SARCOIDOSIS VASCULITIS AND DIFFUSE LUNG DISEASES 2010; 27; 111-120

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Sarcoidosis in Ireland: Regional differences in prevalence and mortality from 1996-2005

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ABSTRACT. Background: Sarcoidosis is a common multisystem disease of unknown cause and Ireland is among the countries with the highest reported prevalence of disease worldwide. Despite this, reports on the geographical distribution of disease and differences in mortality due to sarcoidosis within Northern Ireland (NI) and the Republic of Ireland (ROI) are currently lacking. Objective: This study was performed to examine sarcoidosis prevalence and mortality in Ireland (NI and ROI) to specifically determine if geographical or temporal clusters of disease are present and if any differences in mortality exist between NI and ROI. Design: A retrospective study, examining hospital discharge data for NI and ROI and data on deaths due to sarcoidosis, obtained from the relevant official government agencies. Results: For 1996-2005, the prevalence of sarcoidosis was 28.13 per 100,000 for ROI compared with 11.16 per 100,000 for NI (p=0.002). Two significant spatial clusters of disease were detected in the Northwest (Prevalence = 44.9 per 100,000) and also the Midlands region (32.1 per 100,000). Two lower-prevalence spatial clusters were also detected in the South and Southeast of ROI. Temporal clustering was also present throughout ROI and NI for the years 2000 to 2004, while space-time clustering was found in three regions, the West (ROI), the East (ROI) and Northeast (ROI and NI). The case fatality rate for ROI was 0.84%, and for NI was 1.44% (p=0.03). Conclusion: Considerable heterogeneity in disease prevalence is evident in Ireland as significant spatial, temporal and space-time clusters of sarcoidosis are demonstrated in this study. Prevalence rates are also higher than that previously reported for Ireland and are comparable to those of Scandinavian countries. Although case-fatality is low in both ROI and NI, it is significantly lower in ROI. Further study is needed to investigate these findings and the creation of an all-island sarcoidosis registry would provide a mutually beneficial means of capturing this data more effectively. (Sarcoidosis Vasc Diffuse Lung Dis 2010; 27: 111-120)

KEY WORDS: sarcoidosis, Ireland, prevalence, mortality, spatial cluster, temporal cluster

INTRODUCTION

Sarcoidosis is a common multisystem disorder of unknown cause and has a particularly high preva-

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lence in Ireland and other northern European countries. The diagnosis is usually established when clinical and radiological findings are supported by histological evidence of typically non-caseating epithelioid cell granulomas. The disease affects both sexes, all races and all ages, and throughout the world there is considerable heterogeneity in prevalence, the mode of presentation and the severity of disease (1). Geographic, temporal, and familial clustering of cases have been identified through epidemiological study (2-6), and many putative environmental or genetic causes of sarcoidosis have been proposed as a

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result. The ACCESS study, the most extensive performed to date, examined possible aetiological agents (7, 8) and identified associations consistent with previous work (9-17). Unfortunately it did not provide conclusive evidence for a specific causal agent.

The first studies of the prevalence of sarcoidosis in Ireland were in 1964, reporting a prevalence of 20.5 to 40.2 per 100,000 for the Republic of Ireland (18), and 0 to 19.8 per 100,000 for Northern Ireland (19). A later study from the United Kingdom reported that Northern Ireland had among the highest rates of sarcoidosis in the UK (20). Worldwide however, the highest prevalence with 50 cases per 100,000 is seen among the African-American population in the United States and also in Denmark and Sweden, while the remainder of Europe has more modest prevalence rates in the region of 10-20 per 100,000 (15, 21).

Death due to sarcoidosis occurs in 1 to 5% of patients with the disease (1). This is largely dependent on the mode of presentation at diagnosis or the severity of pulmonary involvement. There are considerable regional and racial differences in this regard also, conferring different prognoses on different populations. Previous reports on mortality due to sarcoidosis in Ireland estimated a case fatality rate of 1% (22), comparable to worldwide reports.

