

Exhibit 247

Case-control study of high risk occupations for bladder cancer in New Zealand

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We conducted a nationwide case-control study of bladder cancer in adult New Zealanders to identify occupations that may contribute to the risk of bladder cancer in the New Zealand population. A total of 213 incident cases of bladder cancer (age 25–70 years) notified to the New Zealand Cancer Registry during 2003 and 2004, and 471 population controls, were interviewed face-to-face. The questionnaire collected demographic information and a full occupational history. The relative risks for bladder cancer associated with ever being employed in particular occupations and industries were calculated by unconditional logistic regression adjusting for age, sex, smoking and socio-economic status. Estimates were subsequently semi-Bayes adjusted to account for the large number of occupations and industries being considered. An elevated bladder cancer risk was observed for hairdressers (odds ratio (OR) 9.15 95% Confidence Interval (95%CI) 1.60–62.22), and sewing machinists (OR 3.07 95%CI 1.35–6.96). Significantly increased risks were not observed for several other occupations that have been reported in previous studies, including sales assistants (OR 1.03 95%CI 0.64–1.67), painters and paperhangers (OR 1.42 95%CI 0.56–3.60), sheet metal workers (OR 0.39, 95%CI 0.15–1.00), printing trades workers (OR 1.11 95%CI 0.41–3.05) and truck drivers (OR 1.36 95%CI 0.60–3.09), although the elevated odds ratios for painters, printers and truck drivers are consistent with excesses observed in other studies. Nonsignificantly increased risks were observed for tailors and dressmakers (OR 2.84 95%CI 0.62–13.05), rubber and plastics products machine operators (OR 2.82 95%CI 0.75–10.67), building workers (OR 2.15, 95%CI 0.68–6.73), and female market farmers and crop growers (OR 2.05 95%CI 0.72–5.83). In conclusion, this study has confirmed that hairdressers and sewing machinists are high risk occupations for bladder cancer in New Zealand, and has identified several other occupations and industries of high bladder cancer risk that merit further study.

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Occupational exposure to a range of carcinogens remains widespread. For example, it has been estimated that 23% of the European Union workforce (or 32 million workers) is currently exposed to one or more agents in their workplace that have been classified by the International Agency for Research on Cancer (IARC) as recognized (Group 1), probable (Group 2A), or selected possible (Group 2B) occupational carcinogens.¹ Similarly, Infante² has estimated that 20 million US workers are exposed to occupational lung carcinogens, namely 12,864,000 to IARC Group 1 and a further 7,321,000 to Group 2A lung carcinogens.

A recent literature review³ concluded that workplace exposures account for 5–25% of all bladder cancer cases. Aromatic amines are currently the only agents whose association with bladder cancer has been clearly established, but other agents such as paints, dyes, metals, industrial oils/cutting fluids and polycyclic aromatic hydrocarbons (PAHs) have also been linked to increased bladder cancer risks.³ Occupational exposures to these potential bladder carcinogens occur in a number of industries including aromatic amine manufacture, dyestuff manufacture and use, rubber and

cable manufacture, textile and leather works, driving occupations, and the coal, tar, aluminium, and gas industries.³

It is unlikely that New Zealand workplace conditions differ markedly from those in other developed countries in terms of their occupational cancer risk, but the type and range of industry may differ in New Zealand. In 2001, the Massey University Centre for Public Health Research and the New Zealand Department of Labor, therefore, commenced a project to evaluate occupational contributions to the development of leukemia, non-Hodgkin's lymphoma and bladder cancer.⁴ The controls for the 3 studies have been pooled to provide greater precision for the control exposure prevalence estimates. Here, we present findings for the bladder cancer study to identify occupations that may also contribute to the risk of bladder cancer in the New Zealand population.

Methods

Potential cases in the study were all incident cases of bladder cancer, aged 25–70 years, reported to the New Zealand Cancer Registry during 2003 and 2004, a total of 381 notifications nationwide. Both the treating clinician and general practitioner (GP) of the patient were sent a letter explaining the study and asking for consent to contact the patient. For 23 (6.0%) of the notifications, either the clinician or the GP did not provide consent to contact the patient. Of the 358 remaining cases, for 80 no contact could be established by mail and a further 46 were not eligible (e.g. never worked in New Zealand, mental health problems, bladder cancer was not the primary cancer). From the 232 remaining cases, 213 (91.8%) cases were interviewed for the study. Three of these were next of kin interviews. Thus, among those eligible for the study, the response rate was ~64%.

