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SOFT-TISSUE SARCOMA, NON-HODGKIN'S LYMPHOMA AND OTHER CANCERS IN NEW ZEALAND FORESTRY WORKERS

John REIF[1,2,4], Neil PEARCE[2], Ichiro KAWACHI[2] and James FRASER[3]

[1]Department of Environmental Health, Colorado State University, College of Veterinary Medicine and Biomedical Sciences, Fort Collins, CO 80523, USA; [2]Department of Community Health, Wellington School of Medicine, Wellington: and [3]National Health Statistics Center, Wellington, New Zealand.

Several studies have suggested that forestry workers are at increased risk for certain types of cancer including soft-tissue sarcoma (STS) and non-Hodgkin's lymphoma (NHL). We now report a series of national case-control studies based on the New Zealand Cancer Registry (NZCR). These involved 19,904 male patients with cancer for the period 1980–1984 who were aged 20 years or more at the time of registration. For each cancer site, the registrations for the remaining sites formed the control group. Current or most recent occupational titles were coded. There was an increased risk for STS (OR = 3.24) in forestry workers which was confined to men under 60 years of age at registration. An elevation in risk for NHL (OR = 1.84) was due to an increase in risk for lymphosarcoma and reticulosarcoma (ICD 200) (OR = 3.18). Acute myeloid leukemia was also associated with forestry work, although the estimate of risk was imprecise (OR = 2.24). Among other cancer sites, an increase in risk of neoplasia of the upper gastro-intestinal tract (ICD 150, 151, 152) was demonstrated. Odds ratios were elevated for cancer of the esophagus (OR = 1.77), stomach (OR = 2.22), small intestine (OR = 5.22), gall-bladder (OR = 4.13) and pancreas (OR = 1.79), as well as for nasopharyngeal cancer (OR = 5.56). These increases in cancer risk were not present in sawmill workers in New Zealand during the same period. The factors responsible for the increased cancer risks in forestry workers remain unclear and require further study.

Occupational mortality analyses of forestry workers in the United States and Sweden have shown that overall cancer rates are generally not elevated in this occupational group (Milham, 1976; Edling and Granstam, 1980; Stellman and Garfinkel, 1984). Excess mortality from cancer of the stomach and prostate among loggers, and cancer of the respiratory, digestive, lymphatic and hematopoietic systems among professional foresters were found in the state of Washington (Milham, 1976). An analysis of mortality in Swedish lumberjacks (Edling and Granstam, 1980) also showed an increase in risk of lymphatic and hematopoietic cancer. Excess risks of lung (Harrington *et al.*, 1978) and bladder (Stellman and Garfinkel, 1984) cancer have been described among lumber, sawmill and forestry workers.

Case-control and cohort studies of soft-tissue sarcoma (STS) and malignant lymphoma among forestry workers have been conducted to assess potential associations with occupational exposure to phenoxyherbicides and chlorophenols, compounds used in forestry and the lumber industry. Excess risks of STS (Balarajan and Acheson, 1984; Wiklund and Holm, 1986) or non-Hodgkin's lymphoma (NHL) (Wiklund *et al.*, 1988) were not detected in 3 recent studies of agricultural and forestry workers. These studies did not include specific exposure data for chemicals.

previous studies from New Zealand have demonstrated small excess risks for malignant lymphoma (Pearce *et al.*, 1985) and leukemia (Pearce *et al.*, 1986*a*) among persons engaged in the broad occupational category of agriculture, forestry and fishing. Therefore, we conducted a series of case-control studies based on the NZCR to further examine the risks of soft-tissue sarcoma, malignant lymphoma and leukemia in forestry workers, and to assess the association between forestry work and other cancers.

MATERIAL AND METHODS

The study included all 24,762 male cancer cases aged 20 years or more registered with the NZCR for the period 1980 to 1984. During this period the NZCR obtained practically complete population coverage from public and private hospitals throughout the country, as well as from death certificates and autopsy findings (Foster, 1977). Virtually all patients who die of cancer are reported to the NZCR prior to death. Analysis was restricted to the 19,904 men who had a recorded occupation, 80% of the total sample. Persons for whom no job classification was available, including some retired and some unemployed men, were not included in the analysis (Table I).

