

Helensburgh Cancer Cluster Investigation

1 Background

In December 2008 a review of leukaemia cases in the Illawarra was undertaken in response to community concerns regarding a possible increase in cases of leukaemia among young people (0–19 years) in Helensburgh. The review was conducted at the postcode level (the smallest administrative area for which cancer incidence data are routinely available) and used appropriate analytic methods for detecting areas with higher-than-expected leukaemia incidence. This review found no evidence for increased leukaemia rates among young people in any Illawarra postcode including postcode 2508, which includes Helensburgh. In October 2012 members of the Helensburgh community again raised concerns regarding the incidence of leukaemia, as well as non-Hodgkin's lymphoma, in children. The current assessment was undertaken to update the 2008 review to include additional cancer notification data that were not available in December 2008 and broaden the study area to include the entire Illawarra Shoalhaven Local Health District (ISLHD). It required access to 2011 Census population data which were only released in August 2012.

2 Aims

The aims of this review were to:

- I. Ascertain the number of cases of leukaemia and non-Hodgkin's lymphoma among residents aged 0–19 years of the ISLHD
- II. Assess the geographic distribution of leukaemia or non-Hodgkin's lymphoma incidence within the ISLHD; and
- III. Assess whether the incidence of leukaemia and/or non-Hodgkin's lymphoma is an unexpected occurrence

3 Methods

3.1 Study area, units and population at-risk

The study population was defined as persons resident in Kiama, Shellharbour, Shoalhaven and Wollongong local government areas between 1 January 1996 and 31 December 2008. Three geographic units were used for analysis in this review: postcode, suburb and Census Collection District (CCD) of residence at diagnosis. Postcode is the smallest geographic unit at which cancer notification data are routinely reported in NSW and an updated analysis at this level was undertaken for consistency with the 2008 review. However, postcodes include multiple localities, which make it difficult to assess the public health significance of incidence alarms when a single locality is of principal interest. For this reason, we also conducted analyses using 2006 suburbs and CCDs of residence data. These spatial units represent on average 250 households and permit risk assessments at very fine geographical resolutions (i.e. sub locality).

3.2 Case ascertainment

Incident cases of leukaemia and non-Hodgkin's lymphoma diagnosed in Illawarra Shoalhaven Local Health District residents aged 0–19 years and geocoded to 2006 CCDs were obtained directly from the NSW Central Cancer Registry (CCR) for the period 1 January 1996 to 31 December 2011. These data had to be extracted manually from the CCR and so it was not feasible to obtain equivalent data for the remainder of NSW. We therefore extracted data for non-ISLHD residents using the Health Outcomes Information and Statistical Tool kit (HOIST) using International Classification of Diseases version 10 codes C91–C95 (all leukaemias) and C82–C85 (non-Hodgkin's lymphoma). These data were complete to 31 December 2008. More recent data were not available due to lengthy delays in the release of Australian Bureau of Statistics' death data, which is used to identify incident cancers diagnosed at autopsy. Cancer reports obtained from the CCR included all Helensburgh cases ascertained from local general practitioners.

3.3 Statistical methods

Standardised incidence ratios (SIR) for persons 0–19 years and their exact Poisson 99% confidence intervals (99% CI) were calculated and reported for each of the 25 postcodes in the study area for 1996 to 2008 using Urban NSW (excluding Illawarra and Shoalhaven areas) as the reference population rate (externally standardised) and for 1996 to 2011 using all ISLHD as the reference population rate (internally standardised). Preliminary analyses were performed using the discrete Poisson space-time scan statistic to identify potential clusters in time and space for further investigation. The likelihood that statistically significant clusters from the space-time scan were random events was then evaluated by estimating the probability of obtaining a similar or more extreme occurrence in one of NSW's equivalent geographical units by chance in any consecutive similar time period from 1996-2008 using $1 - ((1-p)^n)^t$, where p is the Poisson probability of observing the number of cases or more in the significant cluster, n is the number of comparable geographic units in NSW, and t is the number consecutive similar time periods. This was done for the three geographic units based on postcode, suburb and CCD.