Controls were randomly selected from the New Zealand Electoral Roll for 2003, frequency matched by age according to the age distribution of cancer registrations for NHL, bladder cancer and leukemia in 1999. A letter of invitation was sent to 1,200 individuals, of which 100 were returned to sender and thus considered ineligible. Of the remaining 1,100, for 348 (32%) contact could not be established. Their addresses were subsequently compared to the most recent Electoral Rolls of 2005 and 2006. Of the 348 nonresponders, 20 did not appear or appeared with another address on the new Electoral Roll and were thus considered ineligible. Of the 752 for whom contact could be established, 92 were ineligible because of other reasons (e.g. never worked in New Zealand). Of the remaining 660 controls, 187 declined to participate (28%), and

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473 population controls were interviewed. Thus, among those eligible for the study, the response rate in the controls was ~48%.

A face-to-face interview was conducted at the home of the case or control by a trained interviewer with an occupational health nursing background. The questionnaire collected information on demographics, smoking and a full occupational history. Each job held since leaving school was listed, including the start year, year of termination, department and job title, and name, location and activity of employer. For each job held at least 12 months, additional information was sought, including a task description, use of machines and materials, self reported exposures, workplace ventilation and use of protective equipment. When the same job was held at 2 different time periods, a single set of additional information was obtained.

Each job was coded according to the 1999 New Zealand Standard Classification of Occupations (NZSCO 1999)⁵ (hereafter referred to as the occupational code) and the Australian and New Zealand Standard Industrial Classification (New Zealand use version 1996)⁶ (hereafter referred to as the industry code). The occupational code was based on the full job and task description, rather than on the occupational title alone, to ensure that the code covered the actual tasks of each job. The industry code was based on the activity of the employer. All coding was done 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. To identify these, we conducted a PubMed search from 1980 onwards for English-language publications of studies that contained both of the key words 'bladder cancer' and 'occupation' or 'occupational exposures' and prepared summary tables of the positive findings. These were then reviewed by the OSH Cancer Panel⁴ which identified occupations and occupational exposures for which it was considered that there was evidence of a probable increased risk of bladder cancer. The final list included hairdressers, salespersons, horticultural workers, painters, metal workers, blacksmiths and toolmakers, mechanics, printing trades workers, tailors and dressmakers, operators in mining and mineral processing, metal processing, and chemical processing, rubber workers, textile workers, drivers, and building workers.

Unconditional logistic regression using SAS V9.1 was applied to estimate the odds ratio (OR) and its 95% confidence interval (95%CI), for ever being employed in a certain occupation/industry, compared to never being employed in that occupation/industry. ORs were calculated for all 958 occupational codes. Of these, only 229 had 10 study subjects or more that ever worked in these occupations, and only the results of these occupations were evaluated. ORs were also calculated for each industry code. Of these 684 codes only 222 contained 10 subjects or more.

ORs were adjusted for age (5 year age groups), gender, Maori ethnicity, and smoking (never, ex, ever). Cases and controls were considered current smokers if they reported to have stopped smoking less than 2 years before the interview. Logistic regression models were also adjusted for socioeconomic status, based on the New Zealand Socioeconomic index of Occupational Status (NZSEI)⁷ (continuous variable ranging between 20 and 90) of the longest held occupation. Whether a longer duration in a certain occupation was associated with an increased risk was studied through categorical variables for duration of each job (1–2 years, 2–10 years, more than 10 years).

Semi-Bayes adjustment

Because of the large number of occupations and industries being considered, this type of study carries the risk that some of the findings involving elevated odds ratios will be due to chance. A semi-Bayes (SB) approach was therefore applied to determine which of the findings were the most robust. The basic idea of empirical Bayes (EB) and SB adjustments for multiple associations is that the observed variation of the estimated relative risks around their geometric mean is larger than the variation of the true (but unknown) relative risks. In SB adjustments, an *a priori* value for

TABLE I – CHARACTERISTICS OF THE STUDY PARTICIPANTS

	Bladder cancer cases		Population controls	
	n	%	n	%
Total	213	100%	471	100%
Gender				
Men	165	54%	221	47%
Women	48	46%	250	53%
Age at interview				
20–50	29	20%	62	13%
51–60	57	37%	137	29%
61–70	110	40%	260	55%
71–	17	3%	12	3%
Smoking				
Never	63	30%	232	49%
Ex	97	46%	200	42%
Current	50	23%	36	8%
NZSEI (occupational class)				
Class 1 (75–90) highest	5	2%	8	2%
Class 2 (60–75)	14	7%	31	7%
Class 3 (50–60)	27	13%	58	12%
Class 4 (40–50)	37	17%	90	19%
Class 5 (30–40)	59	28%	170	36%
Class 6 (10–30) lowest	71	33%	114	24%

the extra variation is chosen so that the true relative risks have a reasonable range of variation, and is then used to adjust the observed relative risks.⁸ The adjustment consists in shrinking outlying relative risks towards the overall mean (of the relative risks of all the different 'exposures' being considered). The larger the individual variance of the relative risks, the stronger is the shrinkage, *i.e.*, the shrinkage is stronger for less reliable estimates based on small numbers. Typical applications in which SB adjustments are a useful alternative to traditional methods of adjustment for multiple comparisons are large occupational surveillance studies, where many relative risks are estimated with few or no *a priori* beliefs about which associations might be causal.⁸ SB estimates were calculated using R (free software for statistical computing and graphics).⁹ The input for SB adjustments were the maximum likelihood estimate of β (logOR), resulting from the multivariate logistic regression for each occupation and industry. The variance of the distribution of the true logOR was assumed equal to 0.25. Assuming a normal distribution of the logORs, this choice implies that the true ORs are within a 7-fold range of each other.¹⁰

