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Leukaemia and occupation: a New Zealand Cancer Registry-based case–control Study

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Background To examine the association between occupation and leukaemia.

Methods We interviewed 225 cases (aged 20–75 years) notified to the New Zealand Cancer Registry during 2003–04, and 471 controls randomly selected from the Electoral Roll collecting demographic details, information on potential confounders and a comprehensive employment history. Associations between occupation and leukaemia were analysed using logistic regression adjusted for gender, age, ethnicity and smoking.

Results Elevated odds ratios (ORs) were observed in agricultural sectors including horticulture/fruit growing (OR: 2.62, 95% confidence interval (CI): 1.51, 4.55), plant nurseries (OR: 7.51, 95% CI: 1.85, 30.38) and vegetable growing (OR: 3.14, 95% CI: 1.18, 8.40); and appeared greater in women (ORs: 4.71, 7.75 and 7.98, respectively). Elevated ORs were also observed in market farmers/crop growers (OR: 1.84, 95% CI: 1.12, 3.02), field crop/vegetable growers (OR: 3.98, 95% CI: 1.46, 10.85), market gardeners (OR: 5.50, 95% CI: 1.59, 19.02), and nursery growers/workers (OR: 4.23, 95% CI: 1.34, 13.35); also greater in women (ORs: 3.48, 7.62, 15.74 and 11.70, respectively). These elevated ORs were predominantly for chronic lymphocytic leukaemia (CLL). Several associations persisted after semi-Bayes adjustment. Elevated ORs were observed in rubber/plastics products machine operators (OR: 3.76, 95% CI: 1.08, 13.08), predominantly in plastic product manufacturing. CLL was also elevated in tailors and dressmakers (OR: 7.01, 95% CI: 1.78, 27.68), cleaners (OR: 2.04, 95% CI: 1.00, 4.14) and builder's labourers (OR: 4.03, 95% CI: 1.30, 12.53).

Conclusions These findings suggest increased leukaemia risks associated with certain agricultural, manufacturing, construction and service occupations in New Zealand.

Keywords Leukaemia, occupation, case–control study, agricultural workers, plastics industry

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Introduction

The aetiology of adult leukaemia is largely unexplained, with only a relatively small proportion of cases able to be attributed to known hereditary, environmental and medical risk factors.[1] Smoking is believed to be a relatively weak risk factor for acute myeloid leukaemia (AML),[2,3] while predisposing genetic conditions and retroviral infections occur relatively rarely in the population. It has been estimated that up to 10% of cases in the USA[4] and Europe[5] are attributable to occupational exposures, and that the worldwide mortality and morbidity from leukaemia arising from occupational exposure to benzene, ionising radiation and ethylene oxide alone was 6800 deaths and 101 000 disability-adjusted life years (DALYs) in the year 2000.[6]

Although many other associations between exposure to specific agents and occupations have been observed in the last few decades, the findings have not been consistent.[7] Industries and occupations implicated include agriculture,[8,9] nuclear power generation,[10] electrical utilities,[11] nursing and health care,[12] oil refining and petrochemicals,[13] textile manufacturing,[14] welding,[15] driving[9] and the rubber industry.[16,17]

New Zealand studies of occupational risk factors for leukaemia have observed increased risk in electrical workers, electricians, telephone line workers, welders/flame cutters and radio/television repairers.[18–20] Elevated risk has also been observed in New Zealand agricultural and forestry workers,[21] abattoir workers,[22,23] particularly in those with over 2 years' employment in the industry and involved in contact with animals or animal tissues in their work,[24] and in livestock farmers.[21]

We conducted a population-based case–control study of adult-onset leukaemia and occupation in New Zealand. This study was conducted as part of an ongoing series of cancer registry-based case–control studies investigating occupational cancer in New Zealanders[25] which also included studies of non-Hodgkin's lymphoma[26] and bladder cancer.[27] We report here the leukaemia findings by occupation and industry.

Materials and methods

All incident cases of leukaemia (ICD-10, C91–C95) aged 20–75 years notified to the New Zealand Cancer Registry during 2003–04 were potential participants in this study. On receipt of notifications from the Cancer Registry, both the treating clinician and general practitioner (GP) were sent a letter explaining the study and asking for consent to contact their patients. From the total of 464 notifications nationwide, in 83 (17.9%) cases either the clinician or the GP did not provide consent to contact the patients. Of the 381 remaining cases, for 60 no contact could be established by mail and a further 73 were not eligible (e.g. never worked in New Zealand, current mental health problems or leukaemia was not the primary cancer). From the 248 remaining cases, 225 cases were interviewed for the study with 11 of these being next of kin interviews. Thus, if those known to be ineligible for the study are excluded, the response rate was approximately 57%.

Controls were randomly selected from the 2003 New Zealand Electoral Roll, frequency matched by age according to the age distribution of New Zealand cancer registrations for NHL, bladder cancer and leukaemia in 1999. A letter of invitation was sent to 1200 individuals, of which 100 were returned to sender and thus considered ineligible. Of the remaining 1100, for 348 (32%) contact could not be established. The addresses of these 348 non-responders were subsequently compared with the most recent electoral rolls of 2005 and 2006, and the 20 individuals who did not appear on the new electoral roll (or appeared with another address) were considered ineligible. Of the 752 for whom contact could be established, 92 were ineligible because of other reasons (e.g. never having worked in New Zealand). Of the remaining 660 controls, 187 declined to participate (28%), and 473 population controls were interviewed. Thus, if those known to be ineligible for the study are excluded, the response rate in the controls was approximately 48%.