The study design involved a series of case-control studies, each based on the overall group of 19,904 cancer registrants. Site and subsite were categorized according to the ICD. For each site, the registrants for other sites formed the control group. For example, in the analysis for cancer of the esophagus (ICD code 150) the case group consisted of the 385 registrants with this cancer type and the control group comprised the other 19,519 cancer registrants. A similar procedure was followed for the other cancer sites, except for subtypes of leukemia, where other forms of leukemia were excluded from the control group.

Occupation was defined in the National Cancer Registry as the individual's current or most recent occupation at the time of registration, and coded using the ***New Zealand Standard Classification of Occupations*** (NZSCO) (Department of Statistics, 1980), a modification of the ***International Standard Classification of Occupations*** (International Labour Office, 1968). The NZSCO category of forestry workers included loggers and other forestry workers. As a check on the findings in forestry workers, a similar analysis was conducted with wood preparation workers (principally sawmill workers). Loggers and other forestry workers were deleted from this latter analysis.

All analyses were conducted using the Statistical Analysis System (SAS Institute, 1985). Age-adjusted odds ratios were estimated (Mantel and Haenszel, 1959) using 10-year age intervals, and 95% confidence intervals were calculated by the approximate method (Miettinen, 1976). Analyses were performed according to the ICD codes as shown in Tables I and II, except as otherwise indicated.

RESULTS

There were 134 forestry workers among the 19,904 adult male cancer registrants for the years 1980–1984. The age-

[4]To whom reprints should be sent, at Colorado State University.

Abbreviations: International Classification of Diseases 9th edition (ICD); odds ratio (OR); confidence interval (CI).

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TABLE I - NUMBER OF CANCER CASES BY SITE IN MALES AGED 20 YEARS OR MORE. NZCR 1980–1984

Site	ICD category	Cases with occupation recorded (%)	Total cases
Buccal cavity	140–146,148–149	649 (74)	872
Nasopharynx	147	49 (82)	60
Esophagus	150	385 (83)	463
Stomach	151	1,014 (81)	1,258
Small intestine	152	63 (83)	76
Colon	153	2,043 (82)	2,500
Rectum	154	1,376 (82)	1,679
Liver	155	184 (83)	223
Gall-bladder	156	120 (87)	138
Pancreas	157	571 (82)	695
Larynx	161	303 (82)	379
Lung	162	4,224 (84)	5,031
Bone	170	49 (83)	59
Soft-tissue sarcoma	171	142 (83)	171
Malignant melanoma	172	1,116 (77)	1,448
Prostate	185	2,435 (73)	3,340
Testis	186	399 (92)	435
Bladder	188	912 (72)	1,259
Kidney	189	542 (81)	666
Brain, nervous system	191,192	452 (89)	506
Hodgkin's disease	201	170 (91)	186
Non-Hodgkin's lymphoma	200,202	535 (82)	652
Multiple myeloma	203	295 (83)	355
Leukemia	204–208	534 (82)	649
Other cancers		1,342 (81)	1,662
Total	140–208	19,904 (80)	24,762

adjusted odds ratios for specific cancer sites are shown in Table II. A general increase in risk of cancer of the digestive organs and peritoneum (ICD 150–159) was found (OR=1.49, 95% CI 1.04–2.14). Odds ratios were elevated for cancer of the esophagus (OR=1.77, 95% CI 0.66–4.75), stomach (OR=2.22, 95% CI 1.26–3.91), small intestine (OR=5.22, 95% CI 1.44–18.88), and gall-bladder (OR=4.13, 95% CI 1.42–12.04). The odds ratio for pancreatic cancer was also elevated (OR=1.79), although the estimate was imprecise. Several other related sites, including liver and colon, did not show increased risks.

An increase in risk of nasopharyngeal cancer (ICD 147) was found (OR=5.56, 95% CI 1.59–19.48). No cases of cancer of the nose and nasal sinuses (ICD 160) were recorded among forestry workers, although the expected frequency was only 0.3.

