Historical Analysis of Leukaemia Rates in Helensburgh

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Background

The public health unit was recently notified of three leukaemia diagnoses in the Helensburgh area among persons aged less than twenty years in the previous 18 months. As part of the response to this notification, leukaemia incidence rates for the period 1992–2006 were reviewed for evidence of increased risk. This represents the most current period for which data were available from the NSW Central Cancer Registry; however, it did not include the period during which the most recently notified leukaemia cases were diagnosed. As such, this analysis assesses whether there is any historical evidence of increased leukaemia risk.

Study Area and Population at Risk

The study area was defined by the Kiama, Shellharbour and Wollongong local government areas; a largely metropolitan area referred to collectively as the Illawarra. The unit of analysis within this study area was postcode of residence at diagnosis, which was the finest level of spatial resolution reported in the case data set. Unfortunately, no time series of Australian postcode population counts exists, so geographically weighted recasting was used to define the population at risk for the study period using 2001 postal areas as the standard geography: postal areas are Census approximations of Australia Post postcode boundaries. Census Collection District (CCD) digital boundaries for the years 1991, 1996, 2001 and 2006 were intersected with 2001 postal area digital boundaries using ArcGIS 9.2 and the proportions of each CCD in each postal area calculated. Quinquennial Census population estimates for each CCD were then apportioned into postal areas using these geographic weights. Population counts were aggregated by sex and five year age group within postal areas and the proportion of the total study area population in each age-sex cell calculated for each Census period. These population weights were then used to apportion annual estimated resident populations for the entire Illawarra area to individual 2001 postal areas within the reference bands: 1992–1993, 1994–1998, 1999–2003, 2004–2006 ±2: that is, the age-sex distribution was assumed to remain constant for the five years centred on each Census period.

Cases

Incident cases of leukaemia diagnosed in Illawarra area residents were obtained from the NSW Central Cancer Registry for the period 1 January 1992 to 31 December 2006 using International Classification of Diseases version 9 codes of 204–208 and version 10 codes of C91–C95. Past investigations have indicated that this passive surveillance system provides for 100% ascertainment of incident cancer cases; [1] however it is a relatively untimely data collection with a current delay of nearly two years, hence the focus on pre-alarm incidence. Cases were extracted based on area health service and postcode of residence at time of diagnosis.

Statistical Methods

The potential clustering of leukaemia disease was assessed using the space-time scan statistic for Poisson process data.[2] This method runs a cylindrical scan window of varying diameter (space) and height (time) across the study area and compares the rates of disease inside and outside sets of scan windows to identify candidate clusters using a maximum likelihood algorithm. A test statistic is then derived by Monte-Carlo sampling comparing the observed maximum likelihood ratio to 999 simulated ratios under a null of uniform risk. This approach avoids the preselection bias inherent in many cluster analyses because neither the areal resolution nor temporal epoch of the cluster is defined by the data triggering the alarm. [3, 4, 5]

Space-time analyses were undertaken using SaTScan 7.0 software.[6] The areal and temporal units of analysis were postcode of residence and calendar year at diagnosis as recorded in the NSW Central Cancer Registry. The analysis tested for purely spatial, purely temporal and space-time clusters for the period 1 January 1992 to 31 December 2006 using 2001 postal area centroids as the foci for scan windows. Analyses were undertaken for persons aged <20, 20-49, 50+ years and all ages using a multivariate extension of the scan statistic.[7] The significance of identified clusters was evaluated at the 5% level.

Standardised incidence ratios (SIR) for postcode 2508 (including Helensburgh) are reported for the periods 1992–1996, 1997–2001 and 2002–2006 despite previous caveats about applying focused analytic methods *a posteriori*. Ratios are reported as they are consistent with the results of the spatial scan statistic analysis and provide a more easily communicated incidence metric. However, they should not be used to make inferences about disease risk, which would be biased and overly liberal.[3, 4, 5]

Results

From 1 January 1992 to 31 December 2006 there were 523 incident cases of leukaemia in the Illawarra area: 57 among people <20 years, 62 among people 20–49 years; and 404 among people 50+ years. Twelve incident cases of leukaemia were recorded for people resident in postcode 2508 at time of diagnosis: 4 were among children aged less than <20 years and 6 cases were male. The standardised incidence ratios for postcode 2508 were 1.4 (95% CI: 0.4–3.2) for 1992–1996, 0.2 (95% CI: 0.0–1.3) for 1997–2001 and 1.2 (95% CI: 0.4–2.5) for 2002–2006.

