ORIGINAL ARTICLE

Update of a prospective study of mortality and cancer incidence in the Australian petroleum industry

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Aims: To update the analysis of the cohort mortality and cancer incidence study of employees in the Australian petroleum industry.

Methods: Employees from 1981 to 1996 were traced through the Australian National Death Index and the National Cancer Statistics Clearing House. Cause specific mortality and cancer incidence were compared with those of the Australian population by means of standardised mortality ratios (SMRs) and standardised incidence ratios (SIRs). Associations between increased incidence of specific cancers and employment in the petroleum industry were tested by trends according to period of first employment, duration of employment, latency, and hydrocarbon exposure, adjusting for personal smoking history where appropriate. Total follow up time was 176 598 person-years for males and 10 253 person-years for females.

Results: A total of 692 of the 15 957 male subjects, and 16 of the 1206 female subjects had died by the cut off date, 31 December 1996. In males, the all-cause SMR and the SMRs for all major disease categories were significantly below unity. There was a non-significant increase of the all-cancer SIR (1.04, 95% CI 0.97 to 1.11). There was a significant increase of the incidence of melanoma (SIR 1.54, 95% CI 1.30 to 1.81), bladder cancer (SIR 1.37, 95% CI 1.00 to 1.83), and prostate cancer (SIR 1.19, 95% CI 1.00 to 1.40), and a marginally significant excess of pleural mesothelioma (SIR 1.80, 95% CI 0.90 to 3.22), leukaemia (SIR 1.39, 95%CI 0.91 to 2.02), and multiple myeloma (SIR 1.72, 95% CI 0.96 to 2.84).

Conclusions: Most cases of mesothelioma are probably related to past exposure to asbestos in refineries. The melanoma excess may be the result of early diagnosis. The excess bladder cancer has not been observed previously in this industry and is not readily explained. The divergence between cancer incidence and cancer mortality suggests that the ''healthy worker effect'' may be related to early reporting of curable cancers, leading to increased likelihood of cure and prolonged mean survival time.

Health Watch is a health surveillance programme of employees of the major sectors of the Australian petroleum industry. The mortality and cancer incidence of the Health Watch cohort to 31 December 1989 has been reported previously.[1 2] In this report we present the mortality and cancer incidence of the Health Watch cohort updated to the end of 1996.

METHODS

Health Watch was established in 1980–83 with an interview survey of employees of Australian Institute of Petroleum member companies. Information was obtained on work areas and tasks, and on smoking. Head office staff and those at facilities with fewer than 10 employees were excluded. Subjects were admitted to the cohort on completion of five years of service. More members were admitted to the cohort following three further surveys, the fourth survey being completed in 2000. At these surveys existing cohort members still employed were reinterviewed. Although participation is voluntary, the overall participation rate was over 90%. Follow up information is obtained twice yearly from Australian Institute of Petroleum (AIP) member companies, giving details of retirements, redundancies, and transfers. Those no longer employed by member companies are followed by periodic mailings to obtain an update of smoking and other information.

Jobs are coded according to the system developed by the American Petroleum Institute.[3 4] Total hydrocarbon exposure was derived from job codes and was ranked by a committee of industry occupational hygienists into seven categories of exposure. The distribution of person-years across these categories is unequal, most jobs being in the fourth ranked category. It is a somewhat crude measure of exposure: a more detailed, quantitative estimate of benzene exposures has been undertaken as part of a nested case-control study of leukaemia cases in the cohort.[5]

Names of cohort members are periodically submitted to the National Death Index (NDI) for matching to identify deceased members and ICD-9 coding for principal cause of death. The National Cancer Statistics Clearing House (NCSCH), a consolidated database from all State and Territory cancer registries, is searched for cancer registrations.

Standardised mortality ratios (SMRs) and standardised cancer incidence ratios (SIRs), adjusted by age and calendar year of occurrence by five year groupings, were generated by comparison of mortality and cancer incidence with national rates. Exact 95% confidence intervals were calculated: these do not rely on large numbers for validity.[6 7] Tests for constant SMRs and SIRs across several categories were carried out using Poisson regression.[8] Cancers with raised SIRs were analysed to detect trends in relation to period of first employment and duration of employment. To allow for uncertainties in latency, estimates were made of variation in incidence with time since first employment. Analyses were

Abbreviations: CI, confidence interval; Exp, expected; NCSCH, National Cancer Statistics Clearing House; NDI, National Death Index; Obs, observed; RIR, relative incidence ratio; SIR, standardised cancer incidence ratio; SMR, standardised mortality ratio

Main messages

- An excess of mesothelioma was found, and is probably the legacy of past exposures to asbestos in the petroleum industry. In contrast to earlier findings in this cohort, the excess of leukaemias is not statistically significant.
- There is an excess bladder cancer in the Australian petroleum industry, and a work related cause cannot be excluded.
- The ''healthy worker effect'', at least in the case of cancer, may be due to diagnosis occurring at earlier stages of cancer in occupational cohorts, with increased cure rates and prolonged mean survival time, rather than to lowered cancer incidence.

