

# Increased risk of oesophageal adenocarcinoma among upstream petroleum workers

Jorunn Kirkeleit,<sup>1,2</sup> Trond Riise,<sup>1,3</sup> Tone Bjørge,<sup>1</sup> Bente E Moen,<sup>1</sup> Magne Bråtveit,<sup>1</sup> David C Christiani<sup>2,3</sup>

<sup>1</sup>Department of Public Health and Primary Health Care, University of Bergen, Bergen, Norway

<sup>2</sup>Department of Environmental Health, Harvard School of Public Health, Boston, Massachusetts, USA

<sup>3</sup>Department of Epidemiology, Harvard School of Public Health, Boston, Massachusetts, USA

## Correspondence to

Jorunn Kirkeleit, Research Group for Occupational and Environmental Medicine, Department of Public Health and Primary Health Care, University of Bergen, PO Box 7804, N-5020 Bergen, Norway; [Jorunn.Kirkeleit@isf.uib.no](mailto:Jorunn.Kirkeleit@isf.uib.no)

Accepted 24 September 2009

## ABSTRACT

**Objectives** To investigate cancer risk, particularly oesophageal cancer, among male upstream petroleum workers offshore potentially exposed to various carcinogenic agents.

**Methods** Using the Norwegian Registry of Employers and Employees, 24 765 male offshore workers registered from 1981 to 2003 was compared with 283 002 male referents from the general working population matched by age and community of residence. The historical cohort was linked to the Cancer Registry of Norway and the Norwegian Cause of Death Registry.

**Results** Male offshore workers had excess risk of oesophageal cancer (RR 2.6, 95% CI 1.4 to 4.8) compared with the reference population. Only the adenocarcinoma type had a significantly increased risk (RR 2.7, 95% CI 1.0 to 7.0), mainly because of an increased risk among upstream operators (RR 4.3, 95% CI 1.3 to 14.5). Upstream operators did not have significant excess of respiratory system or colon cancer or mortality from any other lifestyle-related diseases investigated.

**Conclusion** We found a fourfold excess risk of oesophageal adenocarcinoma among male workers assumed to have had the most extensive contact with crude oil. Due to the small number of cases, and a lack of detailed data on occupational exposure and lifestyle factors associated with oesophageal adenocarcinoma, the results must be interpreted with caution. Nevertheless, given the low risk of lifestyle-related cancers and causes of death in this working group, the results add to the observations in other low-powered studies on oesophageal cancer, further suggesting that factors related to the petroleum stream or carcinogenic agents used in the production process might be associated with risk of oesophageal adenocarcinoma.

## INTRODUCTION

Oesophageal adenocarcinoma among white men has been increasing in incidence since the mid-1970s and has replaced squamous cell carcinoma as the most common type of oesophageal cancer in the United States and western Europe.<sup>1 2</sup> Present knowledge indicates that the two forms of cancer have distinct causative profiles. While the strongest proven risk factors associated with squamous cell carcinoma are smoking<sup>3</sup> and alcohol,<sup>3</sup> the strongest causative factors for adenocarcinoma include Barrett's oesophagus,<sup>4</sup> gastro-oesophageal reflux disease,<sup>5</sup> increased body mass index (BMI),<sup>6 7</sup> and to a lesser degree smoking.<sup>3</sup>

Although an increasing number of studies indicate an association between an elevated risk of oesophageal adenocarcinoma and exposure to occupational

## What this paper adds

- ▶ Although an increasing number of studies indicate an association between an elevated risk of oesophageal cancer and exposure to occupational agents, including those found in the petroleum industry, occupationally related chemical exposure has not yet been proved to be a causal factor.
- ▶ We found an increased risk of oesophageal adenocarcinoma, but not squamous cell carcinoma, among upstream petroleum workers.
- ▶ The results add to the observations in other low-powered studies, further suggesting that factors related to the petroleum stream or carcinogenic agents used in the production process increase the risk of oesophageal adenocarcinoma.
- ▶ The results underline the importance of distinguishing between carcinoma subtypes when assessing the role of specific occupational agents in oesophageal cancer.

agents,<sup>8–10</sup> occupationally related chemical exposure has not yet been proved to be a causal factor. Assessment of the role of occupational hazards in oesophageal cancer is mainly hampered by its relative rarity, at least in high income countries, and the fact that most studies have not distinguished between the carcinoma subtypes.