Table 1 shows the results of the space-time scan analysis. The most likely cluster for each age grouping is identified by the number one; secondary clusters are identified by the numbers 2, 3, etc. All maximum likelihood ratio test statistics for candidate clusters were non significant at the 5% level, indicating no evidence of disease clustering in postcode 2508 or any other area in the Illawarra for the study period. Postcode 2508 was included in secondary clusters for children aged <20 years and adults aged 50+ years; however, neither were statistically significant as indicated previously. Figure 1 shows the geographical location of the (non significant) most likely clusters.

Table 1 Most likely leukaemia incidence clusters identified using the space-time scan statistic by age group, Illawarra 1992–2006

Age group	Cluster postcodes	Temporal period	Observed cases	Expected cases	SIR	LR statistic	p-value
00–19	1. 2527	1997	3	0.3	10.4	4.38	0.742
	2. *2508*, 2515, 2516, 2517, 2518, 2519, 2525, 2500, 2526	2006	8	2.6	3.1	3.98	0.862
20–49	1. 2527, 2533, 2529, 2528, 2530, 2506	1996-1998	14	4.6	3.0	6.92	0.124
	2. Whole study area*	1996-1998	19	11.2	1.7	2.85	0.997
50+	1. 2528	2004-2006	23	10.7	2.1	5.47	0.459
	2. 2519, 2518, 2500, 2517	1996	17	8.3	2.0	3.54	0.966
	3. 2502, 2505	2000	7	2.4	2.9	2.96	0.997
All ages	1. 2528, 2529	2006	20	7.8	2.6	6.83	0.162
	2. 2527	1997	6	1.4	4.3	4.15	0.878
	3. *2508*, 2515	2005	8	2.7	3.0	3.43	0.983
	4. 2519	1998-2000	15	7.2	2.1	3.24	0.993
	5. 2517	1998	5	1.5	3.5	2.66	0.999

* Purely temporal cluster; bold type face indicates primary or “most likely” clusters; SIR = standardised incidence ratio; LR = Likelihood ratio

