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## The distribution of travel-associated Legionnaires' disease within selected European countries, and a comparison with tourist patterns

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### SUMMARY

Much data has been gathered by the EWGLINET scheme on the distribution of cases of travel-associated Legionnaires' disease (TALD) by country of infection, but less analysis has been carried out on the distribution of these cases within countries. Travel-associated cases with onset in 2002 linked to France, Italy, Spain and Turkey were mapped. Rates of Legionnaires' disease per 100 000 tourists were calculated for internal and foreign visitors for the regions of each country, and mapped. Rates of 1·5 cases/100 000 and 2 cases/100 000 tourists were classified as 'high' and 'very high' respectively. Cases of TALD were concentrated in certain regions, but when rates were calculated using tourist data, the results were relatively constant throughout each country. Rates were higher among foreign visitors than internal visitors; three of the countries had at least one region with 'high' rates, whilst Turkey additionally had three regions with 'very high' rates.

### INTRODUCTION

In 1976, legionella bacteria were responsible for a large outbreak of Legionnaires' disease (LD) in an American hotel [1]. Since then, awareness of the disease has heightened, and the number of cases detected by national surveillance systems continues to increase. In 1986 an expert group – the European Working Group for Legionella Infections (EWGLI) – was established, and in 1987 EWGLI launched an international surveillance scheme (EWGLINET) to monitor the occurrence of travel-associated Legionnaires' disease (TALD) across Europe [2]. EWGLINET now collects data on these cases of LD from 37 countries.

LD is often travel-associated, although nosocomial and community infections are also a significant public health problem in many countries [3]. EWGLINET

has published many articles on the distribution of TALD between the countries of Europe [4], but less is known about the distribution of these cases within each individual country. Some spatial analysis of LD has been previously carried out for community-acquired cases in Scotland, but the travel-related cases were not analysed [5, 6].

Additionally, Italy [7], France [8] and Spain [9] have all carried out preliminary mapping of TALD in their own countries. However, each chose to plot clusters rather than individual cases and, since the periods under study also varied, comparisons with the data presented in this paper are difficult to make.

This paper aims to investigate whether travel-associated cases are clustered in particular areas of selected countries, and whether the distribution changes when tourist patterns are accounted for.

### METHODS

Data were provided by the EWGLINET scheme on all cases of TALD with onset in 2002 that had been

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reported by its (then) 36 collaborating countries. EWGLINET accepts any microbiologically proven case defined as having stayed overnight in public accommodation in the 2–10 days prior to onset (the incubation period for LD) [2]. The dataset for this study included variables such as date of onset, age and sex of case, towns and regions visited, and dates of travel. The countries of infection associated with the most cases in 2002 – France, Italy, Spain and Turkey – were selected as study countries. Countries visited by fewer cases were not included in the study because the numbers would be too small for statistical analysis.

Cases often visit more than one accommodation site during their incubation period. For the purposes of this study each case was allocated to one visit per country based on the number of nights spent at each site and prioritized to the place where the case spent the most nights inside the incubation period. This method was selected in order to allow for an uncomplicated mapping process. It was not felt that a more intricate analysis was required, as this paper is intended only as a preliminary spatial investigation. If in future a more detailed analysis of a specific country or region is carried out, it would be necessary to take all visits into account, adjusted by the number of nights spent at each accommodation site.

Cases that had stayed in private accommodation or in accommodation that was notified to EWGLINET as ‘unknown’, were removed from the dataset. MapInfo was then used to produce maps showing the distribution of cases in each country for 2002.

Tourist data were requested from the EWGLINET collaborator in each country under study. Each country was able to provide 2002 visitor numbers by region, split into foreign and internal visitors, except Italy, who were able to provide data for 2001. The Italian data came from their National Statistics Institute [10], the Spanish data were taken from the Spanish Department of Statistics [11], the French data were provided by the government’s Strategic Planning, Education and Statistics Department [12], and the Turkish data came from the Ministry of Tourism Department of Statistics [13].