From the existing literature, it is apparent that prevalence rates in Ireland are relatively high compared with the rest of the world, while mortality rates are relatively low. However, no study has been performed to investigate if any regional differences in prevalence or mortality exist within Ireland. The aims of this study were to: 1) Examine and compare disease prevalence and mortality throughout Ireland (ROI and NI); and 2) Investigate if any spatial, temporal or space-time clusters of disease exist.

Methods

Data collection

For ROI, population data was obtained from the official census figures for 1996, 2002, and 2006, available from the Central Statistics Office (CSO), Cork. Linear interpolation was used to estimate intercensal populations. Mortality data for sarcoidosis was also obtained from the CSO. Data on discharges from public hospitals participating in the Hospital In-Patient Enquiry (HIPE) database with a diagnosis of sarcoidosis was obtained from the Economic and Social Research Institute (ESRI), Dublin. The diagnostic codes used were: ICD-09 CM Code 135 (for 1996-2004), ICD-10 Code D86 (2005). For Northern Ireland, population data were obtained using official census figures for 1991, 2001 and 2006, available from the Census Office for Northern Ireland, Belfast. Intercensal population estimates were obtained from the Northern Ireland Statistics & Research Agency. Mortality data and data on number of discharges from hospital with a diagnosis of sarcoidosis in any diagnostic portion were obtained from the Department of Health, Social Services & Public Safety (DHSSPS) for Northern Ireland, Belfast. The diagnostic codes used were: ICD-09 Code for Sarcoidosis 135 (for 1996-2000), ICD 10 Code for Sarcoidosis: D86 (2001 onward). Although the codes used for NI and ROI differed for the years 2001 to 2004, we did not find any significant differences in prevalence in these areas as a result and conclude that any differences in coding practices during these years had little effect on our overall results.

Statistics

Prevalence was taken as the number of cases recorded annually based on county or area of residence using the HIPE discharge data available for NI and ROI. Statistical analysis was performed using SPSS, Statistical Software Package, Version 18.0. Where appropriate, Analysis of Variance (ANOVA) with Bonferroni adjustment for multiple comparisons was used. A p-value of <0.05 was considered statistically significant. Age-adjusted mortality was calculated using the World Health Organisation standard population 2000-2025. Spatial and temporal clustering analysis was performed using SaTScan[™] software where the number of cases of sarcoidosis in each county for each year was used as the case file, the county population for each year as the population file, while the coordinates file contained the latitude and longitude of the centroid of each county of residence for ROI or health board area of residence for NI.

The Kulldorff spatial scan statistic uses a variable circular window to detect spatial clusters, and if

identified, determines the significance while adjusting for the inherent problems of multiple testing. There are recognised sensitivites of the results to the choice of input parameters (23). As a result, a number of different thresholds were used, beginning initially at 50% of the population, the default setting within SaTScan[™], and then progressively decreasing this in increments of 5%, to the 5% threshold. The resultant spatial clusters were then visually inspected to ensure a particular population threshold detected a spatial cluster that did not include a large number of low-prevalence areas. This was performed using methods previously described (24), whereby for each year a county was assigned a binary variable based on whether prevalence was above or below that expected. These were then summed for each county within a cluster, and from this, the proportion of counties within a cluster with higher than expected prevalence was calculated.

Temporal cluster analysis detects clustering of events without regard to the proximity of locations with one another. Clusters are detected using the scan test, which determines if the maximum number of cases observed in a series of sequential time-periods is greater than expected by chance. Additional analyses can then be performed to determine if the temporally-clustered cases are also clustered simultaneously in time and space. The space-time method operates similarly to the spatial scan method outlined above, except it includes a temporal component by including a cylindrical window above the geographic location of the space point. The height of the cylindrical window reflects the time-period of the potential cluster.