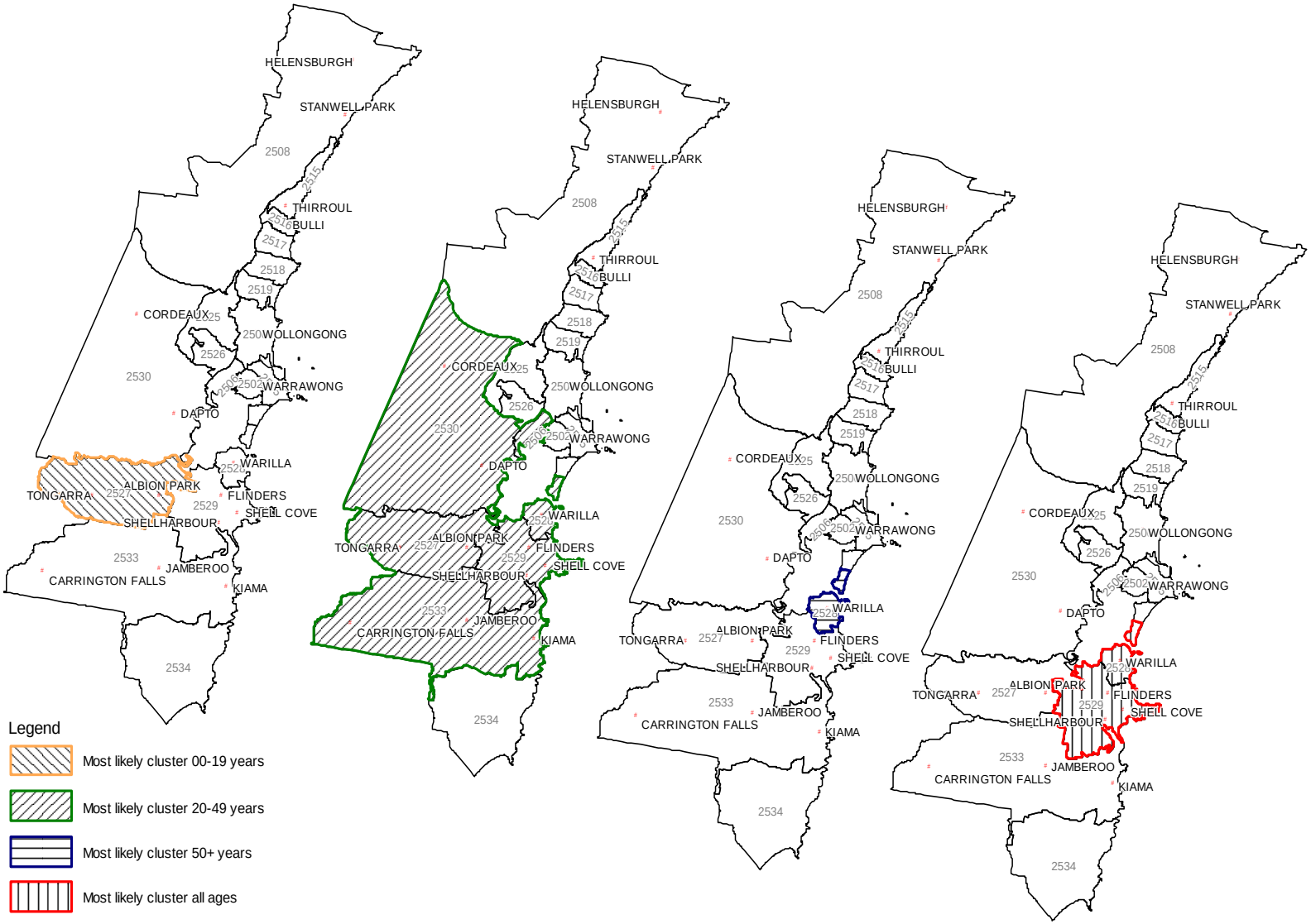

Figure 1 Non significant space-time clusters of leukaemia incidence by age group, Illawarra 1992–2006 (see Table 1 for temporal details)

Conclusion

This analysis found no evidence of increased risk or clustering of leukaemia incidence in postcode 2508, which includes the Helensburgh township, from 1992–2006. The most likely clusters identified by the analysis were located in the southern region of the Illawarra area and centred on postal area 2527 for persons <20 and 20–49 years and 2528 for persons aged 50+ years and all persons. However, none of these potential clusters were statistically significant indicating no evidence of increased disease risk in any Illawarra postcode for the study period 1992–2006.

There are a number of important limitations to this analysis that need to be considered. First, cases and populations at risk come from independent data sets that are spatially misaligned. This is because the Census data used to rebase populations at risk is a "best fit" approximation of Australia Post postcodes using Census Collection District areal units. This misalignment may lead to an over or under estimate of the population at risk; however, in the Illawarra, there is good agreement between actual postcodes and Census approximated postal areas, so spatial misalignment is unlikely to be a major source of bias. Related to this issue is the permanence of postcode boundaries across time. An intrinsic but often neglected characteristic of postcodes is that they are designed for the efficient delivery of mail and are re-drawn intermittently to facilitate this purpose. Redistribution of postcode boundaries can result in the spatial misalignment of cases across time. Geocoding cases to address-level latitude and longitude coordinates mitigate this problem by allowing cases to be aggregated to standard space-time areal units; but this was beyond the scope of the analysis. A review of postal area boundary 2508 indicated very few changes from 1991 to 2006, suggesting case misalignment is unlikely to be a significant source of bias in the analysis of the substantive hypothesis test of average leukaemia risk in the Helensburgh (postcode 2508) area.

References

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