The interview was conducted face-to-face at the home of the case or control by a trained interviewer with an occupational health nursing background. The questionnaire collected information on demographic factors, smoking and a full occupational history. Each job held since leaving school was listed, including the start date, date of termination, department and job, and the name, location and activity of the employer. Then, for each job with a minimum duration of 12 months, more detailed questions were asked, including a task description, types of equipment and materials used, self-reported exposures, workplace ventilation and use of protective equipment.

Each job was coded according to the New Zealand Standard Classification of Occupations (NZSCO 1999)[28] and the Australian and New Zealand Standard Industrial Classification (ANZSICO 2004—New Zealand use version 1996).[29] Coding of occupation was based on the full job and task description, rather than simply on the occupational title provided, to ensure that the code covered the actual tasks of each job. The industry code was based on the description of the activity of the employer. All coding was conducted blind to the case–control status of the participants.

Before the data analyses were conducted, a broad list of *a priori* high-risk occupations was constructed based on the international literature. This included teaching professionals, hairdressers and beauty therapists, market farmers and crop growers, market-oriented animal producers, painters and

paperhangers, electricians, blacksmiths and toolmakers, machinery mechanics and fitters, electrical and electronic instrument mechanics, leather goods makers, chemical processing plant operators, power generating plant operators, chemical products machine operators, rubber and plastics products machine operators, wood products machine operators, textile bleaching, dyeing and cleaning machine operators, slaughterers and leather goods assemblers. A similar list of *a priori* high-risk industries was also constructed, including agriculture, horticulture and fruit growing, plant nurseries, vegetable growing, kiwi fruit growing, beef cattle farming, sheep farming, other livestock farming, textile fibre, yarn and woven fabric manufacture, textile product manufacture, knitting mills, clothing manufacture, plastic product manufacturing, metal product manufacturing, iron and steel manufacture, electrical services, painting and decorating services, preschool education, school education, post-school education and other education.

We used unconditional regression using SAS V9.1 to estimate the odds ratio (OR) and 95% confidence interval (CI) for ever being employed in a specific occupation or industry, compared with never being employed in that occupation or industry. While ORs were calculated for all 958 occupational codes in NZSCO 1999 and all 684 industry codes in ANZSICO 2004, only those for the 235 occupations and 220 industries in which 10 or more study subjects had ever worked were evaluated further. ORs were adjusted for age (5-year age groups), gender and smoking. Study subjects were categorized as never-, ex- or ever-smokers, with those who reported having stopped smoking less than 2 years before the interview being considered current smokers. Logistic regression models were also adjusted for occupational class, using a continuous variable ranging between 20 and 90 based on the New Zealand Socio-Economic Index (NZSEI),[30] of the longest held occupation. Internal analyses were also conducted to establish whether increased duration in a certain occupation or industry was associated with an increased risk, using categorical variables for duration of each job (<2 years, 2–10 years and >10 years).

Semi-Bayes adjustment

Because of the large number of occupations and industries being considered, and the risk that the multiple comparisons inherent in this type of study would result in elevated ORs due to chance, a semi-Bayes (SB) approach[31] was also applied to determine which of the findings were the most robust. SB estimates were calculated using *R*, free software for statistical computing and graphics.[32] The input for the SB adjustments were the maximum likelihood estimates of beta (LogOR), resulting from the multivariate logistic regression for each occupation and industry. The variance of the true LogOR was assumed to be equal to 0.25. Assuming a normal distribution of the LogORs, this choice implies that the true LogORs are ranging from −1 to 1 and the ORs are within a 7-fold range of each other.[33]

For those occupations or industries which were not considered *a priori* to be of high risk for leukaemia, estimates were shrunk towards the mean for all occupations or industries. Similarly, for those occupations/industries which were considered *a priori* to be of high risk for leukaemia, estimates were shrunk towards the mean for all such occupations or industries. Here we report the findings for *a priori* high-risk occupations and industries, and for other occupations and industries that showed elevated or decreased risks in the current analyses.

The study had ethical approval from the Auckland Ethics Committee, approval number AKL/99/172.

Results

We interviewed 225 leukaemia cases and 473 population controls. Of these, two controls were excluded due to missing values in key variables, leaving 225 cases and 471 controls available for analysis (Table 1). Cases were 61% male while controls were 47% male, with a mean age of 56.2 in cases and 59.2 in controls. There were no significant differences between genders in the distribution of age, smoking and social class.

The proportions of notifications by major leukaemia subtypes were chronic lymphocytic leukaemia (CLL)—54%, AML—23%, chronic myeloid leukaemia (CML)—3.5%, acute lymphoblastic leukaemia (ALL)—4% and other—15.5%. As both the patient's treating clinician and GP had to consent before an approach could be made to schedule an interview, the elapsed time between the original notification to the Cancer Registry and case interviews was significant. The median time to interview was 9 months (Q25-5 months, Q75-18 months). By subtype the proportion of notified cases that were interviewed and included in the study were CLL—54%, CML—100%, AML—41%, ALL—56% and other—30%.