Policy implications

- Further exploration of the findings on bladder cancer in the petroleum industry, including attempts to identify any causal exposure, should receive priority.
- Policies of elimination of asbestos exposure need to be maintained.
- The finding of normal or above-normal rates of cancer incidence but significantly low mortality indicates that there is great scope for reduction in cancer mortality from screening for some cancers, such as melanoma and bowel and bladder cancer.

also performed for increasing hydrocarbon rank score—both for the highest ranked job ever held, and the rank score of the job held longest. The measure of effect in these analyses was relative incidence ratios (RIR), being the measure relative to a baseline stratum, adjusted by age, calendar year and, where appropriate, smoking. Poisson regression was used for the relative incidence rate calculations using the method described by Berry[9] and Breslow and Day.[10]

Names of subjects whose vital status was uncertain were submitted to the Australian Electoral Commission in 2001 (that is, five years after the cut off date). Subjects still on the electoral roll were categorised as still alive. Subjects whose names appeared on the NCSCH but not on the NDI were categorised as alive and their follow up continued to the cut off date. A total of 1258 males (8%) and 323 females (27%) remained untraced and their person-years of observation were censored from the date of last contact, if that date preceded the cut off date. Less than 2% of male person-time was lost from censoring.

RESULTS

Table 1 shows details of the cohort at 31 December 1996. Table 2 shows mortality by major cause. For men the all-cause SMR was 0.68 (95% CI 0.63 to 0.73). Mortality by each major disease category was also significantly below unity in males. In females the all-cause SMR was 0.70 (95% CI 0.40 to 1.14). Thirteen of the 16 female deaths were due to cancer, with an all-cancer SMR of 1.22 (95% CI 0.65 to 2.08).

Table 3 shows cancer mortality and cancer incidence in males. The SMR was significantly less than unity (0.84, 95% CI 0.74 to 0.94). There were no cancers of any major anatomical site for which the SMR significantly exceeded unity. The lung cancer SMR was significantly less than unity (0.66, 95% CI 0.51 to 0.85).

The SIR for all cancers was 1.04, a non-significant increase (95% CI 0.97 to 1.11). There were significant excesses of the incidence of melanoma (SIR 1.54, 95% CI 1.30 to 1.81), bladder cancer (SIR 1.37, 95% CI 1.00 to 1.83), and prostate cancer (SIR 1.19, 95% CI 1.00 to 1.40). Pleural mesothelioma (SIR 1.80, 95% CI 0.90 to 3.22), all leukaemias combined (SIR 1.39, 95% CI 0.91 to 2.02), and multiple myeloma (SIR 1.72, 95% CI 0.96 to 2.84) occurred in marginally significant excess. The incidence of lung cancer was significantly below unity (SIR 0.65, 95% CI 0.51 to 0.82).

All 11 pleural cancers were mesotheliomas. There were no peritoneal mesotheliomas. Not all occupational histories of the 11 cases of mesothelioma are sufficiently detailed to assess whether asbestos exposure during employment in the petroleum industry was responsible. Ten cases occurred in refinery workers, of whom six were fitters, welders, or maintenance workers, and two had probably had significant asbestos exposure prior to entering the petroleum industry. Three other refinery workers had had possible prior asbestos exposure before entering the industry (in one case this was in the petroleum industry in another country). The occupation of one refinery worker is not known. In the one case who was not a refinery worker, asbestos exposure may have occurred prior to entering the industry but not since. Inspection of the work histories of the individual cases suggests that most of the asbestos exposures occurred prior to the 1970s.

Both lung cancer incidence and lung cancer mortality were significantly reduced compared with the general male population. Lung cancer incidence was strongly associated with the amount of tobacco use. Former smokers had a relative incidence rate below that of those who smoked 1–19 cigarettes per day. There was only one lung cancer among lifelong non-smokers (1 per 59 635 person-years).

The incidence of melanoma was significantly raised overall, and the excess was significantly increased in refinery, terminal, and airport personnel. There was no significant association with decade of hire, duration of employment, time since hire, or hydrocarbon exposure ranking. Despite the excess incidence the mortality rate from melanoma was low, although not significantly different from that of the general population (SMR 0.82, 95% CI 0.41 to 1.47).