RESULTS

Prevalence

For 1996 to 2005, there was a mean of 990 cases of sarcoidosis per year in ROI, and 186 per year in NI. Annual prevalence (95%CI) of disease for ROI and NI is shown in Table 1 and Figure 1. Overall, ROI had a significantly higher prevalence than NI at 28.13 per 100,000, compared to 11.16 (p=0.002).

	r			
Year	ROI	NI	p*	
1996	20.45	7.75	0.007	
1997	22.04	8.23	0.012	
1998	24.12	8.21	0.007	
1999	32.23	11.74	0.012	
2000	31.21	16.35	0.14	
2001	25.45	12.30	0.017	
2002	29.68	12.21	0.002	
2003	37.66	10.12	0.002	
2004	38.71	12.57	0.003	
2005	19.72	12.10	0.044	
Mean	28.13	11.16	0.002	

 Table 1. Mean prevalence of sarcoidosis 1996-2005

Prevalence rates per 100,000 population

ROI: Republic of Ireland, NI: Northern Ireland

*Mann-Whitney U-test performed

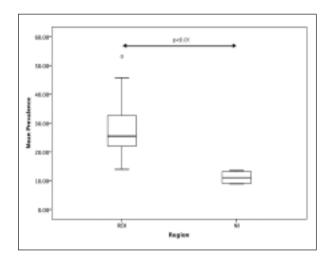


Fig. 1. Mean annual prevalence of Sarcoidosis for ROI and NI. Mean prevalence per 100,000 population. ROI: Republic of Ireland, NI: Northern Ireland

Spatial Cluster Analysis

Table 2 and Figure 2 show the results of the spatial cluster analysis, identifying clusters at varying population thresholds. At the highest population threshold (50%), one large primary cluster was identified in the Northwestern region of ROI (Northwest/Midlands cluster). This comprised 11 counties: Mayo, Galway, Sligo, Roscommon, Leitrim, Clare, Longford, Cavan, Westmeath, Donegal, and Offaly. The prevalence of sarcoidosis in this region was 38.2 per 100,000. The Relative Risk for sarcoidosis for

Population Threshold [*]	Region	Proportion§	Radius	RR	Prevalence
(%)			(km)		
10	Northwest ¹	0.78	106.9	2.35	44.9
	Midlands ²	0.65	48.1	1.55	32.1
	Southeast ²	0.55	76.5	1.30	27.0
15	Northwest/Midlands ¹	0.74	93.8	2.21	41.0
	Southeast ²	0.55	76.5	1.30	27.0
	$South^2$	0.65	66.9	1.13	23.8
20	Northwest/Midlands ¹	0.74	158.0	2.13	38.2
	Southeast ²	0.55	76.5	1.30	27.0
25, 30, 40	Northwest/Midlands ¹	0.74	158.0	2.13	38.2
	Southeast ²	0.54	94.9	1.17	24.4
50	Northwest/Midlands ¹	0.74	158.0	2.13	38.2

 Table 2. Sarcoidosis in Ireland - Significant spatial clusters

* Various population thresholds used to identify potential significant clusters, p=0.001 for all clusters shown, 1: Most-likely cluster, 2: Secondary cluster.

[§] Proportion refers to the proportion of counties within a cluster with higher than exected prevalence.

Radius: Radius (in kilometres) of circle used to identify cluster.

Prevalence = Annual prevalence per 100,000 of population.

RR: Relative risk compared with areas not within the cluster

this area was 2.13 compared with the area outside this cluster. Progressively decreasing the population threshold to a 10% level identified two core clusters within this Northwest/Midlands cluster, one situated in the Northwest (Sligo, Leitrim, Roscommon, Mayo), and a second in the Midlands (Westmeath, Longford, Offaly, Meath). Mean prevalence in the Northwest core cluster was 44.9 per 100,000 (RR = 2.35), while in the Midlands core cluster prevalence was 32.1 per 100,000 (RR = 1.55). Decreasing the population threshold further did not identify any smaller clusters within the Northwest or Midlands regions. A more detailed analysis of the strength of these two core clusters showed that 78% of the counties within the Northwest cluster, and 65% of those within the Midlands cluster had high prevalence.