Excess risks were also found for soft-tissue sarcoma (ICD 171) (OR=3.24, 95% CI 1.17–8.98) and for several types of cancer of the lymphatic and hematopoietic systems (Table III). The overall odds ratio for non-Hodgkin's lymphoma was 1.84 (95% CI 0.85–3.97), but 6 of the 7 cases occurred in ICD 200 (lymphosarcoma and reticulosarcoma), producing a risk estimate of 3.18 (95% CI 1.42–7.12). No cases of Hodgkin's disease (ICD 201) occurred in forestry workers (0.3 expected). The odds ratio for all forms of leukemia (ICD 204–208) was not elevated among forestry workers but the odds ratio for acute myeloid leukemia was 2.24 (95% CI 0.72–6.94).

The associations between cancer and forestry work were examined further by separating cases and controls into those aged less than 60 and those 60 and over at the time of registration. Cases of STS and cancer of the small intestine were confined to the younger age group, whereas the elevated risks for cancer of the stomach and pancreas were confined to the older age group. The risk for NHL was similar among the 2 age groups.

When forestry workers were separated into those engaged in logging (n=47) and those involved with other forms of forestry work (n=87) the risk estimates were generally similar in both groups. As an additional check on the findings for forestry workers, risk estimates were calculated for workers engaged in wood preparation, predominantly as sawmill workers (Table IV). Sawmill workers would be expected to have at least as much exposure to wood dust as forest workers and loggers, and may also be exposed to chlorophenols (used as fungicides to prevent sapstain) and other chemicals employed in the treatment of sawn timber (IARC, 1981). There were 139 registrants whose occupation was listed as timber treater (n=2) or sawmiller (n=137). With the possible exception of cancer of the gall-bladder, the elevated risks noted for loggers and foresters were not found among sawmill workers. In particular, there was little evidence for an increased risk of cancer of the esophagus, stomach, small intestine and nasopharynx or for soft-tissue sarcoma, non-Hodgkin's lymphoma or acute myeloid leukemia. No cases of soft-tissue sarcoma or nasopharyngeal cancer were observed in sawmill workers but the expected numbers were 1.0 and 0.3 respectively.

DISCUSSION

This study design has been used in several previous NZCR-based case-control studies (Pearce et *al.*, 1985, 1986*a*,*b*, 1987; Smith et al., 1984) and the relevant issues have been described (Pearce and Checkoway, 1988; Smith *et al.*, 1988). The main advantage of using other cancers as controls is the minimization of information bias, as well as the minimization of selection bias due to incomplete cancer registration. The main potential disadvantage is that selection bias may occur if the exposure under study is associated with an increased risk for other cancer sites. Any such bias is generally likely to be small in occupational studies (Smith et *al.*, 1988), although more significant bias may occur if an exposure is associated with a common cancer such as lung cancer. Even in this situation,

TABLE II - AGE-ADJUSTED ODDS RATIOS AND 95% CONFIDENCE INTERVALS FOR CANCER IN FORESTRY WORKERS, NZCR 1980-1984

ICD number	Site	Exposed cases	Odds ratio	95%CI
140-146,148-149	Buccal cavity	3	0.71	0.23-2.19
147	Nasopharynx	2	5.56	1.59-19.48
150	Esophagus	4	1.77	0.66-4.75
151	Stomach	13	2.22	1.26-3.91
152	Small intestine	2	5.22	1.44-18.88
153	Colon	7	0.51	0.24-1.09
154	Rectum	10	1.22	0.64-2.34
155	Liver	1	0.81	0.11-5.80
156	Gall-bladder	3	4.13	1.42-12.04
157	Pancreas	6	1.79	0.79-4.05
161	Larynx	2	1.14	0.28-4.65
162	Lung	30	1.27	0.84-1.91
170	Bone	1	1.72	0.22-13.30
171	Soft-tissue sarcoma	4	3.24	1.17-8.98
185	Prostate	12	0.72	0.39-1.31
186	Testis	6	0.99	0.38-2.61
188	Bladder	4	0.68	0.25-1.84
189	Kidney	2	0.58	0.15-2.30
191-192	Brain/nervous system	4	1.19	0.44-3.25
200,202	Non-Hodgkin's lymphoma	7	1.84	0.85-3.97
203	Multiple myeloma	1	0.53	0.08-3.72
204-208	Leukemia	4	0.96	0.36-2.61
	Other cancer	6	0.65	0.29-1.47
	Total	134		

the appropriate approach is not always clear, since excluding exposure-related cancers from the control group may actually increase the net bias (Pearce and Checkoway, 1988).