Occupational class distribution was similar for cases and controls, except for the lowest occupational class (Class 6), which had a higher frequency in the cases (34%) than in the controls (24%). We studied whether this difference in occupational class between cases and controls could have been a result of response-bias in the controls, i.e. that controls with lower occupational class were less likely to participate in the study. For this purpose, we compared the gender, age and occupational class distributions between the 471 participating controls and the 729 non-participating controls using the information available from the electoral roll. This showed that both gender and age were determinants of non-participation within the controls, with men and younger ages less likely to participate. Logistic regression, adjusting for age and gender, showed that being in the lowest occupational class (Class 6) was

Table 1 Characteristics of the study participants

	Study population				Males				Females			
	Cases		Controls		Cases		Controls		Cases		Controls	
	n	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%
Total	225	100	471	100	137	61	221	47	88	39	250	53
Age at interview												
20–50	54	24	62	13	28	20	26	12	26	30	36	14
51–60	72	32	137	29	45	33	63	28	27	30	74	30
61–70	85	38	260	55	57	42	126	57	28	32	134	54
71–75	14	6	12	3	7	5	6	3	7	8	6	2
Smoking[a]												
Never	91	40	232	49	50	36	91	41	41	48	141	57
Ex	94	42	200	42	67	49	109	49	27	31	91	37
Current	38	17	36	8	20	15	21	10	18	21	15	6
NZSEI (occupational class)												
Class 1 (75–90) highest	6	3	8	2	5	4	4	2	1	1	4	2
Class 2 (60–75)	15	7	31	7	10	7	13	6	5	6	18	7
Class 3 (50–60)	25	11	58	12	13	10	35	16	12	14	23	9
Class 4 (40–50)	39	17	90	19	21	15	40	18	18	20	50	20
Class 5 (30–40)	63	28	170	36	48	35	82	37	15	17	88	35
Class 6 (10–30) lowest	77	34	114	24	40	29	47	21	37	42	67	27

[a]Five missing values in female participants.

a determinant of non-participation in controls (OR: 1.8, 95% CI: 1.2–2.8). When compared with the highest occupational class, all other occupational classes had ORs of 1.0–1.1 for non-participation. Logistic regression models were therefore also adjusted for occupational class, although this adjustment did not alter the risk estimates.

A priori high-risk occupations and industries

Tables 2 and 3 list the findings for the *a priori* high-risk occupations and industries, both adjusted for and stratified by gender.

Teaching professionals

A reduction in risk was observed in those employed in the education sector overall (OR: 0.78, 95% CI: 0.51–1.20), particularly in teaching professionals (OR: 0.52, 95% CI 0.28–0.96) and in Primary school teachers (OR: 0.29, 95% CI: 0.10–0.84). The only educational occupation in which an elevated OR was observed was that of technical and further education (OR: 3.25, 95% CI: 1.09–9.70), and an increase with increasing duration of employment was suggested (ORs of 0.96, 1.64 and 2.71 for employment for <2 years, 2–10 years and >10 years, respectively).

Agricultural workers

A marginal elevation in ORs was observed in all agricultural and fisheries occupations (OR: 1.37, 95% CI: 0.94–1.99), with elevated risk apparent in market farmers and crop growers (OR: 1.84, 95% CI: 1.12–3.02), field crop and vegetable growers (OR: 3.98, 95% CI 1.46–10.85), market gardeners (OR: 5.50, 95% CI: 1.59–19.02), and nursery growers and workers (OR: 4.23, 95% CI: 1.34–13.35). In each instance, the increase appeared greater in women (ORs 3.48, 7.62, 15.74 and 11.70, respectively) than in men (ORs 1.15, 2.38, 2.25 and 0.52, respectively), although no clear trend of increasing risk with increasing duration of employment was evident. There were similar findings for employment in the agricultural sector overall (OR: 1.42, 95% CI: 0.95–2.11), with elevated ORs observed in horticulture and fruit growing (OR: 2.62, 95% CI: 1.51–4.55), plant nurseries (OR: 7.51, 95% CI: 1.85–30.38), vegetable growing (OR: 3.14, 95% CI: 1.18–8.40) and other livestock farming (OR: 9.06, 95% CI: 1.86–44.23). The excess risks appeared greater in women in horticulture and fruit growing (OR: 4.71, 95% CI: 2.09–10.62), plant nurseries (OR: 7.75, 95% CI 1.83–32.90) and in vegetable growing (OR: 7.98, 95% CI: 1.33–47.75), while the excess risk in other livestock farming was predominantly in men (OR: 16.04, 95% CI: 1.91–134.9).

Rubber and plastics workers

Elevated ORs were also observed in rubber and plastics products machine operators (OR: 3.76,