Cases in the dataset were divided into internal tourists (e.g. French people travelling in France) and foreign tourists. Rates were calculated for each region of each country for the number of cases/100 000 internal tourists (using internal tourist figures only) and the number of cases/100 000 foreign tourists (using the foreign visitor numbers only). These

rates were then grouped into bands and mapped using MapInfo (the bands used were 0 to <0.1, 0.1 to <0.25, 0.25 to <0.5, 0.5 to <1.5, 1.5 to <2, and  $\geq 2$  cases/100 000). A rate of 1.5 cases/100 000 tourists was categorized as ‘high’, whilst a rate of 2/100 000 tourists was labelled ‘very high’.

These rate bands can be compared to the overall rates of LD reported by individual countries in the annual dataset collected by EWGLI each year [3]. These latter figures take account of all categories of legionella infection, including travel, nosocomial and community cases, and they use ‘total population’ for the denominator figures. Although not completely comparable to the other rates presented in this paper, they do give some indication of the overall rates in each country. In 2003, France reported a rate of 1.7 cases/100 000 population, whilst Italy reported 0.97 cases/100 000. Spain’s rate was 2.87 cases/100 000 population, and because Turkey only reported one case for 2003, they had a very low rate of <0.002 cases/100 000.

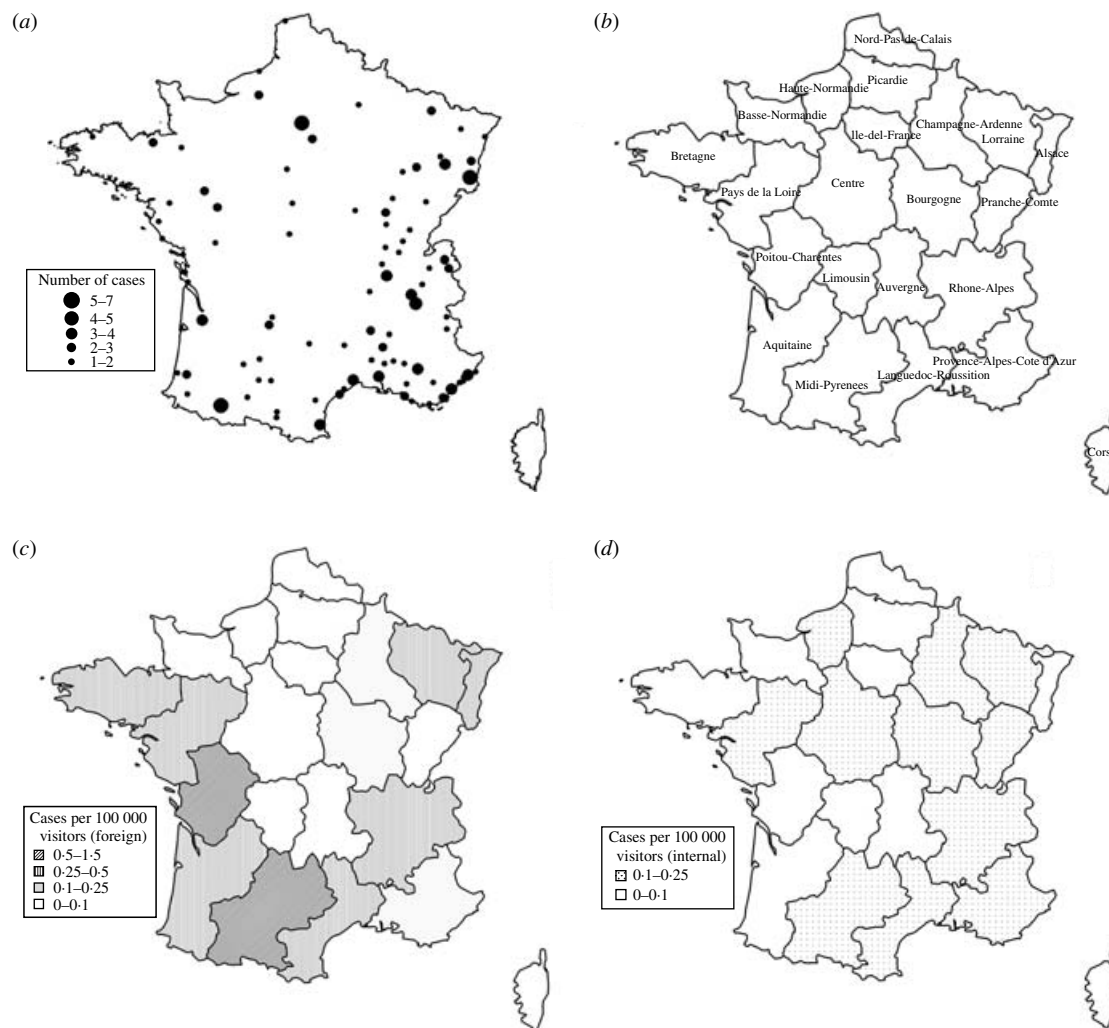
## RESULTS

### France

A total of 149 cases were reported to EWGLINET and linked to travel in France in 2002, 81 among French nationals and 68 among foreign visitors. The internal rates for French regions were generally low – a range of 0–0.24 cases/100 000 internal tourists with an