In a historical cohort study of petroleum workers, we previously found that petroleum workers employed on Norway's continental shelf from 1981 to 2003 had a higher risk of developing acute myelogenous leukaemia and multiple myeloma than the general working population.<sup>11</sup> The increased risk was found in the work category assumed to have the most extensive contact with crude oil and its derivatives. However, petroleum workers involved in producing crude oil are exposed to a wide range of carcinogenic agents.<sup>12</sup> We therefore analysed cancer incidence within this historical cohort to investigate whether the risk of other cancer types was increased. This article examines the risk of major cancer types with a particular focus on oesophageal cancer among workers in the upstream petroleum industry offshore and discusses the petroleum workers' risk in relation to suspected risk factors for oesophageal cancer.

## MATERIALS AND METHODS

### Study population and study design

We carried out a historical cohort study of cancer incidence among employees in Norway's upstream petroleum industry offshore. The cohort was

established using information from the Norwegian Registry of Employers and Employees which contains records from 1981 onwards. All Norwegian employers are required to register their employees using a personal identification number, industrial classification code (International Standard Industrial Classification (ISIC) or the Classification of Economic Activities in the European Union (NACE)), county of work and the first and last date of all their work engagements. On 31 July 2004, the Registry included 1 961 711 workers with 2 126 699 work engagements.<sup>13</sup> Kirkeleit *et al*<sup>11</sup> described the establishment of the cohort previously. In brief, we included all individual workers registered with any of the offshore-related industrial classification codes or having Norway's continental shelf (North Sea) as the work location. Based on the workers' location of work (onshore or offshore) and the industrial classification codes for their first registered engagement in the offshore-related petroleum industry, we categorised the offshore workers into five job categories: (1) upstream operators, (2) drilling and well maintenance, (3) catering personnel, (4) others offshore and (5) petroleum workers onshore.

The category 'upstream operators' only contains workers registered with the industrial classification codes ISIC 22 and NACE 11100 (extraction of crude oil and natural gas), and includes job categories such as process technicians, laboratory engineers, control operators and other job groups involved in the production process such as mechanics, electricians and turbine operators, hydraulics technicians and other support personnel. The category 'drilling and well maintenance offshore' includes the ISIC code 50230 (oil drilling) and NACE code 11200 (service activities incidental to oil and gas extraction excluding surveying), the latter comprising activities such as drilling of wells and installation, disassembling and maintenance of drilling towers at site on contract. The category 'catering offshore' includes job groups such as catering crew and housekeeping personnel. The category 'others offshore' includes miscellaneous industrial codes and comprises activities contracted out to oil field service companies, such as construction and maintenance personnel, logistics and technical consultancy activities. Since there are no onshore oil fields in Norway, 'petroleum workers onshore' contains mainly workers involved in administering, planning and coordinating the activities offshore.

We selected up to six referents per petroleum worker at random from the general working population, using the same Norwegian Registry of Employers and Employees and the same

year of first engagement of the corresponding petroleum worker. Statistics Norway did this by randomly selecting individuals available in the registry having the same sex, age and community of residence as the petroleum worker in question. To gain information on cancer incidence in the five job categories, the total cohort was linked to the Cancer Registry of Norway in April 2006, including all cases of cancer reported up to 31 December 2003, with information on the diagnosis (location and morphology) and date of diagnosis.