As would be expected, when other exposure-related cancers were deleted from the reference group, the effect estimates increased. For example, the odds ratio for STS rose from 3.24 to 4.00 (95%CI 1.46-11.05) and the odds ratio for NHL rose from 1.84 to 2.25 (95% CI 1.05-4.86) when other cancers with elevated risks among forestry workers were excluded. The more conservative relative risk estimates obtained by including all other cancers as controls have been presented here but the risks may actually be slightly higher. Previous New Zealand studies of the occupational category involving farming, forestry and fishing have suggested that valid effect estimates can be obtained by including all other cancers as controls (Smith *et al.*, 1988; Pearce and Checkoway, 1988), and this procedure has been followed in the current study.

The major disadvantage of using registry data for case-control analyses of occupational cancer risks is the relatively crude nature of the occupational data and the absence of exposure data. The cancer registry records current or most recent occupation at the time of registration rather than a complete occupational history. Misclassification will thus occur if the period several decades before registration is of prime concern. This misclassification will tend to bias the estimate of risk towards the null value (Copeland et *al.*, 1977). More importantly, the data do not permit the examination of dose-response relationships based on duration of employment in an industry, or estimation of risks for specific departments or processes.

Increased risks for cancer of several sites within the gastrointestinal system and related organs were found among New Zealand forestry workers. There was a general increase in risk for cancer of the digestive organs and peritoneum (ICD 150-159) (OR=1.49), consistent with a previous report of mortality in forestry workers (Milham, 1976). Conversely, a recent analysis of deaths in timber cutters and loggers in New Hampshire (Schwartz, 1988) failed to show significantly elevated proportionate mortality ratios (PMRs) for cancer of the gastrointestinal and lymphopoietic systems, although increased risks

TABLE III - AGE-ADJUSTED ODDS RATIOS AND 95%CONFIDENCE INTERVALS FOR CANCER IN FORESTRY WORKERS, BY AGE-GROUP, NZCR 1980-1984

Site (ICD)	Age group (years)					
	20-59			60+		
	Exposed cases	OR	95%CI	Exposed cases	OR	95%CI
Nasopharynx (147)	1	3.53	0.55-22.59	1	13.36	2.74-65.06
Esophagus (150)	1	1.55	0.21-11.33	3	1.85	0.59-5.80
Stomach (151)	3	0.71	0.23-2.19	10	2.35	1.23-4.49
Small intestine (152)	2	11.18	3.43-36.44	0	—	—
Gall-bladder (156)	1	6.34	1.10-36.64	2	3.52	0.93-13.34
Pancreas (157)	0	—	—	6	2.38	1.06-5.36
Soft-tissue sarcoma (171)	4	4.86	1.78-13.28	0	—	—
Non-Hodgkin's lymphoma (200,202)	4	1.97	0.70-5.57	3	1.70	0.54-5.35
Lympho/reticulosarcoma (200)	4	4.21	1.56-11.33	2	2.16	0.54-8.59
Acute myeloid leukemia (205.0)	2	2.79	0.70-11.03	1	1.61	0.23-11.54

TABLE N - AGE-ADJUSTED ODDS RATIOS AND 95% CONFIDENCE INTERVALS FOR SELECTED SITES AND SUBTYPES OF CANCER IN SAWMILL WORKERS, NZCR 1980–1984

ICD number	Site	Exposed cases	odds ratio	95% CI
147	Nasopharynx	0	—	—
150	Esophagus	2	0.72	0.18–2.90
151	Stomach	7	0.95	0.44–2.05
152	Small intestine	0	—	—
156	Gall-bladder	2	2.30	0.59–9.07
157	Pancreas	2	0.47	0.12–1.83
171	Soft-tissue sarcoma	0	—	—
200,202	Non-Hodgkin's lymphoma	4	1.17	0.43–3.17
200	Lympho/reticulosarcoma	2	1.11	0.27–4.48
204–248	Leukemia	2	0.52	0.13–2.07
205.0	Acute myeloid leukemia	1	0.89	0.12–6.39