4 Results

Between 1996 and 2008 there were 61 (SIR=1.04, 99% CI=0.73–1.44) and 11 (SIR=0.92, 99% CI=0.36–1.90) incident cases of leukaemia and non-Hodgkin's lymphoma among Illawarra Shoalhaven Local Health District children aged 0-19 years, respectively: a further 17 leukaemia and 2 non-Hodgkin's lymphoma cases were reported from 2009–2011. Aggregate SIRs indicated similar leukaemia incidence rates to Urban NSW and ISLHD for all postcodes including 2508 (see Table 1). Non-Hodgkin's lymphoma incidence was also similar to Urban NSW and ISLHD for all Illawarra Shoalhaven postcodes. There were no notified cases of non-Hodgkin's lymphoma in children 00–19 years for postcode 2508 during the period 1996 to 2011.

4.1 Statistical assessment of the chance of occurrence of geographic clustering

Space-time scans identified two statistically significant potential clusters of high leukaemia rates in ISLHD between 2005 and 2008. The first potential cluster was identified at the postcode level and included 6 cases in postcode 2508. The second cluster was observed at the CCD level and involved five adjoining CCDs in Helensburgh, Otford and Stanwell Park localities. Standardised incidence ratios for these clusters (and non-cluster) periods within potential cluster areas are reported in Table 2. Sensitivity space-time scans using the ISLHD standardised data for 1996 to 2011 identified the same space-time clusters but importantly found no evidence of high leukaemia rates after 2008. No statistically significant potential clusters were identified for non-Hodgkin's lymphoma and so the remaining analyses focus on leukaemia.

4.1.2 Using postcode as a geographical comparison unit

The probability of observing ≥ 6 cases of leukaemia in postcode 2508 from 2005-2008 given an expected value of 0.55 is 0.000024 and the probability of this not occurring in the postcode is $1 - 0.000024 = 0.999976$. Postcode 2508 is one of 605 postcodes in NSW, so the probability of not observing an event this unusual in any NSW postcodes is $(0.999976)^{605} = 0.985554$. There are nine possible consecutive 4-year periods from 1996-2008, so the probability of not observing an event this unusual in any NSW postcode in any 4 consecutive years is $(0.985554)^9 = 0.877251$. Therefore there is a $1 - 0.877251 = 0.122748$ or 12.3% probability of observing an event of this magnitude or more extreme in one of NSW's 605 postal areas by chance in any four consecutive years between 1996 and 2008.

Note that a problem with this method is the great disparity in postcode population sizes, with 2508 being a reasonably small postcode, and hence much more likely to have erratic rates for rare diseases over different time periods while other very much larger population postcodes are much less likely to have a chance high or low rate.

4.1.2 Using suburb as a geographical comparison unit

The SIR for leukaemia incidence in Helensburgh locality was additionally calculated for the period of the most likely cluster (2005–2008) on the grounds it contributed two-thirds of cases (n=4) to the

postcode 2508 total. The expected incidence based on urban NSW population rates was 0.36178, giving an SIR of 11.06 (99% CI: 1.86–34.81). Helensburgh is one of 2,953 suburbs in NSW. After adjusting for pre-selection bias using the methodology described previously, the likelihood of observing an event of this magnitude or more extreme by chance in any one suburb in NSW in any 4 consecutive years between 1996 and 2008 is $1 - ((1 - 0.000535)^{2,953})^9 = 0.94584$ or 94.6%.

Note that the great disparity in suburb population sizes is also a problem for this method, with Helensburgh being a reasonably small suburb, and hence much more likely to have erratic rates for rare diseases over different time periods while other very much larger population suburbs are much less likely to have a chance high or low rate.

4.1.3 Using CCD as a geographical comparison unit

Space-time analysis also identified a potential cluster of high leukaemia incidence in five adjacent CCDs across Helensburgh, Otford and Stanwell Park localities. This potential cluster included the six cases from 2005 to 2008. The expected incidence based on urban NSW population rates was 0.23, giving an SIR of 26.39 (99% CI: 6.68–68.09). There are 11,901 CCDs in NSW and at least 74,738 unique combinations of 5 adjoining CCDs. Therefore the likelihood of observing an event of this magnitude or more extreme by chance in any 5 adjoining CCDs in NSW in any 4 consecutive years between 1996 and 2008 is $1 - ((1 - 0.00000017)^{74,738})^9 = 0.107385$ or 10.7%.

Note that all CCDs for non-remote locations are all approximately the same size, so this method is considered to better reflect the probability of the observed number of cases by chance. Note also that the number of 5 CCD combinations in NSW is much greater than the 74,738 used in this estimation as we have not included combinations that cross grid boundaries, so this calculation will, if anything, be a significant underestimate.

4.1.4 Conclusion

The probability that a cluster of leukaemias occurring at the rates observed for Helensburgh in 2005-2008 would occur in a similar area is most likely between about 10% and almost 95%.