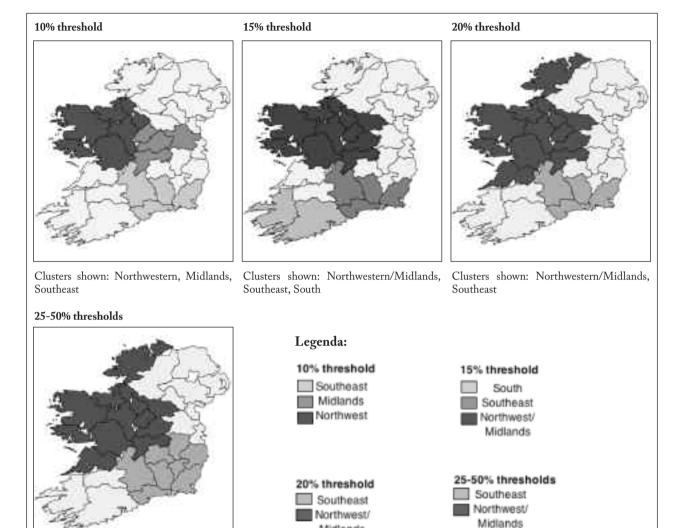
Two other geographical clusters were also identified, in the Southeast (Waterford, Kilkenny, Tipperary, Wexford) with a prevalence of 27 per 100,000 and also the South (Cork, Kerry), with a prevalence of 23.8 per 100,000. Although significant, when compared with the Northwest and Midlands clusters, these clusters contained a lower proportion of high prevalence counties, at 55% and 65% respectively (Table 2). Figure 3 shows the relative risk of sarcoidosis for all of the spatial clusters identified. The Northwestern core cluster had the highest risk of sarcoidosis that was 2.35 times that of areas outside of the cluster.

Temporal cluster analysis

A temporal cluster of sarcoidosis for all regions within NI and ROI was identified between the beginning of 2000 and the end of 2004 (p=0.001). Prevalence during this period was 23.5 per 100,000, RR was 1.23 compared to all other years.

Space-time cluster analysis

A significant space-time cluster was found in the Western region (Galway and Mayo) for 1999 to 2000, p=0.001, illustrated in Figure 4 and Table 3. Prevalence in this cluster was 96.55 per 100,000. Two other secondary clusters were also identified; one in the Eastern area (Dublin, Wicklow, Kildare) for the years 1996 to 1998, and another in the Northeast (ROI: Cavan, Leitrim, Longford, Louth, Meath, Monaghan, Westmeath, and NI: Eastern, Southern, Western) for the years 2004 to 2005. Prevalence in the Eastern cluster was 23.49 while in



Midlands

Clusters shown: Northwestern/Midlands, Southeast

Fig. 2. Spatial clusters of Sarcoidosis in Ireland

the Northeastern cluster was 42.46. It is notable that this latter space-time cluster comprised regions from both Northern Ireland and ROI.

Mortality differences between NI and ROI

There were 8 deaths per year due to sarcoidosis in ROI, compared to 3 deaths for NI. However, when one accounts for the differences in prevalence between the regions, the case-fatality rate (95%CI) was found to be significantly higher for Northern

Ireland at 1.44% (1.02-1.86), whereas for ROI the case-fatality rate was 0.84% (0.53-1.15), p=0.03.

Gender-specific prevalence and mortality (ROI)

Mean prevalence was 26.65 per 100,000 for males, and 24.43 for females (p=0.2), while the case fatality rate (95%CI) was 1.21% for males and 0.63% for females (p=0.005). Data on gender of patients with sarcoidosis at a county-level were not available, however the overall ROI prevalence for males was

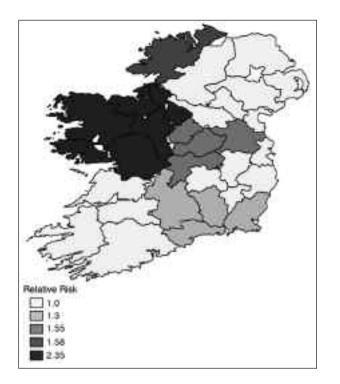


Fig. 3. Relative Risk for Sarcoidosis based on spatial clustering.

not significantly different to that for females. To investigate if the proportion of males to females in the

population within a cluster had a significant influence on the clustering results obtained, further examination of the data was performed. This is summarised in Table 4. No significant difference was found in male/female ratio of the populations inside a cluster compared with the population outside a cluster.