Table 2 ORs and 95% CIs for *a priori* high-risk occupations

A priori high-risk occupation for leukaemia	All (225 cases, 471 controls)			Men (137 cases, 221 controls)			Women (88 cases, 250 controls)		
	Cases/controls (*n*)	OR	95% CI	Cases/controls (*n*)	OR	95% CI	Cases/controls (*n*)	OR	95% CI
Teaching professionals									
23-Teaching professionals	17/73	0.52	0.28–0.96	6/21	0.47	0.18–1.24	11/52	0.55	0.23–1.29
231-Tertiary teaching professionals	3/21	0.38	0.11–1.36	2/8	0.47	0.09–2.38	1/13	0.27	0.03–2.24
232-Secondary teaching professionals	6/28	0.47	0.17–1.30	3/5	0.88	0.20–3.91	3/23	0.27	0.06–1.27
233-Primary and early childhood teaching professionals	10/39	0.55	0.24–1.55	1/11	0.16	0.02–1.28	9/28	0.87	0.34–2.22
Agricultural workers									
6-Agriculture and fishery workers	73/118	1.37	0.94–1.99	51/75	1.30	0.81–2.08	22/43	1.37	0.72–2.63
61-Market-oriented farmers and crop growers	73/118	1.37	0.94–1.99	51/75	1.30	0.81–2.08	22/43	1.37	0.72–2.63
611-Market farmers and crop growers	37/44	1.84	1.12–3.02	19/29	1.15	0.61–2.19	18/15	3.48	1.54–7.86
6111-Field crop and vegetable growers	11/7	3.98	1.46–10.85	5/5	2.38	0.65–8.70	6/2	7.62	1.33–43.76
61112-Market gardener and related worker	9/4	5.50	1.59–19.02	3/3	2.25	0.43–11.64	6/1	15.74	1.66–149.1
6112-Fruit growers	17/20	2.01	0.99–4.10	8/10	1.55	0.57–4.18	9/10	2.52	0.88–7.22
6113-Gardeners and nursery workers	15/18	1.45	0.69–3.03	7/14	0.70	0.26–1.84	8/4	5.02	1.35–18.63
61131-Nursery grower, nursery worker	9/5	4.23	1.34–13.35	1/3	0.52	0.05–5.39	8/2	11.70	2.28–59.91
61133-Grounds or green keeper	1/10	0.19	0.02–1.55	1/9	0.19	0.02–1.59	0/1	–	–
612-Market-oriented animal producers	39/81	0.98	0.62–1.54	33/50	1.23	0.72–2.10	6/31	0.49	0.18–1.33
6121-Livestock producers	21/43	1.10	0.62–1.97	18/28	1.30	0.67–2.54	3/15	0.58	0.15–2.26
61211-Dairy farmer, dairy farm worker	13/32	0.83	0.41–1.67	11/21	0.94	0.43–2.08	2/11	0.47	0.09–2.46
61212-Sheep farmer, sheep farm worker	4/14	0.73	0.23–2.32	4/10	0.86	0.25–2.90	0/4	–	–
6122-Mixed livestock producers	7/19	0.81	0.33–2.03	6/11	1.00	0.35–2.84	1/8	0.34	0.04–3.16
6125-Crop and livestock producers	13/29	0.91	0.44–1.89	12/20	1.10	0.50–2.41	1/9	0.37	0.04–3.31
Painters and paperhangers									
7124-Painters and paperhangers	4/10	0.61	0.18–2.07	4/10	0.60	0.18–2.02	0/0	–	–

(continued)

Table 2 Continued

A priori high-risk occupation for leukaemia	All (225 cases, 471 controls) Cases/controls (*n*)	OR	95% CI	Men (137 cases, 221 controls) Cases/controls (*n*)	OR	95% CI	Women (88 cases, 250 controls) Cases/controls (*n*)	OR	95% CI
Electricians									
713-Electricians	5/5	1.69	0.46–6.22	5/5	1.63	0.45–5.93	0/0	–	–
Blacksmiths, toolmakers and related workers									
722-Blacksmiths, toolmakers and related workers	5/6	1.71	0.49–5.92	5/6	1.69	0.49–5.81	0/0	–	–
Machinery mechanics and fitters									
7231-Machinery mechanics and fitters	9/23	0.65	0.29–1.50	8/22	0.55	0.23–1.31	1/1	6.29	0.37–106.4
72311-Machinery mechanic	5/8	1.05	0.33–3.41	5/7	1.16	0.35–3.82	0/1	–	–
72312-Motor mechanic	6/18	0.57	0.21–1.51	5/18	0.43	0.15–1.21	1/0	–	–
Chemical processing plant operators									
815-Chemical processing plant operators	2/8	0.32	0.06–1.73	2/8	0.37	0.07–1.88	0/0	–	–
Chemical products machine operators									
822-Chemical products machine operator	3/7	0.58	0.14–2.45	3/5	0.82	0.18–3.75	0/2	–	–
Rubber and plastics products machine operators									
823-Rubber and plastics products machine operators	9/4	3.76	1.08–13.08	9/3	4.62	1.19–17.99	0/1	–	–
Textile bleaching, dyeing and cleaning machine operator									
8264-Textile bleaching, dyeing and cleaning machine operator	6/10	2.07	0.70–6.09	1/0	–	–	5/10	2.20	0.68–7.08
Slaughterer									
82712-Slaughterer	14/16	1.44	0.65–3.21	13/14	1.57	0.67–3.68	1/2	2.50	0.22–28.99

Numbers were too small (fewer than 10 cases and controls) for the following *a priori* high-risk occupations: hairdressers, electrical and electronic instruments mechanics, leather goods manufacturers, power generating and related plant operators, wood products machine operators, meat processing workers, leather goods assemblers.
OR adjusted for gender, age group, smoking status, Maori ethnicity and occupational status.