Bladder cancer incidence was significantly raised. As table 4 shows, increased incidence (but non-significant) was found in all workplace types except onshore production. After adjustment for the effects of age, calendar period of follow up, and smoking, the relative incidence ratio (RIR) of bladder cancer showed no significant association with period of hire, duration of employment, or time since hire. Based on the highest hydrocarbon rank score ever held, there is a clear and significant trend of increasing incidence with increased hydrocarbon exposure ($p = 0.02$). In the analysis based on the total hydrocarbon ranking of the job held longest, and there is a marginally significant ($p = 0.09$) tendency for increasing relative incidence with increasing hydrocarbon ranking.

Table 1 Employment details and vital status of cohort members

	Males	Females
Persons alive	14006	867
Vital status at cut off date unknown	1258	323
Deaths in Australia	684	16
Deaths overseas	8	0
Total	15956	1206
Total person-years	176598	10253
Median duration of employment (y)	16.3	13.0

Table 2 Mortality by major cause

	Males			Females		
Cause (ICD-9)	**Obs/Exp**	**SMR**	**95% CI**	**Obs/Exp**	**SMR**	**95% CI**
Cancer (140–208)	280/334.2	0.84	0.74 to 0.94	13/10.7	1.22	0.65 to 2.08
Ischaemic heart disease (410–414)	188/263.0	0.71	0.62 to 0.82	2/2.9	0.68	0.08 to 2.47
Stroke (430–438)	28/48.6	0.58	0.38 to 0.83	0		
Respiratory disease (460–519)	30/58.5	0.51	0.35 to 0.73	0		
Digestive system diseases* (570–579)	18/33.5	0.54	0.32 to 0.85	0		
Accidents/violence (800–999)	71/115.3	0.62	0.48 to 0.78	0		
All other causes	69/156.6	0.44	0.34 to 0.56	1/9.2	0.1	0 to 0.6
All causes	684/1009.7	0.68	0.63 to 0.73	16/22.8	0.70	0.40 to 1.14

*Disorders of liver and biliary tract, pancreas, gastrointestinal haemorrhage other than from peptic ulcer, and intestinal malabsorption.

There was a non-significant excess of all leukaemias combined (SIR 1.39, 95% CI 0.91 to 2.02). This contrasts with the previous report of this cohort in which there was a significant leukaemia excess.[2] The numbers of the main individual leukaemia types (acute/chronic lymphatic, acute/chronic myeloid) were too low for meaningful analysis. However, there was a significant excess of ''all other leukaemias''—that is, those not included in the four leukaemia types specified above. The excess of all leukaemias combined was present in all workplace types except onshore production, but was not significant in any (table 5). There is a marginally significant trend towards increasing relative incidence with earlier periods of first employment ($p = 0.09$) but no association with duration of employment or time since hire. The RIR of leukaemia increases significantly with increasing rank score of hydrocarbon exposure, based on the highest rank score ever held ($p = 0.05$). Based on the rank score of the job held longest there is a marginally significant increase in risk with increased hydrocarbon exposure ($p = 0.07$). Analyses of leukaemia in table 5 show RIRs after adjustment for smoking; because of uncertainty as to whether smoking is an independent cause of leukaemia, RIRs were also computed without adjusting for smoking, with no material difference in the results.

The incidence of prostatic cancer shows no association with any workplace type, decade of hire, duration of employment, time since hire, or hydrocarbon exposure ranking. Mortality from prostatic cancer was close to unity (SMR 0.98, 95% CI 0.58 to 1.55).

Mortality from heart disease was significantly below unity (SMR 0.71, 95% CI 0.62 to 0.82). Ischaemic heart disease mortality was strongly related to the degree of tobacco use, with the reduction in former smokers almost down to that of lifelong non-smokers.

Shift workers showed no difference in all-cause mortality, all-cancer mortality, heart disease mortality, mortality from accidents and/or violence, and cancer incidence compared with non-shift workers. Relative to the general population the SMRs were significantly below unity, but cancer incidence was slightly increased (SIR 1.09, 95% CI 0.95 to 1.25).