Age-specific and age-adjusted prevalence and mortality (ROI)

The highest age-specific prevalence was 47.69 per 100,000 in the 50-59 year old age group. However, the highest age-specific case fatality rate was 7.6% in the above 80 years age group (Table 6). Data on the age groups of patients within a county were not available, however from inspection of the ROI data in Table 6 it is apparent that there is considerable variation in age-specific prevalence. The ageadjusted prevalence for ROI was 23.64 per 100,000. To investigate if the age-composition of a cluster influenced the results on prevalence, further analysis was therefore performed. Table 5 shows the age distribution of the population within a cluster compared to population not within a cluster. No significant differences were found.

a) Western space-time cluster: Jan 1999 to Dec. 2000



Shaded counties: Galway, Mayo.

b) Northeastern space-time cluster: Jan. 2004 to Dec. 2005



Shaded areas: ROI – Cavan, Leitrim, Longford, Louth, Meath, Monaghan, Westmeath. NI – Western, Southern, Northern.

c) Eastern space-time cluster: Jan. 1996 to Dec. 1998



Shaded counties: Dublin, Kildare, Wicklow.

Fig. 4. Space-time clusters of Sarcoidosis. Space-time clusters identified in Ireland from 1996 to 2005

Region	West	East	Northeast
Years	1999, 2000	1996, 1997, 1998	2004, 2005
Area	Galway, Mayo	Dublin, Kildare, Wicklow	ROI Cavan, Leitrim, Longford, Louth, Meath, Monaghan, Westmeath. NI Eastern, Southern, Western.
Observed/Expected	1.73	1.36	1.23
Mean Prevalence	96.55	23.49	42.46
р	0.001	0.001	0.001

Table 3. Sarcoidosis in Ireland – Space-time Cluster analysis.

Table 4. Male to Female ratio within Northwest/Midlands cluster compared with population outside cluster

Population threshold*	Inside cluster	Outside Cluster	р
50%	1.02	0.99	0.08
25%	1.02	0.99	0.05
20%	1.02	1.00	0.18
15%	1.01	1.00	0.31
10%	1.01	1.00	0.46

Unpaired t-test performed.

*Population threshold as utilised by SaTScan

Table 5. Proportion of population in each age-group within the

 NWM cluster compared with population outside NWM cluster

Age Group	Inside cluster	Outside Cluster	p^*
0-9	0.14	0.14	0.59
10-19	0.16	0.16	0.25
20-29	0.14	0.15	0.06
30-39	0.14	0.15	0.08
40-49	0.14	0.13	0.12
50-59	0.11	0.11	0.11
60-69	0.08	0.07	0.05
70-79	0.06	0.05	0.08
80+	0.03	0.03	0.12

* Mann-Whitney U Test performed

NWM: Northwest/Midlands Cluster

Discussion

This study further describes the high prevalence of sarcoidosis in Ireland, and identifies considerable differences in rates of disease between ROI and NI, findings consistent with previous work (18-20, 22). However, it most importantly identifies significant

Table 6. Age-specific	prevalence and	case fatality ra	te for ROI

0 1	1	5	
Age group	Mean Prevalence (10-years)	Mean Deaths per year	Case-fatality rate (10-year)
0-9	.09	0	0
10-19	1.08	0	0
20-29	27.67	0.4	1.45
30-39	38.15	0.3	.79
40-49	41.11	1.2	2.92
50-59	47.69	2.6	5.45
60-69	40.15	2.9	7.22
70-79	27.84	1.1	3.95
80+	11.85	0.9	7.60

geographical and temporal clustering of disease within Ireland, with prevalence rates higher than those previously reported and among the highest in the world.