were found among pulp and paper-mill workers for these sites. In the current study, odds ratios were elevated for cancer of the esophagus (OR=1.77), stomach (OR=2.22), small intestine (OR=5.22), gall-bladder (OR=4.13) and pancreas (OR=1.79), although some of the estimates were imprecise. Previous studies of persons engaged in forestry and logging have shown an increase in risk of stomach cancer (Milham, 1976; Siemiatycki *et al.*, 1986), a finding also associated with carpentry and cabinet-making (Stellman and Garfinkel, 1984; Dubrow and Wegman, 1983), plywood millworking (Milham, 1976) and pulp and paper-mill work (Schwartz, 1988; Milham and Demers, 1984). A 4-fold excess in mortality from small intestinal cancer among pulp and paper-mill workers (Milham, 1976) and elevated PMRs for pancreatic cancer in sawmill workers (Milham, 1976) and pulp and paper-mill workers (Milham and Demers, 1984) have also been described.

The finding of an increased risk of gall-bladder cancer in both forestry workers and sawmill workers requires further investigation. An elevated PMR for cancer of the gall-bladder was also found in a study of mortality among pulp and paper-mill workers in Washington State (Milham, 1983). In the current study, the risk estimates for hepato-biliary cancer (ICD 155 and 156) were 2.07 (95% CI 0.77–5.53) for forestry workers and 2.47 (95% CI 1.04–5.90) for sawmill workers, suggesting that a common mechanism may exist for the 2 closely related sites. For liver cancer risk, this might possibly reflect the fact that much of the forestry is conducted in an area of New Zealand where hepatitis B virus carrier rates and hepatocellular carcinoma rates are high (Milne *et al.*, 1987). With that exception, regional differences in the prevalence of forestry in New Zealand are unlikely to be responsible for the cancer risks found.

One risk factor common to forestry workers and other occupations involving wood is contact with wood dust. Forestry workers have an increased risk of Hodgkin's disease (Abramson *et al.*, 1978), an association shared with other occupational groups exposed to wood dust (Petersen and Milham, 1974; Grufferman *et al.*, 1976; Greene *et al.*, 1978). In the current study no cases of Hodgkin's disease were registered among forestry workers, although less than one was expected, and the risk estimate in sawmill workers was not elevated.

Previous reports have also linked wood-related work with cancer of the nasopharynx, a finding reproduced in this study. An excess of woodworkers was reported among cases of adenocarcinoma of the nasopharynx in the UK (Mould and Bakowski, 1976), while a 7-fold increase in risk of nasopharyngeal cancer associated with exposure to chlorophenols was reported in Northern Sweden where forestry and wood milling are predominant industries (Hardell *et al.*, 1982). There appeared to be effect modification by woodwork, consistent with the well-known relationship between nasal and paranasal sinus cancer and exposure to wood dust (Acheson *et al.*, 1967). No support for a relationship with chlorophenols was found in a Danish case-control study (Olsen and Jensen, 1984). Furthermore, no sawmill workers were found among cases of nasopharyngeal or nasal cancer in the current study, although less than one case of each was expected.

Cigarette smoking has been associated with increased risks of cancer of the nasopharynx, esophagus and pancreas (Doll and Peto, 1983). To evaluate the role of smoking in the excess risks of these cancers among forestry workers, we examined data on smoking and occupation from the 1981 New Zealand census (Department of Statistics, 1983). A higher proportion of forestry workers were current smokers (49.2%) or ever-smokers (65.5%) compared to the total full-time male labor force, among whom 37.7% smoked currently and 59.6% had ever smoked. The principal impact of cigarette smoking is on the risk of lung cancer, and some elevation in the risk of lung cancer among forestry workers was found (OR= 1.27). Therefore, the increased risks of these cancers may be due, at least in part, to cigarette smoking. However, no increase in risk was noted for several other sites associated with smoking (larynx, bladder, oral cavity, lip) and exposures to chain-saw exhausts containing polycyclic aromatic hydrocarbons such as benzo[α]pyrene could have been partially responsible.