For those occupations (or industries) which were not considered to be of *a priori* high risk for bladder cancer, estimates were shrunk towards the mean for all occupations (or industries). Similarly, for those occupations (and industries) which were considered to be of *a priori* high risk for bladder cancer, estimates were shrunk towards the mean for all such occupations (or industries).

The findings for all occupations and industries, both before and after SB adjustment, will be made available on web-based tables. Here, we report the findings for *a priori* high risk occupations and industries and for other occupations and industries that showed statistically significant elevated or decreased risks in the current analyses.

Results

The study included 213 interviews with bladder cancer cases, and 473 interviews with population controls. Of these, 2 controls were excluded because of missing values in key variables, leaving 213 cases and 471 controls available for analysis (Table I). Cases were 77% male (23% female) and controls were 47% male (53% female), with a mean age of 59.9 years in cases and 59.2 in controls. Current smoking was more common in the cases (23%) than in the controls (8%) (OR 3.75, 95%CI 2.35–5.97). Ever smoking was more common in the cases (69%) than in the controls (50%) (OR 2.29, 95%CI 1.62–3.24).

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 (33%) than in the controls (24%), whereas there was a difference in the other direction for class 5 (28% vs. 36%), and the proportions for Class 5 and 6 combined were similar in cases (61%) and controls (60%). We studied whether these differences 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 sex, age and occupational class distributions between the 471 participating controls and the 729 nonparticipating controls using the information available from the electoral roll. This showed that both sex and age were significant determinants of nonparticipation within the controls, with men and younger ages less likely to participate. Logistic regression showed that the lowest occupational class (Class 6) was a statistically significant determinant of nonparticipation in controls (OR = 1.8, 95%CI 1.2–2.8), adjusting for age and sex, while all other occupational classes had ORs for nonparticipation of 1.0–1.1 compared to the highest occupational class. Logistic regression models were therefore also adjusted for occupational class.

A priori high risk occupations and industries

Tables II and III list the findings for the *a priori* high risk occupations and industries, both adjusted for and stratified by sex.

Hairdressers. Hairdressers had an elevated risk of bladder cancer (Odds Ratio (OR) 9.15 95% confidence interval (95%CI) 1.60–62.22). The same pattern was observed for the industrial classification of 'hairdressing and beauty salons' (OR 5.35, 95%CI 1.37–20.9). The association appeared to be present in both males and females, but the numbers for males were small and there were no exposed controls. However, there were no consistent patterns by duration of employment (see web tables) although the numbers were relatively small. For hairdressers, the OR was 2.87 (95% CI 0.59–13.89) in ever smokers and 9.66 (95% CI 0.62–151.42) in nonsmokers.

Salesworkers. Overall, there was little or no evidence of an increased risk in sales workers. Sales assistants had an OR of 1.03 (95%CI 0.64–1.67); there was a suggestion of an elevated risk in males (OR 1.60, 95%CI 0.83–3.10), whereas there was a significantly reduced risk in females (OR 0.42, 95%CI 0.18–0.95). There was also little evidence of an increased risk for work in the retail trade.

Market farmers and crop growers. Overall, there was no increased risk for market farmers and crop growers (OR 0.92, 95%CI 0.50–1.67), although there was a nonsignificantly elevated risk in women (OR 2.05, 95%CI 0.72–5.83). For the industrial category of 'horticulture and fruit growing,' there was a small elevated risk (OR 1.34, 95%CI 0.69–2.60) which was statistically significant in women (OR 3.03, 95%CI 1.06–8.65).

Tailors and dressmakers. Tailors and dressmakers had a nonsignificantly increased risk (OR 2.84, 95%CI 0.62–13.05).

Rubber workers. Rubber and plastics machine operators had a nonsignificantly increased risk (OR 2.82, 95%CI 0.75–10.67), as did work in plastic product manufacturing (OR 2.10, 95%CI 0.72–6.18).