overall rate (regardless of region) of 0.11/100 000. Foreign rates ranged higher from 0–0.58/100 000 foreign tourists with an overall rate of 0.16, but there were no regions that fell into the ‘high’ or ‘very high’ categories. The two regions with the highest rates were Poitou-Charentes with a foreign rate of 0.5/100 000 and Midi-Pyrenees with a foreign rate of 0.58 (Fig. 1).

### Italy

A total of 150 cases were reported to EWGLINET and linked to travel in Italy in 2002, 61 among Italian nationals and 89 among foreign visitors. The rates for internal travel ranged from 0–0.68/100 000 with an overall rate of 0.13, whilst the rates for foreign travel varied between 0 and 1.5/100 000 with an overall rate of 0.25. One region had a foreign rate that fell into the ‘high’ category – Puglia (1.5/100 000 foreign travellers) – and that same region also gave the highest Italian rate for internal cases (0.68/100 000) (Fig. 2).



**Fig. 1.** France. (a) The distribution of cases in France in 2002 (only the main visit per case is shown). (b) France with labelled regions. (c) The rates of cases reported in foreign people travelling in France, per 100 000 foreign travellers. (d) The rates of cases reported in French people travelling in France, per 100 000 internal travellers.

**Spain**

A total of 100 cases were reported to EWGLINET and linked to travel in Spain in 2002, 16 among Spanish nationals and 84 among foreign visitors. The low number of internally reported cases gave rise to low internal rates of between 0 and 0.36 cases/100 000 with an overall rate of 0.05. The foreign rates had an overall rate of 0.32 and a larger range, from 0 to 1.53/100 000, including Navarra with a ‘high’ rate of 1.53 (Fig. 3).