The crude historical cohort included 71 018 'at risk' workers from the petroleum industry and 424 584 referents. Workers in the upstream petroleum industry who had their work location onshore were not included in the analysis. We also excluded subjects from the cohort if they had had a cancer diagnosis before entering into the cohort and excluded referents if they had an earlier engagement in the petroleum industry before they were drawn as referents even if they were not considered to be exposed in that engagement. We allowed subjects to serve as referents for more than one 'subject at risk'. The final cohort included 27 919 offshore workers distributed in the four job categories. There were a total of 3154 (11.3%) female workers in these job categories with the majority working as catering personnel (49.1%), so the analyses were therefore restricted to male workers only. Table 1 provides the characteristics of the final male cohort.

To gain more information on mortality from lifestyle-related diseases, the cohort was linked to the Norwegian Cause of Death Registry. Information on all deaths reported up to 31 December 2003 was included, with information on date of death and underlying cause of death (ICD-8 to ICD-10). The cohort was also linked to the Norwegian Education Registry, including the variable highest completed education, ranging from 1 (elementary school) to 6 (PhD degree), as of September 2004.

### Statistical analysis

We estimated the rate ratios (RRs) for both cancer incidence and mortality comparing the various working categories with the general working population using the Cox proportional hazard regression model. For cancer risk, we censored subjects at the end of follow-up (31 December 2003), the date of death or date of diagnosis of another type of cancer than the one being studied, whichever occurred first. For mortality we censored subjects at the end of follow-up or date of death from another cause of mortality than the one being studied. We checked the

**Table 1** Characteristics of the study population examined to determine whether male workers employed in Norway's upstream petroleum industry offshore have a higher risk of developing cancer than the general male working population in Norway, 1981–2003

Variable	Referents	Onshore workers	Offshore workers (all)	Offshore workers			
				Upstream operators	Drilling and well maintenance	Catering personnel	Others offshore
Number of male workers (% of total)	283002 (77.3)	30611 (71.7)	24765 (88.7)	5853 (86.9)	6722 (95.4)	1231 (50.9)	10959 (93.5)
Age, mean (SD)							
At inclusion in the cohort	34.6 (9.5)	34.7 (9.7)	33.8 (9.0)	34.3 (7.8)	32.5 (8.5)	33.4 (10.0)	34.4 (9.6)
At the end of follow-up	47.2 (11.7)	46.7 (11.8)	47.0 (11.2)	50.6 (11.0)	43.5 (11.2)	50.1 (11.4)	46.8 (10.7)
Mean educational level (1–6, with 6 being the highest)	4.2 (1.5)	5.2 (1.6)	4.0 (1.2)	4.2 (1.2)	4.0 (1.2)	3.5 (1.1)	4.0 (1.3)
Tertiary education (%)	26.9	51.7	15.0	18.1	13.0	8.2	15.3
Intermediate education (%)	61.0	43.4	75.1	74.4	77.0	75.4	74.3
Compulsory education (%)	12.1	4.9	9.9	7.5	10.0	16.4	10.4
Average follow-up (years)	11.4 (6.6)	11.0 (6.6)	12.0 (6.5)	15.1 (6.0)	9.8 (6.5)	15.3 (6.3)	11.4 (6.0)
Person-years of follow-up	3224836	335339	297584	88418	65872	18774	124520

proportional hazards assumption for overall cancer and oesophageal cancer by comparing the estimated  $-\ln(-\ln)$  survivor curves for the groups being investigated. There was no marked deviation from the proportional hazards assumption.

The referents were matched to the petroleum workers by age and year of first registered engagement, but since we used the total reference population for analysing risk in each specific job category, there was no longer an identical distribution of age and year of first registered engagement between the reference group and the job categories. We therefore performed multivariate analysis including these independent covariates, in addition to educational level on a six-point scale. Age was defined at the time of entering into the cohort (time of first registered engagement) and used as a continuous variable in the model. We also performed analysis where age was included as a categorical variable (age at inclusion into the cohort in 5-year intervals). To ensure sufficient adjustment for the year of first engagement, we repeated all analyses of the 'upstream operators' using only the referents drawn for this specific job category. We also repeated the analyses excluding 'upstream operators' registered 1 year or less in the offshore industry.