Textile workers. Textile products machine operators had an increased risk (OR 1.93, 95%CI 0.96–3.88) which was statistically significant for sewing machinists (OR 3.07, 95%CI 1.35–6.96). There was some evidence of an association with duration of employment (see web tables), with odds ratios of 0.77 (95% CI 0.19–3.20), 2.32 (95% CI 0.90–5.96) and 4.53 (95% CI 0.90–22.90) for 1–2, 2–10, and 10+ years of employment as a textile products machine operator. The OR was 1.78 (95% CI 0.74–4.52) in ever smokers and 2.21 (95% CI 0.75–6.50) in nonsmokers. There was a nonsignificantly increased risk for clothing manufacturing (OR 2.04, 95%CI 0.90–4.63), but there was little evidence of an association with duration of employment (see web tables).

Drivers. Overall, there was little evidence of an increased risk in motor vehicle drivers (OR 0.93, 95%CI 0.51–1.69) or heavy truck drivers (OR 1.36, 95%CI 0.60–3.09), or for work in road

transport (OR 1.42, 95%CI 0.72–2.78). However, the latter category showed a significantly increased risk for women (OR 8.52, 95%CI 1.17–61.97), and there was a nonsignificantly increased risk for road freight transport in men (OR 2.03, 95%CI 0.74–5.53).

Building workers. There was a nonsignificantly elevated risk in building workers (OR 2.15, 95%CI 0.68–6.73), but not for work in building construction (OR 1.06, 95%CI 0.60–1.86).

Other a priori high risk occupations. There was little evidence of an increased risk for occupations involving metal work (Table II), but there were nonsignificantly increased risks for metal product manufacturing (Table III). The *a priori* high risk occupations and industries of painting, mining, chemical processing and printing showed little evidence of increased risks.

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 (Table II) and industries (Table III) was associated with only a slight increased risk for bladder cancer (OR_{a priori occupation} 1.01 95%CI 0.69–1.48; OR_{a priori industry} 1.57 95%CI 1.07–2.32). All estimates in Tables II and III were also regressed towards these means using SB adjustment. This generally resulted in an attenuation of the ORs (see web-based tables), and only one of the ORs for the *a priori* high risk occupations (82631 – sewing machinist, OR 2.08 95%CI 1.00–4.35) remained statistically significant at the $p < 0.05$ level after SB adjustment.

Occupations and industries with an observed increased or decreased risk ($p < 0.05$) but not considered an *a priori* high risk occupation, are listed in Table IV. A number of occupations and industries showed a statistically significant decreased risk for bladder cancer, but almost all of these were no longer statistically significant after SB adjustment. Three occupations showed a statistically significant increased risk (see Table IV), in addition to the *a priori* high risk occupations listed in Table II, but none of these remained statistically significant after SB adjustment. Four occupations showed a statistically significant increased risk (see Table IV), in addition to the *a priori* high risk industries listed in Table III, but none of these remained statistically significant after SB adjustment. However, the reduced risk for work in education and the increased risks for work in manufacturing, and specifically in 'other food manufacturing' remained statistically significant after SB adjustment.

Discussion

This study of 213 incident bladder cancer cases diagnosed in New Zealand during 2003 and 2004 and 471 population controls aimed to identify occupations that entail an elevated risk for bladder cancer in New Zealand. After adjustment for age, smoking status, and socioeconomic status, this study showed that hairdressers and some textile workers remain at high risk for bladder cancer, and that several other occupations and industries including horticultural workers (females), tailors and dressmakers, and rubber workers may have an increased risk.

Before discussing the detailed study findings, the strengths and limitations of the study should be acknowledged. The study was population-based with the National Cancer Registry providing virtually complete coverage of incident cancers, and the Electoral Roll providing a near complete population register for the sampling of controls. Interviews were conducted face-to-face and involved a detailed occupational history. The main limitations of the study are the low response rates (estimated as 64% of cases and 48% of controls), and hence the relatively small number of cases interviewed. However, as noted earlier, there is little evidence of systematic response bias, apart from the particularly low response rate in the lowest occupational class in the controls, which was controlled for in the analysis. The small number of cases and controls interviewed is perhaps of greater concern, as there were a number of occupations and industries that showed