The first reports of the prevalence of sarcoidosis in Ireland were in 1964, showing a prevalence of 20.5-40.2 per 100,000 in the Republic of Ireland, based on mass screening examinations for Tuberculosis in the Dublin area (18), and 0-19.8 per 100,000 population for Northern Ireland (19), also based on mass radiographic screening. Cummiskey and Dean (22) later performed a more extensive study using hospital-inpatient data records from throughout ROI and found results similar to those of Logan (18). The mean ROI prevalence rates reported in this present study are comparable to these reports, showing there has been little change in disease prevalence over a forty-year period. Similarly, based on our findings for Northern Ireland, it appears that little change in prevalence has occurred since the first report by Milliken (19).

The finding that distinct differences in prevalence exist between ROI and NI, and that this remains so after forty years in an intriguing one and has not previously been reported. It is also interesting to note that despite the differences in prevalence between NI and ROI, the NI region still has a higher prevalence than areas in Britain (20). Indeed the prevalence of sarcoidosis is higher among Irish people living in London than among native Londoners (25). Considered together, these findings would support the hypothesis that there is a multifactorial aetiology for the disease, with both environmental and genetic factors conferring risk to a particular population.

The spatial cluster analysis yields further interesting results as it identified four regions with prevalence higher than elsewhere in ROI or NI Spatial and temporal clustering of sarcoidosis has been well documented in other countries (3, 4, 12, 14, 26-29), but not Ireland. The prevalence in the Northwest core cluster is 44.9 per 100,000, considerably higher than the ROI population mean. This also represents over twice the increased risk of being admitted to hospital with sarcoidosis compared with the population elsewhere (Fig. 3). Prevalence in the Midlands core cluster was 32.1, representing a 1.55 times increased risk of admission with sarcoidosis. Other clusters were also identified in the South and Southeast ROI.

Interesting temporal and space-time clusters are also identified. While there is a significant increase seen in prevalence throughout ROI and NI between 2000 and 2004, more localised clusters were identified. A Galway/Mayo cluster is seen for the years 1999 and 2000, with a prevalence of 96.55 per 100,000. To our knowledge this is the highestreported prevalence of sarcoidosis for a population from Ireland. It is also among the highest in the world, comparable to rates reported from Scandinavian countries or the African-American population (21). For comparison, Table 7 is included to show data from this present study together with previous studies from Ireland and other European countries.

There is a particularly intriguing space-time cluster occurring in the Northeast region, comprising areas from both NI and ROI (Fig. 4). It is not clear why such clustering should be identified across two regions with distinct health administrations.

Table 7. Current and previously reported prevalence of Sarcoidosis in Ireland compared with other European countries.

Current Prevalence (as reported in this pape	r) 96.6
Western space-time cluster	20.0
North-western spatial cluster	44.9
Republic of Ireland (Mean)	28.1
Northern Ireland (Mean)	11.2
Previous Reports Sweden (34)	55-64
Ireland (18)	33.3
Finland (35)	28.2
Norway (36)	26.7
Netherlands (37)	21.6
England (38)	19
Switzerland (39)	16
Italy (40)	11.7
Northern Ireland (19)	10.3
France (41)	10
Portugal (34)	0.2

* number of cases per 100,000 population

Nonetheless, its presence despite this suggests that the cluster may indeed be significant, as it is present despite any potential differences in detection of disease or reporting practices between NI and ROI. Although this cluster might also reflect familial aggregation of disease in this region, it again raises the possibility of a shared environmental exposure or of a transmissible agent.