Table 3 Standardised incidence ratios (SIRs) and standardised mortality ratios (SMRs) for major cancer types, with 95% confidence intervals (95% CI); males

Cancer site (ICD-9)	**Obs/Exp cancers**	**SIR**	**95% CI**	**Obs/Exp deaths**	**SMR**	**95% CI**
Lip, oral cavity, pharynx (140–149)	39/52.9	0.74	0.52 to 1.00	6/13.0	0.46	0.17 to 1.00
Oesophagus (150)	6/11.8	0.51	0.19 to 1.11	6/11.0	0.54	0.20 to 1.18
Stomach (151)	26/24.5	1.06	0.69 to 1.56	15/14.6	1.03	0.58 to 1.70
Colon (153)	64/68.5	0.93	0.72 to 1.19	27/32.4	0.83	0.55 to 1.21
Rectum (154)	49/47.9	1.02	0.76 to 1.35	11/13.3	0.83	0.41 to 1.48
Liver (155)	6/7.1	0.84	0.31 to 1.84	4/6.9	0.58	0.16 to 1.49
Gall bladder (156)	4/4.4	0.92	0.25 to 2.35	3/2.1	1.41	0.29 to 4.12
Pancreas (157)	16/15.2	1.05	0.60 to 1.71	10/14.6	0.69	0.33 to 1.26
Larynx (161)	14/15.2	0.92	0.50 to 1.55	2/5.3	0.38	0.05 to 1.36
Lung (162)	73/111.9	0.65	0.51 to 0.82	62/93.6	0.66	0.51 to 0.85
Pleura (163)	11/6.1	1.80	0.90 to 3.22	6/3.1	1.96	0.72 to 4.27
Connective tissue (171)	6/7.4	0.81	0.30 to 1.76	2/2.2	0.93	0.11 to 3.35
Melanoma (172)	143/92.9	1.54	1.30 to 1.81	11/13.4	0.82	0.41 to 1.47
Non-melanotic skin (173)	*			2/3.5	0.56	0.07 to 2.04
Prostate (185)	137/115.3	1.19	1.00 to 1.40	18/18.4	0.98	0.58 to 1.55
Testis (186)	14/11.3	1.24	0.68 to 2.08	1/0.82	1.22	0.03 to 6.8
Bladder (188)	46/33.5	1.37	1.00 to 1.83	6/6.1	0.98	0.36 to 2.13
Kidney (189)	28/24.5	1.14	0.76 to 1.65	13/8.8	1.49	0.79 to 2.54
Eye (190)	5/2.7	1.85	0.60 to 4.31	†		
Brain/nervous system (191–192)	16/17.0	0.94	0.54 to 1.53	15/14.2	1.06	0.59 to 1.74
Non-Hodgkin's lymphoma (200–202)	32/33.6	0.95	0.65 to 1.35	11/13.4	0.82	0.40 to 1.47
Multiple myeloma (203)	15/8.7	1.72	0.96 to 2.84	8/4.9	1.63	0.70 to 3.22
All leukaemias (204–208)	27/19.5	1.39	0.91 to 2.02	16/10.9	1.47	0.84 to 2.39
Acute lymphatic leukaemia (204.0)	1/1.2	0.84	0.02 to 4.68	2/1.1	1.81	0.22 to 6.56
Chronic lymphatic leukaemia (204.1)	7/7.2	0.97	0.39 to 2.00	0/1.8	0	
Acute myeloid leukaemia (205.0)	6/5.8	1.04	0.38 to 2.27	5/4.90	1.03	0.33 to 2.39
Chronic myeloid leukaemia (205.1)	4/3.4	1.18	0.32 to 3.02	4/2.0	2.03	0.55 to 5.20
All other leukaemias	9/1.9	4.65	2.13 to 8.83	5/1.2	4.33	1.40 to 10.1
Other and unspecified sites	36/50.9	0.70	0.50 to 0.98	25/27.8	0.90	0.58 to 1.33
All malignant (excluding 173)	813/782.7	1.04	0.97 to 1.11	280/334.2	0.84	0.74 to 0.94

*Not a registrable disease in most Australian cancer registries.
†Expected value could not be computed due to grouping of ICD-9 190 in national data into ICD 190–199.

Table 4 Bladder cancer: SIR by workplace type and RIR by period of hire, duration of employment, years since hire, highest hydrocarbon ranking job held, and hydrocarbon ranking of job held longest, adjusted for age, calendar year; RIRs also adjusted for smoking