Table 3 ORs and 95% CIs for *a priori* high-risk industries

A priori high-risk industry for leukaemia	All (225 cases, 471 controls)			Men (137 cases, 221 controls)			Women (88 cases, 250 controls)		
	Cases/controls (*n*)	OR	95% CI	Cases/controls (*n*)	OR	95% CI	Cases/controls (*n*)	OR	95% CI
Agriculture									
A01-Agriculture	59/101	1.42	0.95-2.11	39/58	1.35	0.81–2.26	20/43	1.38	0.71–2.69
A011-Horticulture and fruit growing	32/32	2.62	1.51–4.55	13/18	1.43	0.66–3.12	19/14	4.71	2.09–10.62
A0111-Plant nurseries	8/3	7.51	1.85–30.38	1/0	–	–	7/3	7.75	1.83–32.90
A0113-Vegetable growing	10/8	3.14	1.18–8.40	5/6	1.73	0.51–5.93	5/2	7.98	1.33–47.75
A0117-Kiwi fruit growing	6/6	2.39	0.74–7.72	3/4	1.41	0.30–6.57	3/2	4.87	0.74–31.87
A012-Grain, sheep and beef cattle farming	14/39	0.77	0.39–1.50	13/24	0.98	0.47–2.07	1/15	0.19	0.02–1.58
A0123-Sheep-beef cattle farming	5/24	0.48	0.17–1.32	4/12	0.59	0.18–1.96	1/12	0.24	0.03–2.04
A0124-Sheep farming	5/18	0.52	0.18–1.51	5/14	0.60	0.20–1.78	0/4	–	–
A013-Dairy cattle farming	12/36	0.68	0.34–1.38	9/24	0.64	0.28–1.45	3/12	0.76	0.19–3.10
A015-Other livestock farming	8/2	9.06	1.86–44.23	7/1	16.04	1.91–134.9	1/1	2.60	0.15–44.62
Textile, clothing, footwear and leather manufacturing									
C22-Textile, clothing, footwear and leather manufacturing	24/50	1.29	0.73–2.27	12/10	1.98	0.80–4.87	12/40	1.06	0.48–2.31
C221-Textile fibre, yarn and woven fabric manufacturing	5/6	1.88	0.50–7.05	4/1	5.54	0.57–54.0	1/5	0.72	0.07–7.27
C222-Textile product manufacturing	8/14	1.31	0.50–3.42	3/4	1.17	0.25–5.57	5/10	1.68	0.49–5.74
C223-Knitting mills	3/7	1.41	0.35–5.68	1/2	1.18	0.10–13.39	2/5	1.64	0.29–9.38
C224-Clothing manufacturing	11/27	1.30	0.59–2.84	3/0	–	–	8/27	0.99	0.40–2.48
Plastic product manufacturing									
C256-Plastic product manufacturing	10/8	2.66	0.98–7.23	8/4	3.78	1.06–13.45	2/4	1.36	0.20–9.30
Metal product manufacturing									
C27-Metal product manufacturing	23/30	1.54	0.84–2.82	16/20	1.28	0.62–2.63	7/10	2.27	0.76–6.75
C271-Iron and steel manufacturing	6/7	2.07	0.65–6.57	5/4	2.15	0.55–8.44	1/3	1.74	0.17–17.44
Electrical services									
E4232-Electrical services	6/10	1.28	0.44–3.73	5/5	1.73	0.48–6.25	1/5	0.63	0.07–5.87

(continued)

Table 3 Continued

A priori high-risk industry for leukaemia	All (225 cases, 471 controls) Cases/controls (*n*)	OR	95% CI	Men (137 cases, 221 controls) Cases/controls (*n*)	OR	95% CI	Women (88 cases, 250 controls) Cases/controls (*n*)	OR	95% CI
Painting and decorating services									
E4244-Painting and decorating services	3/9	0.40	0.10–1.56	2/7	0.34	0.07–1.74	1/2	0.70	0.06–8.35
Education									
N84-Education	45/128	0.78	0.51–1.20	14/39	0.52	0.32–1.26	31/89	1.12	0.63–2.01
N841-Preschool education	5/7	2.05	0.61–6.89	0/0	–	–	5/7	2.01	0.57–7.14
N842-School education	18/85	0.48	0.27–0.87	6/18	0.55	0.21–1.46	12/67	0.47	0.22–1.01
N843-Post-School education	23/37	1.45	0.80–2.65	9/16	0.86	0.35–2.15	14/21	2.05	0.91–4.62
N8431-Higher education	10/24	1.00	0.44–2.23	5/10	0.77	0.24–2.48	5/14	1.23	0.41–3.75
N8432-Technical and further education	14/16	1.84	0.83–4.09	4/8	0.74	0.21–2.64	10/8	3.25	1.09–9.70
N844-Other education	10/51	0.47	0.23–0.98	2/19	0.16	0.04–0.73	8/32	0.95	0.39–2.31

Numbers were too small (fewer than 10 cases and controls) for the following *a priori* high-risk industries: rubber product manufacturing, chemical product manufacturing.
$^*P < 0.05$, $^{**}P < 0.01$.

95% CI: 1.08–13.08), predominantly in men (OR: 4.62, 95% CI: 1.19–17.99) and in those with 2–10 years employment (OR: 8.78, 95% CI: 0.94–81.62). The risk also appeared to be most strongly associated with jobs as plastics rather than rubber machine operators, and a similarly increased risk was observed for work in the plastic product manufacturing industry (OR: 2.66, 95% CI: 0.98–7.23).

Other a priori occupations and industries

Elevated ORs were observed for electricians (OR: 1.69, 95% CI: 0.46–6.22), blacksmiths and toolmakers (OR: 1.71, 95% CI: 0.49–5.92) textile bleaching, dyeing and cleaning machine operators (OR: 2.07, 95% CI: 0.70–6.09) and slaughterers (OR: 1.44, 95% CI: 0.65–3.21). No clear trends of increasing risk with increasing duration of employment were evident.

