Lymphohaematopoietic malignancy around all industrial complexes that include major oil refineries in Great Britain

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Abstract

***Objectives*—To examine the incidence of lymphohaematopoietic malignancy around industrial complexes that include major oil refineries in Great Britain after recent public and scientific concern of possible carcinogenic hazards of emissions from the petrochemical industry.**

***Methods*—Small area study of the incidence of lymphohaematopoietic malignancies, 1974–91, within 7.5 km of all 11 oil refineries (grouped into seven sites) in Great Britain that were operational by the early 1970s and processed more than two million tonnes of crude oil in 1993.**

***Results*—Combined analysis of data from all seven sites showed no significant ($p<0.05$) increase in risk of these malignancies within 2 km or 7.5 km. Hodgkin's lymphoma, but no other malignancy, showed evidence ($p=0.02$) of a decline in risk with distance from refineries, but there was an apparent deficit of cases of multiple myeloma near the refineries ($p=0.04$).**

***Conclusion*—There was no evidence of association between residence near oil refineries and leukaemias, or non-Hodgkin's lymphoma. A weak positive association was found between risk of Hodgkin's disease and proximity to major petrochemical industry, and a negative association with multiple myeloma, which may be chance findings within the context of multiple statistical testing.**

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Keywords: small area; lymphohaematopoietic malignancy; oil refineries

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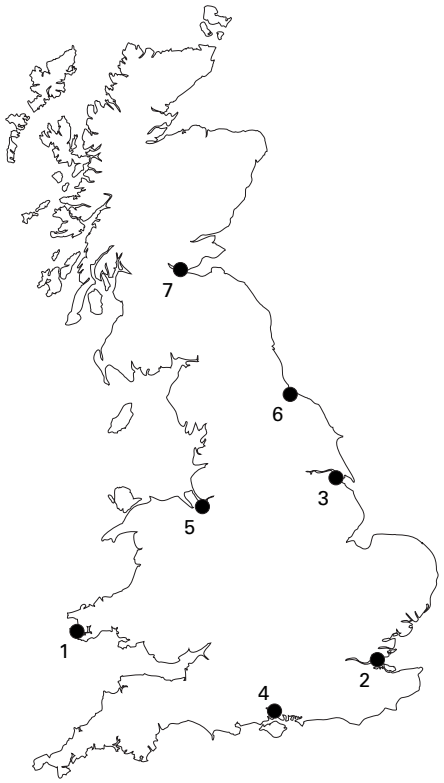
Oil refining and other petrochemical processes may lead to low level emissions of compounds with possible carcinogenic potential including benzene[1] and 1,3-butadiene.[2] A cohort study in the United Kingdom of mortality among oil refinery workers, who would be expected to have higher exposures to these compounds than residential populations, has not shown an excess risk of leukaemia or other haematopoietic malignancy.[3] Few studies of cancer risks among residential populations living near to petrochemical industry have been reported. A United States study found high rates of cancer of the lung, nasal cavity and sinuses, and skin among the resident male population in counties where the petroleum industry is most heavily concentrated, but no significant increase for lymphohaematopoietic malignancy.[4] Another study in the United States suggested high rates of lung cancer near petrochemical plants.[5] A study of the geographical distribution of childhood leukaemia and other childhood cancers in Great Britain reported a tendency for clustering near emission sources of (among other things) volatile petroleum products,[6] although the methodology of this study with residential post codes as a proxy for populations had previously been questioned.[7] A more recent study of the same data set similarly found an association of childhood cancers with emission sources based on comparisons between address at birth and at death.[8] By contrast, studies of cancer incidence and mortality among residents living close to a petrochemical plant in south Wales were largely reassuring.[9 10] We report here a study of lymphohaematopoietic malignancy around all industrial complexes that include major oil refineries in Great Britain.



The seven oil refinery sites. (1) Milford Haven (three refineries: Elf, Texaco and PCC, and Gulf); (2) Coryton (two refineries: Mobil and Shell); (3) Immingham (two refineries: Lindsey and Conoco); (4) Esso, Fawley; (5) Shell, Stanlow; (6) Phillips Imperial, Teeside; (7) BP, Grangemouth.

Table 1 Observed (O) cases, observed/expected (O/E) ratios (95% CI) of lymphohaematopoietic malignancy within 2 km and 7.5 km of industrial complexes that include major oil refineries, and results of Stone's tests