Workplace type	Person-years	Obs/Exp	SIR	95% CI
Refinery	69795	21/14.2	1.48	0.92 to 2.26
Terminal	73373	18/15.1	1.19	0.71 to 1.88
Airport	6877	4/1.4	2.85	0.78 to 7.29
Onshore production	19629	2/2.2	0.9	0.11 to 3.27
Offshore production	6924	1/0.6	1.61	0.04 to 8.96
Period of hire	**Person-years**	**Cases**	**RIR***	**95% CI**
Post-1975	79838	9	1	
1965–74	60283	13	0.82	0.32 to 2.08
1955–64	24837	16	0.98	0.35 to 2.75
Pre-1955	11640	8	0.68	0.21 to 2.24
Years of employment	**Person-years**	**Cases**	**RIR†**	**95% CI**
5–9	45836	4	1	
10–15	43718	10	1.45	0.44 to 4.80
15–19	32976	6	0.74	0.20 to 2.81
20–24	21475	2	0.25	0.04 to 1.45
25+	32593	24	0.99	0.29 to 3.40
Years since hire	**Person-years**	**Cases**	**RIR‡**	**95% CI**
5–9	37624	4	1	
10–14	41147	5	0.68	0.18 to 2.61
15–19	34372	6	0.57	0.15 to 2.21
20–24	23741	6	0.47	0.11 to 1.94
25+	39714	25	0.44	0.12 to 1.65
Highest hydrocarbon ranking job	**Person-years**	**Cases**	**RIR§**	**95% CI**
1	33991	6	1	
2	14986	1	0.79	0.09 to 6.68
3	1912		0	
4	80583	23	2.06	0.83 to 5.08
5	6430	2	2.65	0.53 to 13.2
6	28420	9	2.21	0.78 to 6.26
7	10252	5	3.74	1.14 to 12.3
Hydrocarbon ranking longest job	**Person-years**	**Cases**	**RIR¶**	**95% CI**
1	45922	8	1	
2	15856	1	0.66	0.08 to 5.34
3	2959	0	0	
4	74258	25	2.02	0.91 to 4.48
5	4723	1	1.32	0.17 to 10.6
6	25187	8	1.84	0.69 to 4.92
7	5011	2	2.11	0.45 to 9.95

Tests for trend: *p=0.63, †p=0.60, ‡p=0.24, §p=0.02, ¶p=0.09.

At the cut-off date 16 females had died, 13 from cancer. There was a marginally significant increase in all-cancer incidence (SIR 1.33 95% CI 0.98 to 1.78). There was a statistically significant increase in melanoma incidence (SIR 2.75, 95% CI 1.42 to 4.80) (table 6). The SIR for bladder cancer was 7.13, based on three cases (95% CI 1.47 to 20.82). The all-cancer SMR was 1.22 (95% CI 0.65 to 2.08) (table 2).

DISCUSSION

Low SMRs are common in occupational cohorts, a finding commonly called ''the healthy worker effect''. The ''healthy worker effect'' is reported to abate[11 12] or even to go into reverse[13] with aging of occupational cohorts, and the all-cause SMR of 0.68 compared with 0.63 as reported in the cohort up to 1989[1] suggests that this is also occurring in this cohort.

The ''healthy worker effect'' has been attributed to healthy individuals being selected for employment.[14 15] The discovery of a ''healthy worker effect'' was based on mortality studies, so that the proposition that occupational cohorts have lower disease incidence than the general population is speculative, and can only be clarified by concurrent analyses of disease incidence and mortality. Cancer mortality is an imperfect measure of the occurrence of cancer, being a function not only of cancer incidence, but also of cancer survival and the frequency of death from competing causes. A strength of the present study has been its ability concurrently to examine mortality and cancer incidence; this is in contrast to nearly all studies of the industry in other countries, which have had mortality as their single end-point.

The finding of an all-cancer SIR of 1.04 (an increase of marginal significance) with an all-cancer SMR of 0.84 (significantly reduced) indicates that at least in the case of cancer, the low SMR is not the result of low cancer incidence. An alternative explanation of the low SMR is prolonged survival. The prospect of cure and the survival time from cancer is strongly related to the site of the cancer and the staging at the time of diagnosis. As shown in table 3, the strongest contributor to the difference between SIR and SMR for cancer is melanoma, in which the incidence of disease in Australia is increasing, whereas the mortality rate is stable. This divergence has been attributed to earlier diagnosis.[16] Other contributors to the difference between SIR and SMR in this cohort have been cancers of the colon, rectum, bladder,

Table 5 Leukaemia: SIR by workplace type and RIR by period of hire, duration of employment, years since hire, highest hydrocarbon ranking job held, and hydrocarbon ranking of job held longest, adjusted for age, calendar year; RIRs also adjusted for smoking