Semi-Bayes adjustment of the *a priori* high-risk occupations and industries

Ever being employed in one or more of the *a priori* high-risk occupations and industries was associated with little or no overall increased risk for leukaemia ($OR_{a\ priori\ occupation}$: 0.97, 95% CI: 0.69–1.37; $OR_{a\ priori\ industry}$: 1.25. 95% CI: 0.89–1.77).

All risk estimates for occupations and industries were also regressed towards this mean using SB adjustment. In the *a priori* high-risk occupations, this generally resulted in an attenuation of the ORs, although the adjusted ORs for market farmers and crop growers (OR_{SB}: 1.66, 95% CI: 1.06–2.59) and for field crop and vegetable growers (OR_{SB}: 2.07, 95% CI: 1.00–4.29) remained after SB adjustment. In the *a priori* high-risk industries, the SB adjustment resulted in attenuated risk estimates in all sectors except for horticulture and fruit growing (OR_{SB}: 2.13, 95% CI: 1.30–3.48).

A posteriori high- and low-risk occupations and industries: the occupations and industries in which increased or decreased risk was observed, but which were not considered *a priori* high risk, are listed in Table 4. The occupation of secretary showed a decreased risk, but this was no longer evident after SB adjustment. Four occupations showed increased risk, but only the occupation of physical science and engineering associate professionals remained after SB adjustment (OR_{SB}: 1.74, 95% CI: 1.03–2.94). Although the increase in risk with increasing duration of employment as a physical science and engineering associate professional was not monotonic, the risk for those with >10 years employment was increased (OR: 2.88, 95% CI: 1.32–6.28). No industry categories showed reduced risk, but seven showed an increase in risk. Of these only personal and household good retailing (OR_{SB}: 1.85, 95% CI: 1.25–2.75) and department stores (OR_{SB}: 2.20, 95% CI: 1.19–4.07) remained after SB adjustment.

Although numbers of cases of specific subtypes were small, associations between CLL and AML and ever

Table 4 ORs and 95% CIs for *a posteriori* high- and low-risk ($P < 0.05$) occupations and industries (excluding the *a priori* high-risk occupations listed in Tables 2 and 3)

A posteriori high and low risk occupations and industries for leukaemia	Cases/controls (*n*)	Not adjusted		Semi-Bayes adjusted	
		OR	95% CI	OR	95% CI
Occupations—reduced risk					
4114-Secretaries	7/49	0.41	0.17–0.96	0.63	0.32–1.22
Occupations—increased risk					
31-Physical science and engineering associate professionals	29/27	2.08	1.15–3.79	1.74	1.03–2.94
743-Tailors and dressmakers	6/4	4.73	1.26–17.83	1.84	0.81–4.18
911-Building caretakers and cleaners	25/34	1.85	1.02–3.35	1.60	0.96–2.69
91512-Builder's labourer	13/6	3.56	1.27–9.99	1.98	0.95–4.11
Industries—reduced risk					
None identified					
Industries—increased risk					
E425-Other construction services	9/4	4.33	1.22–15.31	1.83	0.82–4.07
G-Retail trade	98/181	1.45	1.01–2.07	1.39	0.99–1.95
G52-Personal and household good retailing	63/94	2.06	1.35–3.13	1.85	1.25–2.75
G521-Department stores	18/16	3.30	1.57–6.97	2.20	1.19–4.07
G5233-Domestic hardware and houseware retailing	7/6	3.12	1.00–9.76	1.73	0.81–3.70
H573-Cafes and restaurants	20/28	1.94	1.03–3.68	1.64	0.95–2.81
K74-Insurance	7/4	4.23	1.12–15.99	1.70	0.75–3.86
Q9629-Interest groups nec	7/4	5.45	1.49–19.96	1.99	0.88–4.49

OR adjusted for gender, age group, smoking status and occupational status.

being employed in certain occupations where >5 cases were observed were also investigated using the same logistic regression models, and the results are shown in Table 5. For CLL, these also showed reduced ORs for teaching professionals, and elevated ORs for physical science and engineering associate professionals, horticultural industry workers, tailors and dressmakers, building and related workers, cleaners and builder's labourers. The small number of AML cases included (43) gave little power for this analysis; however, elevated ORs were observed for the subcategories fruit growers and workers and building trades workers.

Discussion

This New Zealand case–control study has confirmed previously observed associations between ever having worked as an agricultural worker and elevated risk for leukaemia. We found elevated ORs in market farmers and crop growers, field crop and vegetable growers, market gardeners and nursery growers, in horticulture and fruit growing and in vegetable growing. For the category Market farmer and Crop growers in particular, and although the numbers were small also for subcategories of this occupational group such as gardeners and nursery workers, the risks appeared to be higher in women than in men. The only animal related agricultural occupation to show an increase in risk was the other livestock farming category which includes pig and horse farming but not sheep, beef, dairy or poultry farming. The gender differences in risk observed persisted after SB adjustment for female market farmers and crop growers (OR_{SB}: 2.24, 95% CI: 1.12–4.46) compared with males (OR_{SB}: 1.14, 95% CI: 0.66–1.95). Although the case numbers for the more detailed occupational subgroups were small, similar differences were suggested for female market gardeners and related workers (OR_{SB}: 2.02, 95% CI: 0.86–4.78) compared with males (OR_{SB}: 0.87, 95% CI 0.43–1.74) and for female nursery grower/nursery worker (OR_{SB}: 2.26, 95% CI: 0.85–5.59) compared with males (OR_{SB}: 1.05, 95% CI: 0.42–2.61). In the analysis by industry the differences remained after SB adjustment for females in horticulture and fruit growing (OR_{SB}: 2.69, 95% CI: 1.34–5.40) compared with males (OR_{SB}: 1.30, 95% CI: 0.70–2.39), and for females in vegetable growing (OR_{SB}: 2.00, 95% CI: 0.79–5.09) compared with males (OR_{SB}: 1.32, 95% CI: 0.61–2.86).