	0 – 2 km		0 – 7.5 km		Stone's tests	
Cell type	O	O/E (95% CI)	O	O/E (95% CI)	Unconditional p	Conditional p
All ages						
All lymphatic and haematopoietic	417	0.95 (0.86 to 1.04)	3827	0.98 (0.95 to 1.01)	0.64	0.51
Multiple myeloma	57	0.74 (0.56 to 0.96)	625	0.89 (0.82 to 0.96)	0.04	0.52
All leukaemias	169	1.06 (0.91 to 1.23)	1446	1.01 (0.96 to 1.07)	0.58	0.78
Lymphoid leukaemias	71	1.00 (0.78 to 1.26)	597	0.94 (0.86 to 1.02)	0.24	0.55
Acute lymphatic leukaemia	27	1.09 (0.72 to 1.59)	197	0.95 (0.82 to 1.09)	0.24	0.17
Chronic lymphatic leukaemia	42	0.99 (0.71 to 1.33)	364	0.91 (0.82 to 1.01)	0.31	0.77
Myeloid leukaemias	81	1.14 (0.91 to 1.42)	666	1.05 (0.98 to 1.14)	0.31	0.38
Acute myeloid leukaemia	44	0.99 (0.72 to 1.33)	420	1.05 (0.95 to 1.16)	0.57	0.50
Chronic myeloid leukaemia	31	1.42 (0.97 to 2.02)	207	1.06 (0.92 to 1.22)	0.25	0.71
Hodgkin's lymphoma	54†	1.01 (0.76 to 1.32)	443	0.97 (0.89 to 1.07)	0.05	0.02
Non-Hodgkin's lymphoma	137	0.92 (0.77 to 1.08)	1313	1.00 (0.94 to 1.05)	0.99	0.77
Ages 0 to 14						
All lymphatic and haematopoietic	25	0.99 (0.64 to 1.46)	180	0.93 (0.80 to 1.08)	0.37	0.12
All leukaemias	19	1.00 (0.60 to 1.56)	138	0.94 (0.79 to 1.11)	0.73	0.38
Lymphoid leukaemias	16	1.08 (0.62 to 1.76)	104	0.91 (0.74 to 1.10)	0.60	0.38
Myeloid leukaemias	2	0.66 (0.08 to 2.38)	22	0.93 (0.59 to 1.41)	0.74	*
Hodgkin's lymphoma	2	0.77 (0.09 to 2.80)	18	0.89 (0.53 to 1.40)	0.07	*
Non-Hodgkin's lymphoma	4	1.15 (0.31 to 2.96)	24	0.91 (0.58 to 1.35)	0.28	*

*Test did not converge because of small numbers
†Includes 1 duplicate registration. Conditional Stone's test for Hodgkin's disease remained significant (p=0.03) after its exclusion.

Methods

The study was carried out with the Small Area Health Statistics Unit postcoded health database. It examined cancer risk near all 11 oil refineries in Great Britain, operational by the early 1970s, which processed more than two million tonnes of crude oil in 1993. They were grouped into seven sites of one to three refineries (figure). Each was treated as an extended emissions source. The incidence of lymphohaematopoietic malignancy was examined in eight bands around refinery perimeters with outer limits at 0.5, 1, 2, 3, 4.5, 5.6, 6.6, and 7.5 km. For descriptive purposes cancer incidence was also examined at 0–2 km and 0–7.5 km.

The following diagnostic groups of the international classification of diseases 8th (ICD-8) and 9th (ICD-9) revision were studied for all ages and 0–14, 15–64, and ⩾65 age groups: lymphatic and haematopoietic malignancy (ICD-8 200–207; ICD-9 200–208, 238.6); multiple myeloma (ICD-8 203; ICD-9 203, 238.6) (not separately examined for the 0–14 age group); non-Hodgkin's lymphoma (ICD-8 and 9 200, 202); Hodgkin's lymphoma (ICD-8 and 9 201); all leukaemias (ICD-8 204–207; ICD-9 204–208); lymphoid leukaemia (ICD-8 and 9 204); and myeloid leukaemia (ICD-8 and 9 205). Acute and chronic subdivisions of the last two were examined for all ages.

Cancer incidence was studied for all years for which national cancer registration data were available: 1974–89 for England and Wales and 1975–91 for Scotland. Population counts by band around each site were estimated from census small area statistics with the 1981 census for years up to and including 1986, and the 1991 census thereafter. Expected (E) numbers of cancer registrations were calculated by year and band from annual rates in Great Britain stratified by 5 year age group, sex, and quintile of the Carstairs deprivation index to adjust for possible socioeconomic confounding.[11] Rates were further adjusted with disease specific standardised regional registration ratios.[12] Because of the disparity in years for which cancer registration data were available, national rates for 1974 were computed from 1974 registrations for England and Wales and 1975 registrations for Scotland; and 1990 and 1991 rates were computed from 1989 registrations for England and Wales and those for the relevant year in Scotland.

Formal hypothesis tests were based on the maximum likelihood ratio test of Stone.[13] This gives a test of decline in risk with distance against a null hypothesis of constant risk in all the bands. As Stone's unconditional test can be significant either where there is a decline in risk with distance or where the relative risk in at least one of the bands does not equal 1.0, we also carried out a conditional test. This specifically tests for decline in risk[14] and consequently is the test of primary interest. Significance values were based on Monte Carlo methods using 999 simulations. Results from the seven industrial sites were combined by pooling the likelihood ratios from each one and comparing their sum with values obtained from simulated data.