Workplace type	Person-years	O/E	SIR	95% CI
Refinery	69795	10/8.1	1.24	0.59 to 2.27
Terminal	73373	14/8.6	1.63	0.89 to 2.73
Airport	6877	1/0.8	1.24	0.03 to 6.92
Onshore production	19629	1/1.5	0.66	0.02 to 3.67
Offshore production	6924	1/0.5	2.15	0.05 to 11.97
Period of hire	**Person-years**	**Cases**	**RIR***	**95% CI**
Post-1975	79838	7	1	
1965–74	60283	8	1.11	0.36 to 3.39
1955–64	24837	5	1.51	0.34 to 6.69
Pre-1954	11640	7	4.03	0.81 to 20.1
Years of employment	**Person-years**	**Cases**	**RIR†**	**95% CI**
5–9	45836	4	1	
10–15	43718	5	1.14	0.30 to 4.41
15–19	32976	4	1.08	0.24 to 4.82
20–24	21475	4	1.53	0.32 to 7.32
25+	32593	10	1.97	0.43 to 9.13
Years since hire	**Person-years**	**Cases**	**RIR‡**	**95% CI**
5–9	37624	4	1	
10–14	41147	3	0.63	0.14 to 2.89
15–19	34372	3	0.69	0.14 to 3.51
20–24	23741	7	2.14	0.48 to 9.55
25+	39714	10	1.33	0.26 to 6.88
Highest hydrocarbon ranking job	**Person-years**	**Cases**	**RIR§**	**95% CI**
1	33991	1	1	
2	14986	1	3.17	0.19 to 51.9
3	1912	0	0	
4	80583	16	7.14	0.94 to 54.1
5	6430	1	6.65	0.41 to 106.7
6	28420	6	6.9	0.82 to 58.0
7	10252	2	7	0.63 to 77.9
Hydrocarbon ranking longest job	**Person-years**	**Cases**	**RIR¶**	**95% CI**
1	45922	2	1	
2	15856	1	1.79	0.16 to 20.1
3	2959	0	0	
4	74258	17	4.93	1.14 to 21.4
5	4723	1	5.11	0.46 to 56.4
6	25187	6	4.63	0.93 to 23.2
7	5011	0	0	

Tests for trend—*p=0.09, †p=0.34, ‡p=0.37, §p=0.05, ¶p=0.07

and larynx, cancers which have quite a good prognosis if diagnosed early. Thus a plausible explanation of the ''healthy worker effect'', at least in the case of cancer, may be earlier diagnosis than in the general population.

Higher social class has been shown to be associated with earlier presentation of cancer.[17] It is possible that secure employment also confers an advantage in socioeconomic status. Economic factors and health promotion programmes in the petroleum industry may lead to early presentation and diagnosis of cancer and hence the low cancer mortality found in this cohort.

Table 6 SIRs and SMRs for major cancer types; females

Cancer site (ICD-9)	Obs/Exp	SIR	95% CI
Colon (153)	4/2.5	1.63	0.44 to 4.16
Melanoma (172)	12/4.4	2.75	1.42 to 4.80
Breast (174)	12/11.7	1.02	0.53 to 1.79
Cervix (180)	3/1.9	1.61	0.33 to 4.71
Bladder (188)	3/0.4	7.13	1.47 to 20.82
Other	12/13.7	0.88	0.45 to 1.54
All cancers	46/34.5	1.33	0.98 to 1.78

The occurrence of a number of cases of mesothelioma in the Health Watch cohort is consistent with other recently published studies of oil refinery workers,[18–21] and is indicative of past asbestos exposure. Although the likelihood of such exposure in some cohort members might suggest a risk of raised lung cancer incidence, such a risk is not apparent in this cohort. Lung cancer is the only cancer which has a significantly low SIR, despite a smoking prevalence in the cohort very similar to that of the general population (age adjusted prevalence of 24.1% compared with the Australian population rate of 28.2%).[22] The concurrence of mesothelioma and a significantly low rate of lung cancer has been a consistent finding in petroleum industry studies, as has been shown by Tsai and colleagues.[20] Moreover such studies have also shown smoking prevalences similar to those of the comparison populations. The consistently low lung cancer rates suggest that asbestos is making little if any contribution to lung cancer in the petroleum industry. There is some support for the view that asbestos can cause lung cancer at exposures too low to cause asbestosis, although this question

remains controversial.[23–25] The findings in this cohort—in which there has been only one registered death from asbestosis—and in other cohorts in this industry suggest that low level asbestos exposure confers a risk of mesothelioma but not of asbestos related lung cancer.

A possible explanation for the low lung cancer incidence may be differences in the amount smoked—that is, smokers in the petroleum industry smoke less, and ex-smokers quit sooner, than smokers in the general population: lung cancer incidence is very sensitive to these variables.[26] The occurrence of only one lung cancer among life-long non-smokers reaffirms that lung cancer in people who have never been active smokers is a rare disease.

The increased melanoma incidence is unrelated to workplace type, duration of employment, or hydrocarbon exposure, so that occupational causation is unlikely. A plausible alternative explanation is early reporting, resulting from periodic medical examinations, as well as health promotion programmes advising workers of the warning signs of skin cancer, would be expected to lead to a high reporting rate. If this leads to melanomas being reported at an earlier age than in the general population an increased SIR could result. Despite the excess melanoma incidence the mortality rate is low (but not significantly).