Elevated risk was also associated with ever having worked as a rubber and plastics products machine operator, and with ever having worked in the plastic product manufacturing industry. Several other occupations and industries including electricians,

Table 5 Odds ratios and 95% CIs for selected occupations by leukaemia subtype

Occupation	CLL(135 cases, 471 controls)				AML (43 cases, 471 controls)			
	Cases/ controls	OR	95%CI	*P*-value	Cases/ controls	OR	95%CI	*P*-value
1-Legislators and administrators	46/126	1.40	0.89–2.18	0.1419	10/126	0.98	0.44–2.14	0.9511
2-Professionals	31/158	0.77	0.45–1.30	0.3256	8/158	0.49	0.20–1.21	0.1230
23-Teaching professionals	7/73	0.35	0.14–0.85	0.0213	–	–	–	–
3-Technicians and associate professionals	41/138	0.97	0.62–1.53	0.9040	11/138	0.79	0.37–1.68	0.5351
31-Physical Science and Engineering Associate Professionals	19/27	2.42	1.22–4.77	0.0112	5/27	2.97	0.97–9.12	0.0563
4-Clerks	52/192	1.23	0.79–1.91	0.3615	20/192	1.07	0.52–2.20	0.8625
5-Service and sales workers	54/185	1.22	0.78–1.88	0.3825	20/185	1.05	0.52–2.13	0.8890
6-Agricultural workers	47/118	1.50	0.96–2.34	0.0727	14/118	1.41	0.68–2.90	0.3581
611-Market farmers and crop growers	22/44	1.89	1.06–3.37	0.0322	9/44	2.26	0.95–5.39	0.0652
6111-Field crop and vegetable growers	6/7	3.58	1.12–11.43	0.0316	–	–	–	–
61121-Fruit growers, worker	7/20	1.50	0.60–3.75	0.3831	6/20	3.34	1.12–9.99	0.0308
61131-Nursery grower, nursery worker	6/5	3.85	1.06–13.93	0.0401	–	–	–	–
7-Trades workers	39/110	0.96	0.59–1.59	0.8841	9/110	1.10	0.44–2.73	0.8392
71-Building trades workers	14/46	0.80	0.40–1.58	0.5155	7/46	2.86	1.01–8.15	0.0484
743-Tailors and dressmakers	5/4	7.01	1.78–27.68	0.0054	–	–	–	–
8-Plant and machine operators and assemblers	59/149	1.36	0.87–2.13	0.1809	17/149	1.49	0.70–3.17	0.3044
84-Building and related workers	7/6	3.78	1.19–11.98	0.0240	–	–	–	–
9-Elementary workers	39/84	1.56	0.96–2.54	0.0701	10/84	1.17	0.50–2.73	0.7107
91111-Cleaners	15/32	2.04	1.00–4.14	0.0495	5/32	1.58	0.50–5.03	0.4400
91512-Builder's labourers	8/6	4.03	1.30–12.53	0.0159	–	–	–	–

OR: Odds Ratio, adjusted for gender, age group, smoking status, Maori ethnicity and occupational status.
95% CI: 95% confidence interval of the odds ratio.

blacksmiths and toolmakers, textile bleaching, dyeing and cleaning machine operators and slaughterers may also have an increased risk for leukaemia in the New Zealand population. Among the occupations and industries considered *a priori* high risk, SB adjustment indicated that the most robust findings of this study were the increased risks of leukaemia for ever having worked in the agricultural occupations of market farmers and crop growers and field crop and vegetable growers, and also for ever having worked in horticulture and fruit growing.

The study has also identified associations between leukaemia and a number of occupations and industries not considered *a priori* to be linked with leukaemia. These include working in the occupations physical science and engineering associate professionals, tailors and dressmakers, building caretakers and cleaners and builders labourers; and in industries including other construction services (primarily landscaping services), retail trade including personal and household good retailing, department stores and domestic hardware and houseware retailing; in cafes and restaurants; in insurance and in 'interest groups nec'. Of these the associations with physical science and engineering associate professionals, personal and household good retailing and department stores remained after SB adjustment.

One of the advantages of this study was that it was a population-based study using the New Zealand Cancer Registry to identify incident cases. This registry is reported to have maintained ~95% complete registration of tumours from all known sources of cancer diagnoses in public and private hospitals, death certificates and autopsy reports for the period 1983–87,[34] and this situation is reported to have improved further since passage of the Cancer Registry Act 1993[35] which made registration compulsory. The sampling frame used for the selection of controls was the national electoral roll, and as all New Zealand citizens and permanent residents aged 18 years and older are legally required to register to vote the controls in this study represent the source population for the cases. This is reflected in the consistency between occupational distribution of controls in this study and that observed in the national census. For example the broad industry category of agriculture, forestry and fishing employs 7.25% of the employed workforce in New Zealand,[36] while the percentage of

controls in this study who had ever been employed in this industry was 6.8%. Thus, it does not appear that significant selection bias has occurred in the controls, despite the relatively low response rate.