The finding of an increased risk of STS among New Zealand forestry workers is puzzling. An initial possibility is that this association represents a chance finding, particularly since a recent case-control study from the National Cancer Register of England and Wales (Balarajan and Acheson, 1984) and a large cohort study of Swedish agricultural and forestry workers (Wiklund and Holm, 1986) did not find elevated risks for forestry workers.

A second possibility is that the increase in risk is due to exposure to phenoxyacid herbicides or chlorophenois, as suggested by case-control studies in Sweden (Hardell and Sandstrom, 1979; Eriksson *et al.*, 1981). The first Swedish study (Hardell and Sandstrom, 1979) was conducted in an area where forestry was prevalent, and where phenoxyherbicides had been sprayed extensively. Despite the fact that phenoxyherbicides and chlorophenols have been produced in New Zealand and widely used in agriculture and forestry since the 1940s it currently appears unlikely that the increased risk of STS observed in forestry workers is due to exposure to these chemicals, for several reasons.

First, a previous case-control study of STS conducted in New Zealand (Smith *et al.*, 1984) found little evidence of an association between STS and exposure to phenoxyherbicides or chlorophenols. The exposure data were obtained by interview and were presumably more accurate and appropriate than the occupational information available for the current analysis.

No association was found for employment in forestry work, nor was there an increase in risk associated with spraying chemicals or other forms of exposure to herbicides. Second, in previous New Zealand case control studies of cancer which assessed exposure to phenoxyherbicides (Smith et al., 1984; Pearce *et* al., 19866, 1987), only 3 of 81 forestry workers (3.7%) were reported to have sprayed chemicals. Third, potential exposure to chlorophenols in a sawmill or as a timber merchant was not associated with an increase in risk of STS (Smith et al., 1984). An elevated risk was found for log-lumber inspectors and lumber graders in a recent study from Washington State (Woods et *al.*, 1987), but other jobs involving comparable chlorophenol exposure showed no increase in risk of STS. Further, studies of sawmill workers, a highly exposed group who treat wood with sodium pentachlorophenol and manually handle the wood during the sorting and cutting processes, show no increase in risk for STS (IARC, 1981; Sterling, 1982). Finally, the current study showed no comparable increase in risk of STS among New Zealand sawmill workers.

A third possibility is that the increased risk of STS, and other cancers, may be associated with the use of chain saws or other equipment used by forestry workers. Chain saws were widely introduced into the New Zealand forest industry in the 1960s, and the finding that the risk of STS was confined to men aged less than 60 at registration suggests that a recently introduced work practice might be responsible. The use of chain saws results in exposure to fuels, cutting and lubricating oils and emissions of polycyclic aromatic hydrocarbons. Diesel-powered skidders and tractors have been employed for the extraction of logs from the forest in recent years, but only a small proportion of the logging crew are machine operators.

Many of the same considerations apply to the finding of an increase in risk of NHL, particularly of lymphosarcoma and reticulosarcoma (ICD 200), among forestry workers. No increase in risk following exposure to forestry work, employment in a sawmill or as a timber merchant was demonstrated in previous New Zealand case-control studies of NHL based on interview data (Pearce et al., 19866, 1987). In contrast to findings in Sweden where 5- and 8-fold increases in risk of malignant lymphoma (ICD 200, 201 and 202 combined) were associated with exposure to phenoxyherbicides and chlorophenols (Hardell et *al.*, 1981), no increase in risk of NHL could be shown for these exposures in New Zealand, whether the analysis included cases registered under ICD 200 or ICD 202 or whether other cancer cases or general population members were used as controls. A recent Swedish cohort study (Wiklund et *al.*, 1988) showed no excess risk of NHL among timber cutters or other forestry workers. However, an elevated PMR for lymphosarcoma was found in US pulp and paper-mill workers (Milham and Demers, 1984), while Woods *et al.* (1987) found an elevated risk of NHL in persons who reported spraying forests with herbicides.

In summary, the data suggest that employment as a forestry worker in New Zealand carries increased risks of STS, NHL and other cancers. It currently appears unlikely that these are caused by exposure to phenoxyherbicides or chlorophenols, although this hypothesis cannot be excluded. Further studies are needed to confirm that forestry workers are at increased risk of these cancer types, and to ascertain which aspects of forestry may be involved.

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