There was also a significant excess of melanoma in females. An occupational cause is even less likely in female workers, and early reporting is therefore the likely explanation of the raised SIR. That being so, early reporting is likely to have occurred in male workers also.

The increase in bladder cancer incidence is unlikely to be the result of confounding from smoking, despite the important role of smoking in the causation of this cancer. As discussed above, the smoking prevalence in the cohort is comparable with that of the Australian male population. Moreover the low incidence of lung cancer and non-malignant respiratory disease suggests that smokers in the cohort may on the whole have a low level of tobacco use. Evidence for an occupational cause is inconclusive. No tendency to increased incidence is apparent from increasing duration of employment, although there is a trend towards increasing incidence with increasing hydrocarbon exposure. A possible contributing factor to the raised incidence could be an increased reporting rate, as with melanoma. The absence of an increased mortality rate for bladder cancer (SMR 0.98, 95% CI 0.36 to 2.13) would be consistent with early reporting with a high cure rate. Bladder cancer often responds well to treatment: South Australian cancer registry data show that bladder cancer cases outnumber bladder cancer deaths more than 2 to 1.[16] Accordingly the increased bladder cancer incidence may be related to early reporting. This may be a vindication of the practice of periodic medical surveillance of employees in the industry, especially if regular medical testing includes urine testing for the presence of haematuria.

Nevertheless an occupational cause must be considered. Although excess risk of bladder cancer has not been documented previously in this industry, most previous studies have been of cancer mortality rather than incidence. Even in this study bladder cancer mortality was not raised. A potential cause of bladder cancer is exposure to polycyclic aromatic hydrocarbons (PAHs), which have been associated with bladder cancer in the aluminium reduction industry.[27] PAHs are present in a number of diesel and fuel oils, but the heaviest concentrations occur in the furfural extraction units in the lubrication oil refineries, of which there are four in Australia. However, only 11 of the 46 bladder cancers occurred in employees of these refineries, and work in a furfural extraction unit was not mentioned in any of the job histories.

Interpretation of the leukaemia excess is made difficult by the conflicting results of dose-response analysis. Overall the excess was not statistically significant. RIR increased with hydrocarbon rank score but not with duration of employment. A possible explanation is that brief but high benzene exposures may be causally related to leukaemia. On the other hand the dose-response gradient may be partly due to a chance effect. The RIR estimates in table 5 are relative to exposures in the lowest category, where there were very few cases, indeed only a single case for hydrocarbon ranking of job held longest. Using an external comparison, the SIR for leukaemia in the lowest exposure category (category 1) was very low. Combining the two lowest exposure categories, the SIR was 0.46, with a 95% CI of 0.09 to 1.34. Thus if the true SIR were near the upper confidence limit, the trend of increasing risk with increasing hydrocarbon exposure in table 5 would almost be eliminated.

The absence of a significant excess of leukaemia contrasts with the previous report of this cohort,[2] and with the findings of a concurrent case-control study nested within the cohort.[28] Because of this the leukaemia findings have been presented in some detail. Three leukaemia cases (all chronic lymphatic leukaemia) notified by cohort members, and confirmed as real cases, were excluded from the analysis as they were not registered with the NCSCH, so that the leukaemia incidence rate is probably an underestimate. The numbers of individual leukaemia types in this cohort are too low for a causal association to be fully evaluated. As shown in table 3, the only category of leukaemia in significant excess is ''all other leukaemias'', that is, those not classified as acute or chronic myeloid leukaemia or acute or chronic lymphatic leukaemia. This finding prompted a review of ''all other leukaemias'' by a haematologist, who was provided with the histological reports. This review suggested that three of the ''all other leukaemias'' were actually chronic lymphatic leukaemias, making 10 such cases in all, and three were acute myeloid leukaemias, making nine such cases in all. The association between leukaemia and quantitative estimates of benzene exposure is examined in the separate case-control study.

The significantly low SMR from ischaemic heart disease in shift workers is of interest in view of prior epidemiological evidence that shift work is a risk factor for heart disease.[29]

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REFERENCES

1 **Christie D**, Robinson K, Gordon I, *et al.* A prospective study of the Australian petroleum industry. I Mortality. *Br J Ind Med* 1991;**48**:507–10.
2 **Christie D**, Robinson K, Gordon I, *et al.* A prospective study of the Australian petroleum industry II incidence of cancer. *Br J Ind Med* 1991;**48**:511–14.
3 **Tabershaw Occupational Medicine Associates**. *Job code classification system: Part1—Petroleum refineries and selected petrochemical operations*. Washington: API, 1979.
4 **American Petroleum Institute OH Industrial Hygiene Sub-Committee**. *Job code classification system: Part II—Production operations and marketing/ transportation operations*. Washington: API, 1985.
5 **Glass DC**, Gray CN. Estimating mean exposures from censored data: exposure to benzene in the Australian petroleum industry. *Ann Occup Hyg* 2001;**45**:275–82.