TABLE II – ODDS RATIOS AND 95% CIS FOR *A PRIORI* HIGH RISK OCCUPATIONS

<i>A priori</i> high risk occupation for bladder cancer	All (213 cases, 471 controls)			Men (165 cases, 221 controls)			Women (48 cases, 250 controls)		
	cases/ controls (n)	OR	95%CI	cases/ controls (n)	OR	95%CI	cases/ controls (n)	OR	95%CI
Hairdressers, beauty therapists and related workers									
5141-Hairdressers, beauty therapists and related workers	6/6	4.02	1.05–15.36	2/0			4/6	3.99	0.84–18.97
51411-Hairdresser	6/3	9.15	1.60–52.22	2/0			4/3	9.95	1.37–72.21
Salespersons, demonstrators and models									
52-Salespersons, demonstrators and models	36/107	0.85	0.54–1.36	24/30	1.15	0.63–2.11	12/77	0.39	0.17–0.90
521-Salesperson and demonstrators	35/101	0.91	0.57–1.47	23/26	1.29	0.69–2.41	12/75	0.41	0.18–0.92
5211-Salesperson and demonstrators	35/101	0.91	0.57–1.47	23/26	1.29	0.69–2.41	12/75	0.41	0.18–0.92
52111-Sales assistant	35/94	1.03	0.64–1.67	23/21	1.60	0.83–3.10	12/73	0.42	0.18–0.95
Market farmers and crop growers									
611-Market farmers and crop growers	18/44	0.92	0.50–1.67	11/29	0.60	0.29–1.27	7/15	2.05	0.72–5.83
6112-Fruit growers	9/20	1.31	0.56–3.05	5/10	0.94	0.31–2.87	4/10	2.03	0.55–7.48
6113- Gardeners and nursery growers	8/18	0.85	0.35–2.02	6/14	0.70	0.26–1.92	2/4	1.32	0.19–9.05
Painters and paperhangers									
7124-Painters and paperhangers	11/10	1.42	0.56–3.60	10/10	1.28	0.50–3.30	1/0		
71241-Painter, decorator and/or paperhanger	7/6	1.35	0.42–4.39	7/6	1.41	0.44–4.56	0/0		
Metal moulders, sheet-metal and related workers									
721-Metal moulders, sheet-metal and related workers	7/21	0.37	0.15–0.92	7/20	0.41	0.16–1.03	0/1		
7212-Sheet metal workers	7/19	0.39	0.15–1.00	7/19	0.43	0.17–1.10	0/0		
72124-Fitter and welder	4/8	0.65	0.18–2.32	4/8	0.69	0.19–2.42	0/0		
Blacksmiths, toolmakers and related workers									
722-Blacksmiths, toolmakers and related workers	1/6	0.17	0.02–1.55	1/6	0.21	0.02–1.86	0/0		
Machinery mechanics and fitters									
723-Machinery mechanics and fitters	21/23	1.17	0.60–2.29	21/22	1.24	0.63–2.42	0/1		
7231-Machinery mechanics and fitters	21/23	1.17	0.60–2.29	21/22	1.24	0.63–2.42	0/1		
72311-Machinery mechanic	10/8	1.59	0.57–4.40	10/7	1.69	0.59–4.81	0/1		
72312-Motor mechanic	11/18	0.75	0.32–1.73	11/18	0.80	0.35–1.85	0/0		
Printing trades workers									
733-Printing trades workers	7/12	1.11	0.41–3.05	5/8	0.93	0.28–3.03	2/4	1.54	0.22–10.87
7331-Printing trades workers	5/8	1.21	0.36–4.14	4/5	1.08	0.27–4.43	1/3	1.31	0.10–16.84
73317-Printing machinist	4/7	1.31	0.35–4.94	3/4	1.17	0.24–5.70	1/3	1.31	0.10–16.84
Tailors and dressmakers									
743-Tailors and dressmakers	5/4	2.84	0.62–13.05	3/0			2/4	1.16	0.16–8.47
Mining and mineral processing plant operators									
811-Mining and mineral processing plant operators	3/7	0.54	0.13–2.20	3/7	0.55	0.14–2.23	0/0		
Metal-processing plant operators									
812-Metal-processing plant operators	4/9	0.81	0.23–2.88	3/6	0.67	0.16–2.83	1/3	2.08	0.20–21.86
Chemical processing plant operators	3/8								
815-Chemical processing plant operators	3/8	0.45	0.11–1.88	3/8	0.51	0.12–2.08	0/0		
Chemical products machine operators									
822-Chemical products machine operators	3/7	0.50	0.12–2.15	3/5	0.64	0.14–2.88	0/2		
Rubber and plastics products machine operators									
823-Rubber and plastics products machine operator	7/4	2.82	0.75–10.67	7/3	3.45	0.85–14.08	0/1		
Textile products machine operators									
826-Textile products machine operators	17/38	1.93	0.96–3.88	5/3	2.28	0.51–10.17	12/35	1.26	0.52–3.07
8263-Sewing and embroidering machine operators	13/24	2.91	1.31–6.50	2/0			11/24	1.96	0.78–4.92
82631-Sewing machinist	12/23	3.07	1.35–6.96	1/0			11/23	2.26	0.90–5.65
8264-Textile bleaching, dyeing and cleaning machine operators	3/10	0.81	0.19–3.54	3/0			0/10		
Drivers and mobile machinery operators									
83-Drivers and mobile machinery operators	39/55	0.86	0.52–1.43	36/52	0.85	0.50–1.43	3/3	2.48	0.33–18.43
832-Motor vehicle drivers	24/34	0.93	0.51–1.69	22/31	0.88	0.47–1.66	3/3	2.48	0.33–18.43
8321-Car, taxi and light van operators	12/21	0.73	0.33–1.60	11/18	0.75	0.33–1.72	1/3	0.42	0.03–6.77
83211-Taxi driver	3/12	0.50	0.14–1.85	2/10	0.32	0.07–1.53	1/2	1.13	0.04–35.01
83212-Light truck or van driver	9/10	0.86	0.32–2.32	9/9	1.10	0.40–3.03	0/1		
8322-Bus drivers	7/7	1.69	0.55–5.26	5/7	1.21	0.35–4.14	2/0		
83221-Passenger coach driver	7/7	1.69	0.55–5.26	5/7	1.21	0.35–4.14	2/0		
8323-Heavy truck drivers	16/13	1.36	0.60–3.09	16/13	1.61	0.71–3.67	0/0		
83231-Heavy truck or tanker driver	16/13	1.36	0.60–3.09	16/13	1.61	0.71–3.67	0/0		
833-Agricultural, earthmoving and other materials-handling equipment	13/19	0.76	0.35–1.66	13/19	0.83	0.38–1.82	0/0		
8331-Motorised farm machinery operators	5/8	0.64	0.19–2.14	5/8	0.63	0.19–2.15	0/0		
8332-Earthmoving and related machinery operators	6/11	0.57	0.19–1.70	6/11	0.67	0.23–1.98	0/0		
83325-Roading and/or paving machine operator	3/9	0.34	0.08–1.39	3/9	0.40	0.10–1.62	0/0		
Building and related workers									
84-Building and related workers	8/6	2.15	0.68–6.73	7/6	1.63	0.51–5.26	1/0		
91512 – Builders laborer	10/6	2.65	0.92–7.63	10/6	2.59	0.90–7.44	0/0		

