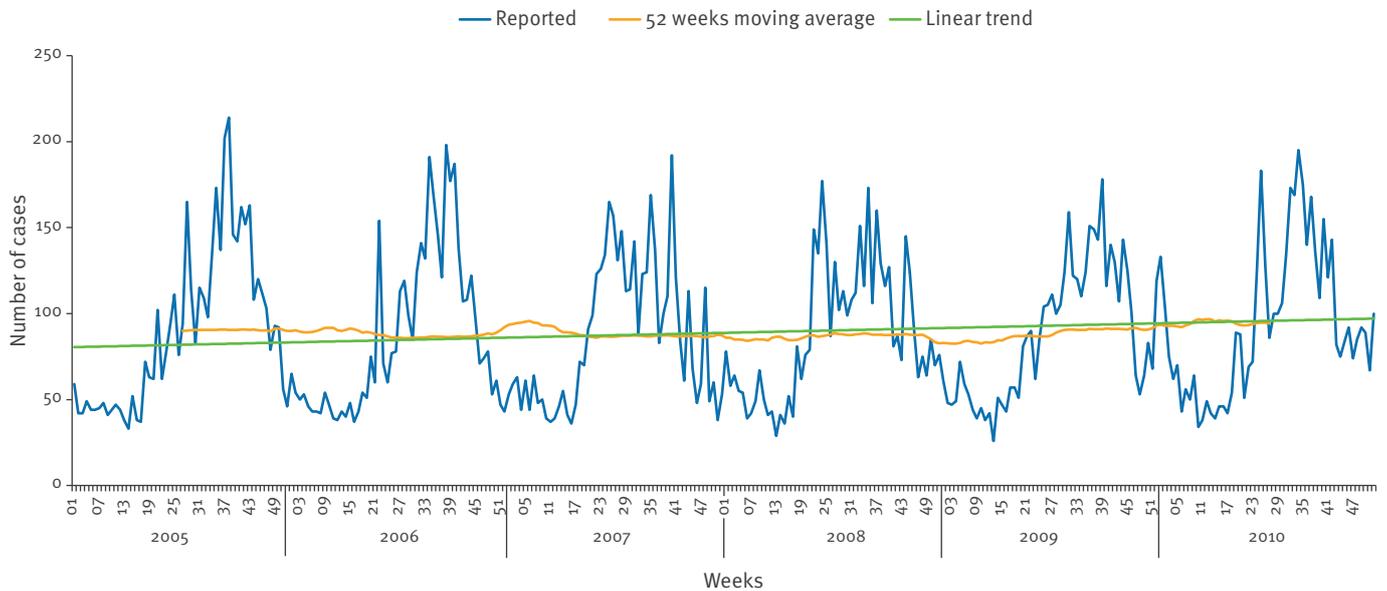
FIGURE 2

Reported cases of community-acquired Legionnaires' disease in France, Germany and the Netherlands by month of disease onset, 2010 and 2008-2009 average (n=3,648)



FIGURE 3

Reported cases of Legionnaires' disease by week of onset, linear trend and 52 weeks moving average, France, Germany, Italy, Spain and the United Kingdom, 2005-2010 (n=27,707)



The increase observed in January was only seen in France. Community-acquired cases reported by France, Germany and the Netherlands did not differ from other cases in terms of age or sex distribution. Cases reported with a date of onset in August and September had a lower CFR as compared to the rest of the year (9 vs. 11%, $p < 0.01$) which again was similar in both years.

Time series analysis of Legionnaires' disease cases reported by France, Germany, Italy, Spain and the United-Kingdom, 2005–2010

Of the 32,493 cases reported during the 2005 to 2010 period, 86% (n=28,194) were reported by the five countries reporting the largest number of cases, namely France (n=8,388), Germany (n=3,164), Italy (n=6,401), Spain (n=7,515) and the United Kingdom (n=2,636). Of these, 99% (n=27,707) had a known date (or month) of disease onset. Overall, a slightly increasing linear trend in the number of reported cases was observed over the period ($p < 0.05$) (Figure 3).

Discussion

Following several years of relatively stable LD notification rates from 2007 to 2009, we observed a 12% increase of the ASR in the EU countries, Iceland and Norway in 2010 compared with 2009. It is noteworthy that this increase mainly occurred in community-acquired cases reported by France, Germany and the Netherlands with dates of disease onset in August and September while Italy and Spain continued to report a high number of cases but similar to what was observed in previous years. It can probably partly be explained by the increasing trend in the reported number of cases

observed since 2005. It is unlikely a random variation and an artefact due to reporting issues can be ruled out, as cases represent true cases checked by the countries participating in the network. None of them reported a change in their surveillance system and the increase was mainly concentrated on two months and three countries.

Most of the excess cases were sporadic cases or part of small clusters which went unnoticed. To our knowledge, the largest outbreak reported in 2009–10 involved a Slovenian nursing home in August 2010 [10]. National reports from France and the Netherlands mentioned increasing numbers of LD cases during summer 2010 but causes remained unclear and were to be further investigated [11,12] The Dutch notification rate in 2010 was the highest ever recorded since introducing LD surveillance in the Netherlands in 1988 [11]. However, since the Netherlands reported fewer cases in 2009 as compared to previous years, the observed increase of the ASR (+82%) should be interpreted with care. If we compared 2010 with 2008 ASR, the increase would be around 40%, more in line with the increase observed in France and Germany. Of note, the 2010 increase in France was more pronounced in eastern regions [12] as previously documented for the period 2002 to 2008 as well [13].

The Dutch region with the highest notification rate was located in the northeast of the country [11]. Having relatively confined regions affected at the same time would suggest a global temporary environmental change such as a heat wave, in conjunction with heavy rains. This

would be supported by previous findings suggesting an impact of climate on the number of cases reported [14-17]. In the absence of any obvious explanatory factor, the summer peak in reported cases may have been related to the exceptionally warm summer observed in 2010 Europe [18]. Unfortunately, since places of residence were not collected at the EU level, it was not possible to introduce environmental variables such as temperature or precipitation with conditions likely to vary substantially from one region to another for a given country. Interestingly, the cases reported during this peak did not differ from other cases in terms of age and sex or outcome.

The 2009-10 data also confirm previous findings regarding the wide range of LD notification rates in Europe. When restricting the calculation of ASR to community-acquired cases, rates observed can be explained neither by environmental conditions nor by national legislation regarding potential sources of exposure such as wet cooling systems [19]. Thus, the number of cases reported in several European countries, from Germany to Greece, remains far below what would be expected. The reservoir of unascertained cases would probably be found in community-acquired cases in countries that have so far been poorly diagnosed and reported. We expect these countries to drive any future increase in the number of cases reported.

Conclusion

LD is an infectious disease leading to the death of around 500 EU citizens every year. In 2010, an as yet unexplained increase of cases of community-acquired LD cases was observed mainly in France, Germany and the Netherlands in August and September. Although consistent with the overall increasing trend observed since 2005, it is striking that this increase was concentrated over a short period of time and in a relatively restricted geographical area. This increase in 2010 indicates an impact on the disease incidence in relation with probable weather conditions or other environmental factors. A possible explanation would be the unusually hot summer 2010. With global warming and an increasing risk of extreme weather in the near future, such situations should be further investigated to target campaigns of information and control measures. More research would be needed to identify the factors associated with sporadic community-acquired cases. The collection of geographical information at sub-national level should help validate the impact of climate on LD incidence at the European level. Last, reasons for the low notification rates observed in eastern and south-eastern European countries need to be elucidated by targeted studies aimed at identifying the causes of under-ascertainment.

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Conflicts of interest

None declared.

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