6 **Pearson ES**, Hartley HO. *Biometrika tables for statisticians*, Cambridge University Press, 1956:1.
7 **Liddell FDK**. Simple exact analysis of the standardised mortality ratio. *J Epidemiol Community Health* 1984;**38**:85–8.
8 **Breslow NE**, Lubin JH, Marek P, *et al*. Multiplicative models and cohort analysis. *Journal of the American Statistical Association* 1983;**78**:1–12.
9 **Berry G**. The analysis of mortality by the subject-years method. *Biometrics* 1983;**39**:173–84.
10 **Breslow NE**, Day NE. *Statistical methods in cancer research: Vol. II—The design and analysis of cohort studies*. Lyon: IARC, 1987.
11 **Monson RR**. Observations on the healthy worker effect. *J Occup Med* 1986;**28**:425.
12 **Wen CP**, Tsai SP, Gibson RL. Anatomy of the healthy worker effect: a critical review. *J Occup Med* 1983;**25**:283–9.
13 **Archer VE**. Reversal of the healthy worker effect. *Int J Occup Environ Health* 1195;**1**:33–6.
14 **McMichael AJ**. Standardized mortality ratios and the ''healthy worker effect'': scratching beneath the surface. *J Occup Med* 1976;**18**:165–8.
15 **Wilcosky T**, Wing S. The healthy worker effect. Selection of workers and work forces. *Scand J Work Environ Health* 1987;**13**:70–2.
16 **South Australian Cancer Registry**. *Epidemiology of cancer in South Australia. Incidence, mortality and survival 1977 to 1999. Cancer series no. 22.* Adelaide: SA Department of Human Services, 2000.
17 **Ionescu MV**, Carey F, Tait IS, *et al*. Socioeconomic status and stage at presentation of colorectal cancer. *Lancet* 1998;**352**:1439.
18 **Gennaro V**, Ceppi M, Boffetta P, *et al*. Pleural mesothelioma and asbestos exposure among Italian oil refinery workers. *Scand J Work Environ Health* 1994;**20**:213–15.
19 **Gennaro V**, Finkelstein MM, Ceppi M, *et al*. Mesothelioma and lung tumors attributable to asbestos among petroleum workers. *Am J Ind Med* 2000;**37**:275–82.
20 **Tsai SP**, Waddell LC, Gilstrap EL, *et al*. Mortality among maintenance employees potentially exposed to asbestos in a refinery and petrochemical plant. *Am J Ind Med* 1996;**29**:89–98.
21 **Lewis RJ**, Schnatter AR, Katz AM, *et al*. Updated mortality among diverse operating segments of a petroleum company. *Occup Environ Med* 2000;**57**:595–604.
22 **Hill DJ**, White VM, Scollo M. Smoking behaviours of Australian adults in 1995: trends and concerns. *Med J Aust* 1998;**168**:209–13.
23 **Weiss W**. Asbestosis: a marker for the increased risk of lung cancer among workers exposed to asbestos. *Chest* 1999;**115**:536–49.
24 **Karjalainen A**, Anttila S, Vanhala E, *et al*. Asbestos exposure and the risk of lung cancer in a general urban population. *Scand J Work Environ Health* 1994;**20**:243–50.
25 **Meldrum M**. *Review of fibre toxicology*. Sudbury: HSE Books, 1996.
26 **Peto R**, Darby S, Deo H, *et al*. Smoking, smoking cessation, and lung cancer in the UK since 1950: combination of national statistics with two case-control studies. *BMJ* 2000;**321**:323–9.
27 **Tremblay C**, Armstrong B, Theriault G, *et al*. Estimation of risk of developing bladder cancer among workers exposed to coal tar pitch volatiles in the primary aluminum industry. *Am J Ind Med* 1995;**27**:335–48.
28 **Glass DC**, Gray CN, Jolley DJ, *et al*. Leukemia risk associated with low-level benzene exposure. *Epidemiology* 2003;**14**:569–77.
29 **Tenkanen L**, Sjoblom T, Kalimo R, *et al*. Shift work, occupation and coronary heart disease over 6 years of follow-up in the Helsinki Heart Study. *Scand J Work Environ Health* 1997;**23**:257–65.