Numbers were too small (less than 10 cases + controls) for the following *a priori* high risk occupations: spray painters, metal moulders, leather goods makers, wood products machine operators, leather goods assemblers.

OR: odds ratio, adjusted for gender, age group, smoking status, Māori ethnicity, occupational status.

95%CI: 95% confidence interval of the odds ratio.

TABLE III – ODDS RATIOS AND 95% CIS FOR A *PRIORI* HIGH RISK INDUSTRIES

<i>A priori</i> high risk industry for bladder cancer	All (213 cases, 471 controls)			Men (165 cases, 221 controls)			Women (48 cases, 250 controls)		
	cases/ controls (n)	OR	95%CI	cases/ controls (n)	OR	95%CI	cases/ controls (n)	OR	95%CI
Horticulture									
A011-Horticulture and fruit growing	16/32	1.34	0.69–2.60	9/18	0.81	0.35–1.90	7/14	3.03	1.06–8.65
A0113-Vegetable growing	4/8	1.03	0.29–3.71	3/6	0.79	0.19–3.33	1/2	1.97	0.16–23.81
Mining									
B-Mining	14/10	1.69	0.69–4.13	14/10	1.69	0.70–4.12	0/0		
Textile, clothing, footwear and leather manufacture									
C22-Textile, clothing, footwear and leather manufacture	20/50	1.47	0.78–2.76	6/10	0.72	0.24–2.18	14/40	1.56	0.68–3.56
C222-Textile product manufacturing	3/14	0.70	0.18–2.75	1/4	0.24	0.02–3.02	2/10	0.90	0.18–4.55
C2221-Made-up textile product manufacturing	3/7	1.75	0.41–7.45	1/2	0.91	0.08–10.33	2/5	1.79	0.31–10.41
C224-Clothing manufacturing	11/27	2.04	0.90–4.63	2/0			9/27	1.20	0.46–3.17
Printing									
C2412-Printing	4/8	1.02	0.28–3.67	3/5	0.87	0.19–3.87	1/3	1.26	0.09–17.53
Plastic product manufacturing									
C256-Plastic product manufacturing	8/8	2.10	0.72–6.18	7/4	2.67	0.72–9.84	1/4	0.95	0.09–9.66
Metal product manufacturing									
C27-Metal product manufacturing	25/30	1.45	0.79–2.65	22/20	1.51	0.77–2.96	3/10	1.18	0.29–4.88
C271-Iron and steel manufacturing	8/7	1.97	0.65–6.02	8/4	2.78	0.79–9.76	0/3		
C274-Structural metal product manufacturing	8/7	2.10	0.69–6.37	6/5	1.49	0.43–5.18	2/2	5.25	0.57–48.69
C276-Fabricated metal product manufacturing	9/10	1.55	0.58–4.13	7/7	1.31	0.43–3.97	2/3	2.27	0.31–16.37
Building construction									
E411-Building construction	26/39	1.06	0.60–1.86	24/36	0.96	0.54–1.72	2/3	4.00	0.54–29.56
E4111-House construction	14/26	0.84	0.41–1.71	13/25	0.81	0.39–1.69	1/1	5.20	0.17–159.08
E4113-Non-residential building construction	7/12	0.94	0.35–2.56	7/11	0.93	0.34–2.55	0/1		
Painting and decorating services									
E4244-Painting and decorating services	7/9	1.13	0.39–3.29	6/7	1.11	0.34–3.56	1/2	1.38	0.10–19.76
Retail trade									
G-Retail trade	73/181	0.93	0.64–1.36	52/70	1.00	0.64–1.59	21/111	0.75	0.37–1.50
G51-Food retailing	25/87	0.76	0.45–1.28	16/28	0.77	0.39–1.51	9/59	0.66	0.28–1.54
G52-Personal and household good retailing	40/94	1.18	0.74–1.89	26/22	1.50	0.79–2.83	14/72	0.78	0.37–1.65
G53-Motor vehicle retailing and services	24/43	0.86	0.48–1.54	20/33	0.76	0.40–1.43	4/10	2.41	0.66–8.77
Road transport									
I61-Road transport	21/23	1.42	0.72–2.78	17/21	1.18	0.57–2.43	4/2	8.52	1.17–61.97
I611-Road freight transport	12/8	1.65	0.61–4.47	12/8	2.03	0.74–5.53	0/0		
I612-Road passenger transport	10/15	1.30	0.55–3.06	6/13	0.73	0.26–2.04	4/2	8.52	1.17–61.97
Hairdressing and beauty salons									
Q9526-Hairdressing and beauty salons	7/5	5.35	1.37–20.9	3/0			4/5	4.79	0.90–25.32