We performed all analysis using SPSS 15.0.

### Ethics approval

We conducted the study with the approval of the Regional Committee for Medical Research Ethics of Western Norway, the Norwegian Data Inspectorate and the Norwegian Directorate of Health.

### RESULTS

The incidence of overall cancer (all sites) among the male offshore workers did not differ significantly from that of the general male working population in any job category (table 2).

Male offshore workers combined had an excess risk of cancer of the oesophagus (RR 2.6, 95% CI 1.4 to 4.8, n=12), larynx (RR 2.3, 95% CI 1.4 to 4.0, n=16) and lung, bronchus and trachea (RR 1.3, 95% CI 1.0 to 1.6, n=92). A deficit of cancer of the colon, rectum and anus of borderline significance was also noted (RR 0.8, 95% CI 0.6 to 1.0, n=71). The excess of cancer of the larynx and lung among male offshore workers is mainly ascribed to an increased risk among 'others offshore'.

For oesophageal cancer, only the adenocarcinoma type was significantly increased (RR 2.7, 95% CI 1.0 to 7.0, n=5), and the increased risk was mainly ascribed to an increased risk among 'upstream operators' (RR 4.3, 95% CI 1.3 to 14.5, n=3) and a non-significant excess among 'others offshore' (RR 3.2, 95% CI 0.8 to 13.9, n=2) (table 2). When we compared 'upstream operators' to a reference group only comprising referents drawn for this specific job category (n=30 714), the risk of oesophageal adenocarcinoma increased (RR 8.1, 95% CI 1.3 to 48.5). Excluding 'upstream operators' registered for 1 year or less in the petroleum industry offshore (n=61) did not change the risk estimates. Including age in the model as a categorical variable resulted in only minor changes in the risk estimates.

In the regression model, the level of education was inversely correlated with the risk of squamous cell carcinoma type in offshore workers (RR 0.6, 95% CI 0.5 to 0.8) for increasing level of education, but not with the risk of oesophageal adenocarcinoma (RR 0.9, 95% CI 0.7 to 1.2).

Table 3 shows the characteristics of the oesophageal cancer cases. All four cases of oesophageal cancer among 'upstream operators' had their first registered engagement prior to 1984 and had an engagement belonging to the job category 'upstream operators' at least until the year of diagnosis. The mean time from first registered engagement offshore until diagnosis was 16 years (range 7–19) for these four cases, and the mean age at

**Table 2** Rate ratios (RR) with 95% CIs for overall cancer and major cancer sites for male workers in the job categories in the upstream petroleum industry versus referents from the general working population of Norway, 1981–2003, adjusted for age at inclusion in the cohort, year of first exposure and education using the Cox proportional hazards model