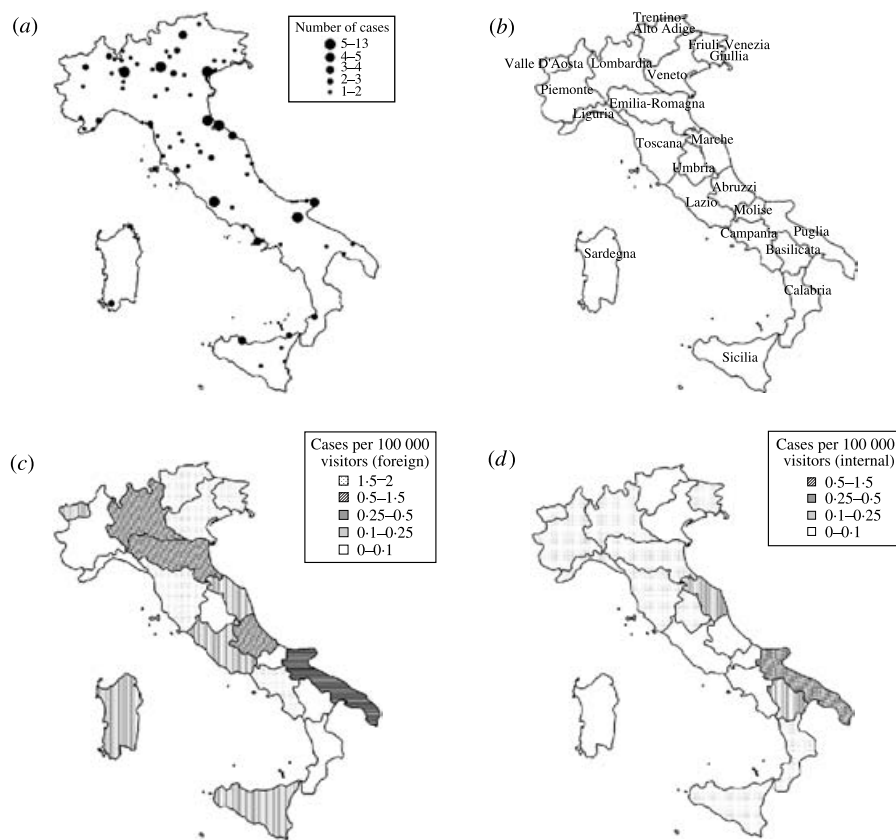
**Turkey**

A total of 83 cases were reported to EWGLINET and linked to travel in Turkey in 2002, none among Turkish nationals (hence no internal map is given). The rates for foreign cases ranged from 0 to

27.81/100 000 foreign tourists with an overall rate of 0.84. One region with a ‘very high’ rate (Corum) is a statistical anomaly – it was only visited by one case but has a very high rate of 27.81/100 000 because of the very low number of foreign visitors. Two other regions had very high rates of foreign cases (Mugla with 2.16, Aydin with 2.27), and one had a ‘high’ rate (Icel with 1.89 cases/100 000) (Fig. 4).

**Statistical analysis**

In every country (excluding Turkey), the overall rate for internal travel was lower than the rate for foreign travel. Analyses were performed for France and Italy to see whether this difference was statistically significant (Spain and Turkey report too few internal cases to give an accurate comparison of rates). In both



**Fig. 2.** Italy. (a) The distribution of cases in Italy in 2002 (only the main visit per case is shown). (b) Italy with labelled regions. (c) The rates of cases reported in foreign people travelling in Italy, per 100 000 foreign travellers. (d) The rates of cases reported in Italian people travelling in Italy, per 100 000 internal travellers.

countries there was strong evidence that the rate of infection of foreign travellers is higher than for internal travellers. France had an incidence rate ratio (IRR) of 1.75 [95% confidence interval (CI) 1.22–2.52,  $P=0.002$ ], whilst Italy's was even higher (IRR 2.49, 95% CI 1.76–3.53,  $P<0.001$ ).

There is also strong evidence that, when foreign and internal rates are taken together, there are significant rate differences between the regions in each country ( $P<0.001$  for both countries). For example in France, Ile-de-France has a lower rate (IRR 0.14, 95% CI 0.06–0.34,  $P<0.001$ ) than Alsace; in Italy the Puglia region has a higher rate (IRR 10.44, 95% CI 1.38–78.71,  $P=0.023$ ) than Abruzzo.

Despite the strong evidence for an overall difference in internal and foreign rates, and differences in total rates of LD between some regions, there was little evidence to suggest an interaction between the regions and the types of visitors in the rates of LD. In Italy, there was no evidence, with a likelihood ratio test giving a  $P$  value of 0.21, and in France there was only weak evidence, with the likelihood ratio test giving a  $P$  value of 0.11.