Numbers were too small (less than 10 cases + controls) for the following *a priori* high risk industries: chemical manufacturing, paint manufacturing.

OR: odds ratio, adjusted for gender, age group, smoking status, Maori ethnicity, occupational status.

95%CI: 95% confidence interval of the odds ratio.

elevated relative risks, consistent with previous studies, which were not statistically significant because of the small numbers involved.

Hairdressers

We found a strongly increased risk (OR 9.15) for hairdressers, and for employment in the hairdressing industry (OR 5.35). Hairdressing has been identified as a risk for bladder cancer in several previous studies.^{11–14} The causative agent is generally assumed to be hair dyes because of their toxicology,¹⁵ although studies of personal use of hair dyes have found only limited evidence for increased bladder cancer risks.^{16–19} However, the finding that permanent hair dye users that are also slow acetylators of aromatic amines are at particularly increased risk of bladder cancer adds to the evidence of a likely causal role of aromatic amines.^{20,21}

Textile workers

We found a significantly increased risk for sewing machinists (OR 3.07). An excess of bladder cancer has previously been reported in workers with textiles,^{12,14,22,23} tailors, dressmakers,

weavers, and upholstery workers,^{24,25} and leatherworkers,^{26–28} but not necessarily sewing machine operators. Claude *et al.*²⁴ showed an increasing trend with employment as a tailor, weaver and upholsterer, with a relative risk of 2.5 at 10+ years. The presumptive causative agent for excess bladder cancer risks in the textile industry is not known, but textile dyes are plausible candidates,²⁹ and once again the likely causative agents are aromatic amines.

Sales workers

A large number of epidemiological studies have reported positive associations between bladder cancer and sales occupations. A recent meta-analysis³⁰ concluded that publication bias explained most of the reported increased bladder cancer risk in men, but sales work still appeared to be associated with a small risk in women. However, the current study found little overall evidence of an increased risk; there was a nonsignificantly increased risk in men (OR 1.60), whereas there was a significantly reduced risk in women (OR 0.42). Possible causal factors include lower frequency of urination and reduced fluid intake.³⁰