A disadvantage of any occupational study where multiple comparisons are made for many occupations is the risk of that some findings may be elevated by chance. For this reason, we calculated SB adjusted estimates. This generally resulted in attenuation of the risk estimates towards the null, particularly for those estimates based on small numbers, although several risk estimates remained elevated.

Due to the size of the study, we were only able to perform analyses by the subtypes CLL and AML, whereas studying leukaemia as a single entity rather than as specific subtypes would tend to dilute any subtype specific effect and hide true associations rather than identifying spurious associations. Although these stratified analyses suggest that CLL predominates in field crop and vegetable growers, nursery growers/workers, tailors and dressmakers, building and related workers, builder's labourers and cleaners, and that AML predominates in fruit growers/workers and building trades workers, both subtypes are elevated in physical science and engineering associate professionals and in market farmers and crop growers.

Agricultural workers

The increased ORs observed in agricultural workers working with crops or livestock is the most striking finding of this study, and is consistent with previous findings in many countries.[7,8,37–40] Apart from the elevated ORs observed in other livestock farming, however, the increased risk in this study was associated primarily with the horticulture and cropping agricultural sectors and jobs rather than with the jobs involving animal contact that have been found previously in other countries,[41,42] and in previous New Zealand studies.[20–23]

The stronger relative risks between occupation and leukaemia found in women rather than in men in agricultural occupations was also a striking finding of this study. This has been found in previous studies of workers in horticultural occupations in Italy[37] and plant farming occupations in the United States,[43] among the wives of pesticide users in Italy[40] and in workers with occupational exposure to agricultural chemicals in the United States[38] and Italy.[37,44] The leukaemia relative risk estimates observed in women with exposure to specific fungicides and insecticides in these studies include statistically significant ORs of up to 8.5, which are within the range of ORs found in the current study. It is not clear why this gender difference exists, but it has been hypothesized that it may be due either to the different tasks (and therefore potential for exposure) traditionally performed by men and women in horticultural occupations, or to the fact that some of these chemicals are endocrine disruptors that affect women in a different way than they do men.[38]

Plastic and rubber products manufacture

There are numerous reports of excess risk in the rubber industry,[15,16] and in this study we found that employment as a plastic and rubber products machine operator was associated with increased risk of leukaemia. Our strongest findings, however, were for employment in the plastics rather than the rubber industry. Elevated ORs have been observed in the synthetic rubber and plastics industries in several countries,[14,39,45] with 1,3-butadiene (which is considered a probable carcinogen by IARC (group 2A) and is being re-evaluated in 2007) implicated as the most likely cause.

Of the other occupations considered *a priori* high risk that showed moderately elevated ORs, similar observations in electricians and slaughterers have been made in New Zealand studies in the 1980s[17–19,21–23] and in numerous studies in other countries.[7] Although occupational classification schemes differ, occupations similar to the category of textile bleaching, dyeing and cleaning machine operators have been observed to have excess risk in studies of drycleaners in dry-cleaning workers in Sweden[46] and North America,[39] and also in textile dye manufacturing in North America.[39] The elevation seen in those employed as a blacksmith and toolmaker is consistent with the excess risk previously observed in the metalwork machinery and equipment industry.[9]

Of the occupations and industries not considered *a priori* of high risk, the elevated ORs observed for employment as a physical science and engineering associate professional remained elevated after SB adjustment. This occupational category includes technicians in a wide range of fields including construction, civil engineering, electrical engineering, telecommunications, avionics, chemical engineering, photography, computers, broadcasting and transmitting, medical radiation, sea transport and air traffic control, which are all jobs with the potential for exposure to a variety of chemicals and electromagnetic fields. Elevated ORs were also observed amongst those working in the retail industry, and in particular in personal and household good retailing or department stores, and these risk estimates also remained after SB adjustment. Although it is difficult to speculate on a possible causative exposure in these occupations, a similar excess has been observed previously in those employed in retail stores for >10 years in the USA.[9]

In conclusion, this study observed a diverse list of high-risk occupations for leukaemia largely in concordance with previous studies in New Zealand and elsewhere. Most notably, leukaemia risk was increased for agricultural workers (and most strongly in women) and for rubber and plastics machine operators. Elevated ORs were observed for several

other occupations and industries previously shown to be associated with leukaemia including electricians, blacksmiths and toolmakers, textile bleaching, tailors and dressmakers, dyeing and cleaning machine operators, cleaners and builder's labourers.

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KEY MESSAGES

- It has been estimated that up to 10% of adult leukaemia in the USA and Europe is attributable to occupational exposures.
- We investigated associations between occupation and adult leukaemia in a population-based case–control study using incident cases notified to the New Zealand Cancer Registry during 2003 and 2004, and controls randomly selected from the New Zealand Electoral Roll.
- Using models adjusted for age, gender, ethnicity and smoking, we observed elevated odds ratios for leukaemia in several occupations and industries, predominantly for CLL, and associations persisted after semi-Bayes adjustment.
- These results suggest increased leukaemia risk in horticultural workers, plastic product manufacturers, tailors and dressmakers, cleaners and builder's labourers.

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