It is possible that some additional variable such as age or sex, month of onset or length of stay differs significantly between internal and foreign visitors and, therefore, provides an underlying explanation for the overall difference in rates of disease. It was proposed to study some of these variables in the French and Italian cases. Unfortunately, the necessary denominator tourist data was not available, so it was not possible to conduct this analysis.

## DISCUSSION

It has been generally assumed that there are certain regions within individual countries that have high rates of TALD. EWGLINET observes that particular towns and regions are regularly visited by the cases reported to its database. This perception seems to be supported when the cases in this study are plotted on maps of France, Italy, Spain and Turkey, and do indeed appear to be clustered in some areas. For example, cases in France seem to be concentrated in the southeast, in Italy most cases are found in the north, whilst in Spain almost all





cases can be found on the eastern coast, and in Turkey all cases are clustered in the western part of the country.

However, it is also true that a predominance of tourists visit the south and east of France, the north of Italy, the east coast of Spain, and the west of Turkey. Indeed, when rates of LD per 100 000 travellers are calculated, these obvious areas of clustering largely disappear and the burden appears to be more standardized across each country. There are exceptions – a small number of individual regions have statistically higher rates of LD than others. These regions should be examined in greater detail by national authorities to ensure that control measures at individual accommodation sites are satisfactory. It would also be worth repeating this analysis over a number of years to account for the influence that individual outbreaks may have on rates of disease. For instance, EWGLI's Spanish collaborator has suggested that the high rate of LD in Navarra in Spain in 2002 may be attributable to a cluster in one hotel in a small town in that region.

It is also worth noting that three of the countries in this study show a relatively similar range of rates of LD. Turkey does stand out as having two regions with 'very high' rates (discounting Corum which is a statistical anomaly) and one region with 'high' rates, as opposed to the other three countries which each had one or no regions with 'high' rates. This is especially interesting because, in recent years, Turkey has come under pressure from other countries to improve its strategies for combating LD. The rates in this paper would appear to give support to the need for this pressure. EWGLINET has, however, observed a sizable decrease in clusters of TALD located in Turkey since 2002, so the situation does appear to be improving.

Dividing the basic dataset to give two different rates for internal and foreign tourists gives interesting results. In every country, the overall rate for internal travel is lower than the rate for foreign travel. In Spain this can be attributed to the low levels of reporting of internal cases, but for France and Italy, who report every case of internal TALD in their country to EWGLINET, an alternative explanation must be sought. It is possible that some additional variable differs significantly between internal and foreign visitors, and, therefore, provides an underlying explanation for the overall difference in rates of disease, but as noted previously, it was not possible to carry out the necessary analysis on this data.

## CONCLUSIONS

All countries where data are available have lower rates of TALD among internal travellers than among foreign visitors. Three of the countries examined in this paper show at least one region with high rates of LD. The prevention measures in these regions should be examined to see whether they differ significantly from those in other regions. Furthermore, it would be interesting to compare local prevention measures between regional authorities and attempt to correlate these with their rates of LD. This, however, is a project that would have to be undertaken at the national level.

When rates for foreign cases are compared across countries, Turkey seems to have more regions with 'high' and 'very high' rates of LD than the other countries. However, recent EWGLINET data suggests that this situation is changing.

There are some areas of further study that would be interesting to examine in the future. Additional variables may differ between internal and foreign travellers, such as the type of accommodation site used. Potentially one group may use more campsites or larger hotels than the other group. It is also possible that there are different levels of susceptibility to LD, for instance, if nationals have some immunity through prior exposure to the specific strains of legionella that circulate in their country, this may offer an explanation for their lower rates of disease.

Potential differences between internal and foreign travellers should be analysed taking denominator differences into account, e.g. differences in age and sex of foreign and internal tourists. Unfortunately, it was not possible to obtain the data to carry out that analysis for this study.

This paper lays the groundwork for identifying areas within countries that may have a problem with LD so that prevention policies can be addressed and modified in a targeted, systematic manner. It would be an interesting area for further investigation by national authorities.

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#### DECLARATION OF INTEREST

None.

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