Table 1 Standardised incidence ratios and 99% confidence intervals for childhood leukaemia and non-Hodgkin's lymphoma by postcode at diagnosis, persons 0–19 years, 1996–2008

Post code	Total population	Leukaemia					non-Hodgkin's lymphoma				
		Observed cases	Expected cases	SIR*	99% confidence interval		Observed cases	Expected cases	SIR*	95% confidence interval	
					Lower bound	Upper bound				Lower bound	Upper bound
2500	89,424	3	4.2	0.7	0.08	2.63	0	0.9	0.0	0.00	5.20
2502	39,386	3	1.9	1.6	0.18	5.84	2	0.4	5.3	0.27	24.49
2505	13,628	0	0.6	0.0	0.00	7.14	0	0.1	0.0	0.00	34.78
2506	28,969	1	1.3	0.7	0.00	5.53	0	0.3	0.0	0.00	15.91
2508	36,164	6	1.7	3.4	0.88	8.96	0	0.3	0.0	0.00	13.49
2515	34,679	2	1.7	1.2	0.06	5.62	1	0.3	3.0	0.01	22.22
2516	21,583	0	1.0	0.0	0.00	4.47	0	0.2	0.0	0.00	22.23
2517	40,064	3	1.9	1.6	0.18	5.75	0	0.4	0.0	0.00	11.94
2518	61,408	2	2.9	0.7	0.04	3.16	1	0.6	1.7	0.01	12.64
2519	54,731	5	2.6	2.0	0.42	5.52	0	0.5	0.0	0.00	8.53
2525	36,746	2	1.7	1.2	0.06	5.34	1	0.4	2.8	0.01	20.78
2526	65,408	6	3.1	1.9	0.50	5.04	1	0.6	1.6	0.01	11.73
2527	84,616	4	4.1	1.0	0.17	3.09	1	0.8	1.2	0.01	9.24
2528	84,351	3	4.0	0.8	0.09	2.77	0	0.8	0.0	0.00	5.56
2529	70,425	3	3.4	0.9	0.10	3.23	0	0.7	0.0	0.00	6.91
2530	105,884	5	5.0	1.0	0.21	2.80	0	1.0	0.0	0.00	4.52
2533	51,917	1	2.4	0.4	0.00	3.10	0	0.5	0.0	0.00	8.84
2534	17,470	0	0.8	0.0	0.00	5.63	0	0.2	0.0	0.00	26.72
2535	20,576	0	1.0	0.0	0.00	4.79	0	0.2	0.0	0.00	22.60
2536	682	1	0.0	29.9	0.15	222.05	0	0.0	0.0	0.00	732.04
2538	7,006	1	0.3	3.0	0.02	22.32	0	0.1	0.0	0.00	67.97
2539	49,729	4	2.3	1.7	0.29	5.38	2	0.5	4.1	0.21	19.04
2540	123,306	4	5.9	0.7	0.11	2.15	1	1.2	0.8	0.00	6.24
2541	90,754	2	4.3	0.5	0.02	2.15	1	0.9	1.1	0.01	8.49
2577	5,740	0	0.3	0.0	0.00	18.01	0	0.1	0.0	0.00	76.42
Total	1,234,644	61	58.5	1.04	0.73	1.44	11	12.0	0.9	0.36	1.90

SIR = Standardised Incidence Ratio; * Calculated using urban NSW population rates

Table 2 Standardised incidence ratios for childhood leukaemia for potential cluster areas before (1996–2004) and during (2005–2008) potential cluster periods

Level of analysis	Period	Location	Total population	Observed cases	Expected cases	SIR*	99% Confidence interval	
							Lower bound	Upper bound
Census Postal Areas	1996-2004	2508	25,265	0	1.23	0.00	0.00	3.76
	2005-2008	2508	10,899	6	0.55	11.00	2.79	28.47
Census Suburbs	1996-2004	Helensburgh	16,596	0	0.82	0.00	0.00	5.59
	2005-2008	Helensburgh	7,511	4	0.36	11.06	1.86	34.81
Census Collection Districts	1996-2004	1190110 1190112 1190101 1190108 1190111	9,534	0	0.47	0.00	0.00	9.75
	2005-2008	1190110 1190112 1190101 1190108 1190111	4,508	6	0.23	26.39	6.68	68.09

SIR = Standardised Incidence Ratio; * Calculated using urban NSW population rates