The reasons for this spatial and temporal clustering are unclear, however it would appear that the prevalence of the disease is particularly high in small areas of Ireland exposed to both coastal and rural factors, and in areas that historically would also have a relatively stable indigenous population. This clustering within ROI is not explained by potential regional differences in healthcare utilisation, as further analysis of the data found no significant regional differences in the proportion of admissions that were related to respiratory illness. Familial aggregation of disease has been previously documented in the Irish population by Brennan and colleagues (5), with as many as 12.3% of patients reporting first-degree relatives with the disease and this may be a relevant factor. However, it is possible that a shared environmental factor or transmissible agent may also be responsible. An association of sarcoidosis with water, coastal, or rural areas has previously been found in other countries (11, 13, 14). Indeed, the ACCESS group found agricultural employment, exposure to mould or mildew in employment or exposure to insecticides was associated with development of the

disease (7, 8). No one environmental agent has been found to date, and although the aetiology of sarcoidosis remains elusive, the prevailing view is that sarcoidosis occurs as a consequence of exposure to one or more environmental agents, interacting with genetic factors (1, 15, 30). The results of this study would appear to support this.

Epidemiological studies of sarcoidosis are beset by difficulties, both in the capturing of data and in the interpretation of the results. Difficulties arise for a number of reasons: the lack of a consistent, precise case definition; variations in methods of case ascertainment; variations in disease presentation and severity, and the lack of adequately sensitive and specific diagnostic tests (31). This is a possible limitation of this study. It is also acknowledged that this study does not provide data on the incidence of sarcoidosis, whereby measurement of incidence might give a greater insight into a possible aetiology of sarcoidosis. However, given that sarcoidosis in Ireland has a relatively low mortality, and its high prevalence may reflect the chronicity of the disease among the population, we believe that prevalence would be considered a superior epidemiological quantifier of disease burden to incidence, as has been suggested by others (32).

HIPE data reflects hospital activity and as there is currently no sarcoidosis registry for ROI or NI, this data source is the only comparable means of capturing disease rates for sarcoidosis. Unfortunately, difficulties exist with using this data for epidemiological research as it reflects the number of patient episodes and not necessarily individual patients. It also does not capture those patients who are managed solely through outpatient facilities, those patients managed through certain private hospitals, or those who may be asymptomatic. Indeed it is for these reasons the authors of previous reports of sarcoidosis utilising HIPE data admit this may have resulted in an underestimation of prevalence, possibly by as much as 30% of actual cases (22). Our data should therefore be considered an underestimation of true prevalence, yet while underestimation is possible, this does not necessarily negatively impact on the interpretation of the geographical or temporal clusters described in this study, as the means of data collection used was the same for all areas.

ECONOMIC IMPLICATIONS

There are clearly significant cost implications associated with such a highly-prevalent disease in terms of utilisation of healthcare resources to confirm the diagnosis, to exclude more sinister pathologies or to subsequently provide specialist long-term follow-up if required. Indeed there are significant economic implications on a wider scale also, as sarcoidosis may impact on a person's ability to work. A report by the Irish Thoracic Society found there were almost 70 working days lost annually per recipient of illness benefit related to sarcoidosis (33). Unfortunately there remains a lack of good quality epidemiological data on sarcoidosis, particularly with regard the time of onset, stage of disease at diagnosis, extent and severity of organ involvement, the length of time a person has the disease and the ultimate cause of death. As such, although the disease has a relatively low mortality in Ireland compared with the rest of the world, its prevalence is high, and the financial burden it places on the health systems and the economy as a whole is currently not quantifiable. This is therefore a major epidemiological and financial issue for the healthcare systems of both regions, yet is an issue that has been addressed by a number of EU countries such as Denmark, Germany and Italy, with initiatives such as the establishment of their respective National Sarcoidosis Registries. Establishment of a similar registry for ROI and NI would address much of the current deficiencies in epidemiological data for sarcoidosis in Ireland.

Conclusion

This study provides an update on the burden of disease due to sarcoidosis in Ireland at the end of the 20th, and beginning of the 21st century. It shows that significant geographical and temporal variation in disease prevalence exists in Ireland. It also shows that there are significant differences in mortality between NI and ROI. We propose that focussed cohort studies within these populations might provide invaluable insight into the genetic-environment interaction of sarcoidosis. Furthermore, given the high prevalence of the disease both North and South, Ireland could be in a unique position geographically to

develop a centralised, mutually beneficial all-island registry for sarcoidosis.

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