Table 2 Observed (O) cases and observed/expected ratios (O/E) by distance from refinery sites: all ages

Outer radius of band (km)	Multiple myeloma		All leukaemias		Hodgkin's lymphoma		Non-Hodgkin's lymphoma	
	O	O/E	O	O/E	O	O/E	O	O/E
0.5	4	0.46	14	0.74	14*	2.18	14	0.81
1	8	0.58	25	0.84	7	0.66	23	0.81
2	45	0.82	130	1.17	33	0.91	100	0.96
3	55	0.83	137	0.99	43	0.93	116	0.92
4.5	103	0.79	275	1.02	101	1.11	250	1.02
5.6	128	0.87	316	1.07	88	0.96	276	1.01
6.6	147	1.03	279	0.96	81	0.88	278	1.02
7.5	135	0.99	270	0.99	76	0.94	256	1.02

*Includes 1 duplicate registration, exclusion of which reduces the O/E ratio within 0.5 km to 2.02

Results

Results are presented here at all ages and for both sexes combined, and at ages 0–14 years. Age specific results, and results for each of the seven grouped industrial sites, are available on request. Over all refinery sites combined, there were 417 cases (439.9 expected) of lymphohaematopoeitic malignancy within 2 km of an oil refinery (observed/expected (O/E) ratio

0.95, 95% confidence interval (95% CI) 0.86 to 1.04); and 3827 cases (3902.4 expected) within 7.5 km (O/E 0.98, 95% CI 0.95 to 1.01, table 1). None of the age and cell type specific subgroups separately examined showed a significant increase in risk within 0–2 km or 0–7.5 km. The conditional Stone's test for Hodgkin's lymphoma, uncorrected for multiple testing, suggested a decline in risk (p=0.02) with distance from the sites, almost entirely due to an excess within 0.5 km (14* observed cases, 6.43 expected, table 2). None of the conditional Stone's tests for other malignancies (including Hodgkin's and non-Hodgkin's lymphoma combined) suggested a decline in risk with distance from the sites (tables 1 and 2). The significant (p=0.04) unconditional Stone's test for multiple myeloma at all ages reflected a deficit of these cancers from 0–7.5 km.

Discussion

Except for Hodgkin's disease, our study provides no evidence to suggest that populations living close to industrial complexes that include large oil refineries in Great Britain have an increased risk of lymphohaematopoeitic malignancy. This is consistent with the findings of broad scale studies of lymphatic and haematopoietic malignancy in areas containing petroleum works in the United States[4 15] and with occupational studies of oil refinery workers in the United Kingdom.[3] Although some studies have reported excesses of leukaemia in refinery workers,[16 17] a recent overview of cohort studies from the United Kingdom and North America suggests no excess for cell type specific leukaemias,[18] and oil refining probably contributes little to environmental levels of benzene and other petroleum products.[19]

The decline in risk with distance from oil refineries for Hodgkin's disease must be viewed in the context of multiple testing and the general tendency of Hodgkin's disease to cluster.[20] That benzene might be a contributory factor in Hodgkin's disease has been hypothesised by Aksoy *et al*,[21] and there have been reported associations of Hodgkin's disease with occupation in the chemical industry,[22] with other occupations entailing handling of chemicals,[23–25] and with exposure to diesel exhaust.[26] However, none of these studies provides direct evidence relating to the petrochemical industry. In our study, there was a twofold risk of Hodgkin's disease (14 cases) within 0.5 km of refineries, and it is this which accounts for the positive Stone's test. This is compatible with a highly localised environmental hazard, although the risk within 2 km was almost identical to the regional expectation, and it was fractionally below expectation within 7.5 km. There was an unexplained deficit of cases of multiple myeloma within 7.5 km.

*Checks on a sample of cases revealed a duplicate registration of Hodgkin's disease in the 15–64 year age-band within 0.5 km of a refinery. After exclusion of this duplicate the O/E ratio for Hodgkin's disease (all ages) within 2 km was 0.99 (95% CI 0.74–1.30); the conditional Stone's test remained significant (p=0.03).

Limitations to the interpretation of the study are imposed by several factors including lack of exposure information. Measurements of volatile organic compounds, including benzene, near petrochemical plants have been made previously.[27 28] For example, near the Baglan Bay plant,[9] most of the measurements were <5 ppb,[28] and with exposure to low concentrations of ambient benzene there is great uncertainty about the possible cancer risks.[29] Other factors limiting interpretation include the small area (ecological) nature of the study, uncertainties about population estimates for years between the census years and migration, and possible unmeasured confounding factors. The results cannot reliably be interpreted for specific cell types and age groups at indivdual sites, given the reliance on routine data sources and the fact that this would depend on multiple and non-independent analyses of subgroups, each with limited statistical power.

Overall the study is estimated to have had 80% power to detect an excess of around 11% in lymphohaematopoeitic malignancy at the 5% level within 2 km of refineries. We conclude that within the limitations of the small area approach based on routine data sources, there was no significant evidence of association between residence near to industrial sites containing major oil refineries and leukaemias or non-Hodgkin's lymphoma, and there was a negative association with multiple myeloma. Weak evidence of a positive association with Hodgkin's disease needs to be considered within the context of there being little, if any, other epidemiological evidence specifically relating Hodgkin's disease with the petrochemical industry.

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