TABLE IV – ODDS RATIOS 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 occupation and industry for bladder cancer	cases/controls (n)	Not Semi-Bayes adjusted		Semi-Bayes adjusted	
		OR	95% CI	OR	95% CI
Occupations—reduced risk					
2331-Primary teaching professionals	3/37	0.26	0.07–0.90	0.62	0.28–1.38
331-Finance and sales associate professionals	23/53	0.53	0.30–0.95	0.63	0.38–1.04
4114-Secretaries	3/49	0.28	0.08–0.95	0.63	0.28–1.39
422-Client information clerks	4/45	0.28	0.09–0.85	0.57	0.27–1.23
Occupations—increased risk					
12213-Production manager (manufacturing)	9/6	2.99	1.01–8.86	1.75	0.83–3.68
311-Physical science and engineering technicians	13/10	2.77	1.15–6.70	1.76	0.89–3.47
8143-Papermaking plant operators	6/1	12.80	1.31–125.11	1.55	0.60–4.02
Industries—reduced risk					
K75-Services to finance and insurance	1/32	0.08	0.01–0.57	0.62	0.24–1.60
K752-Services to insurance	1/24	0.10	0.01–0.80	0.71	0.28–1.79
L77-Property services	3/27	0.18	0.05–0.63	0.53	0.23–1.21
L772-Real estate agents	2/21	0.18	0.04–0.84	0.65	0.27–1.55
N-Education	23/128	0.44	0.26–0.76	0.53	0.32–0.85
N842-School education	13/85	0.49	0.25–0.95	0.63	0.36–1.11
N8421-Primary education	5/45	0.34	0.13–0.92	0.62	0.30–1.28
N844-Other education	3/16	0.18	0.06–0.54	0.49	0.22–1.08
Industries—increased risk					
A015-Other livestock farming	9/2	12.26	2.29–65.80	2.03	0.82–5.04
C-Manufacturing	132/208	1.60	1.20–2.31	1.49	1.05–2.12
C217-Other food manufacturing	13/6	4.92	1.69–14.32	2.19	1.02–4.67
C2179-Food manufacturing NEC	8/2	9.17	1.83–46.06	1.95	0.80–4.77
Q-Personal and other services	38/68	1.64	1.02–2.65	1.47	0.95–2.28

OR: odds ratio, adjusted for gender, age group, smoking status, Maori ethnicity, occupational status.

95%CI: 95% confidence interval of the odds ratio.

Farming

We found a nonsignificantly increased risk in women for the occupational category of 'market farmers and crop growers' (OR 2.05) and a significantly increased risk for the industry category of 'horticulture and fruit growing' (OR 3.03). An excess of bladder cancer has been shown in female field, crop and vegetable farm workers,³⁰ gardeners³¹ and in workers using insecticides^{32,33} and herbicides,³⁴ but was not found in a meta-analysis of cancer among farmers.³⁵ 't Mannetje *et al.*²⁵ have shown an increasing trend with years as a field, crop and vegetable farm worker, with a relative risk of 2.1 at 25+ years of exposure. They postulated that this may be related to exposure to pesticides.

Painters

An excess of bladder cancer in painters has been reported in several studies^{22,24,26,34,36} many showing a significant positive trend with years of employment. Relative risks at 10+ years employment were reported as 1.39,²² 1.6,³⁶ and 8.4,²⁴ and at 20+ years 2.0²⁴ and 4.1.²² Silverman *et al.*³⁶ noted that painters may have been exposed to benzidine, polychlorinated biphenyls, formaldehyde, benzene, dioxane and methylene chloride may have been the causative factors. Elevated risk for bladder cancer has also been reported among artistic painters.^{37,38} However, we found no evidence of an increased risk in the current study.

Metal workers

A number of published studies have shown excess risks of bladder cancer in turners, foundry workers, sheetmetal workers, drill press operatives and blacksmiths,^{24,31,36} in workers exposed to cutting and lubricating oils,^{24,39} and in machinists.^{1,1,40} The associated agents are the cutting and lubricating oils.²⁴ These sometimes contain aromatic amines as additives and *N*-nitrosamines can be found in the semi-synthetic and synthetic cutting fluids. Hours *et al.*³⁹ found an elevated odds ratio of 2.56 (95% CI 1.2–1.4) for bladder cancer cases exposed to cutting fluids after adjusting for socioprofessional status and tobacco smoking, compared to general referents. Several studies reported relative risks for length of exposure.⁴¹ At 10 or more years of employment the relative

risk was 2.4 for drill press operatives,³⁶ 2.3 for foundry workers,²⁴ and 3.2 for female blacksmiths, toolmakers, and machine tool operators.²⁵ We found little evidence of an increased risk for these occupations in the current study.

Drivers

A number of published studies have shown an excess of bladder cancer in truck and other drivers.^{22,24,36} Relative risks associated with 10 or more years of driving have been reported as ranging from 1.5²⁴ to 5.5.³⁶ Increased risks have particularly been associated with exposure to diesel exhaust fumes.^{42–45} In the current study, we found little evidence of an increased risk in truck drivers, although there was a significant association in women for employment in the road transport industry (OR 8.52).

Building workers

We found a nonsignificantly increased risk for building workers (OR 2.15) and builders' laborers (OR 2.65). Increased risks in construction workers have previous been reported by Silverman *et al.*³⁶ and Porru *et al.*⁴³

Conclusions

This study observed a diverse list of high risk occupations for bladder cancer largely in concordance with previous studies in New Zealand and elsewhere. Most notably, bladder cancer risk was increased for hairdressers and textile workers. These are both female-dominant occupations in which the likely causative agents are aromatic amines. There were also nonsignificantly increased risks for tailors and dressmakers, rubber and plastics products machine operators, building workers, and female market farmers and crop growers.

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