ICD-10	Site of cancer	Referents (N = 283002) n	Offshore workers combined (N = 24765)		Upstream operators (N = 5853)		Oil drilling (N = 6722)		Catering personnel (N = 1231)		Others offshore (N = 10959)	
			n	RR (95% CI)	n	RR (95% CI)	n	RR (95% CI)	n	RR (95% CI)	n	RR (95% CI)
	Overall cancer (all sites)	8639	710	1.0 (0.9 to 1.1)	225	0.9 (0.8 to 1.1)	141	1.0 (0.8 to 1.1)	58	1.1 (0.8 to 1.4)	286	1.1 (1.0 to 1.2)
C00–C14	Lip, oral cavity and pharynx	269	23	1.0 (0.6 to 1.5)	5	0.7 (0.3 to 1.7)	6	1.2 (0.6 to 2.8)	6	3.5 (1.5 to 7.9)*	6	0.6 (0.2 to 1.4)
C15	Oesophagus	62	12	2.6 (1.4 to 4.8)*	4	2.8 (1.0 to 7.8)*	2	2.1 (0.5 to 8.6)	1	2.1 (0.3 to 15.3)	5	2.7 (1.1 to 6.9)*
	Adenocarcinoma	22	5	2.7 (1.0 to 7.0)*	3	4.3 (1.3 to 14.5)*	0	—	0	—	2	3.2 (0.8 to 13.9)
	Squamous cell carcinoma	34	5	2.2 (0.8 to 5.6)	1	1.8 (0.2 to 13.1)	1	2.4 (0.3 to 17.4)	1	4.2 (0.6 to 31.3)	2	1.9 (0.4 to 7.8)
C16	Stomach	266	23	1.0 (0.7 to 1.6)	8	0.9 (0.4 to 2.0)	6	1.6 (0.7 to 3.5)	2	1.1 (0.3 to 4.5)	7	0.9 (0.4 to 1.8)
C18–C21	Colon, rectum and anus	1120	71	0.8 (0.6 to 1.0)*	23	0.8 (0.5 to 1.1)	10	0.5 (0.3 to 1.0)	5	0.6 (0.2 to 1.5)	33	1.0 (0.7 to 1.4)
C25	Pancreas	186	8	0.6 (0.3 to 1.1)	3	0.6 (0.2 to 2.0)	2	0.8 (0.2 to 3.1)	1	0.8 (0.1 to 5.9)	2	0.4 (0.1 to 1.4)
C32	Larynx	90	16	2.3 (1.4 to 4.0)*	4	1.7 (0.6 to 4.7)	1	0.7 (0.1 to 5.3)	2	3.0 (0.7 to 12.4)	9	3.7 (1.8 to 7.3)*
C33–34	Lung, bronchus and trachea	892	92	1.3 (1.0 to 1.6)*	31	1.3 (0.9 to 2.0)	12	0.9 (0.5 to 1.5)	8	1.3 (0.6 to 2.5)	41	1.5 (1.1 to 2.0)*
C43	Malignant melanoma (skin)	808	61	0.9 (0.7 to 1.1)	20	0.8 (0.5 to 1.2)	16	1.1 (0.7 to 1.8)	5	1.2 (0.5 to 2.8)	20	0.8 (0.5 to 1.2)
C45	Mesothelioma	45	4	1.2 (0.4 to 3.4)	1	1.0 (0.1 to 7.1)	0	—	0	—	3	2.2 (0.7 to 7.2)
C61	Prostate	1377	110	1.1 (0.9 to 1.3)	31	1.0 (0.7 to 1.4)	22	1.1 (0.7 to 1.7)	3	0.3 (0.1 to 1.0)	54	1.4 (1.1 to 1.8)*
C62	Testis	537	51	1.1 (0.8 to 1.4)	19	1.6 (1.0 to 2.5)	8	0.6 (0.3 to 1.3)	5	1.9 (0.8 to 4.5)	19	1.0 (0.6 to 1.5)
C64	Kidney	264	29	1.3 (0.8 to 1.9)	8	0.92 (0.4 to 2.0)	6	1.1 (0.5 to 2.7)	3	1.7 (0.6 to 5.4)	12	1.6 (0.9 to 2.8)
C67	Bladder	457	41	1.1 (0.8 to 1.6)	9	0.74 (0.4 to 1.4)	8	1.2 (0.6 to 2.4)	6	1.7 (0.7 to 4.2)	18	1.3 (0.8 to 2.2)
C70–C72	Central nervous system	477	34	0.8 (0.6 to 1.2)	9	0.7 (0.4 to 1.3)	8	0.9 (0.4 to 1.8)	3	1.1 (0.4 to 3.5)	14	0.9 (0.5 to 1.5)
C91–C95	Leukaemia	188	18	1.1 (0.7 to 1.9)	11	2.1 (1.1 to 3.8)*	4	1.2 (0.4 to 3.2)	0	—	3	0.5 (0.2 to 1.6)
C90	Multiple myeloma	124	17	1.7 (1.0 to 2.9)*	10	2.6 (1.3 to 5.1)*	3	1.7 (0.5 to 5.3)	2	2.3 (0.6 to 9.5)	2	0.6 (0.2 to 2.5)
C81	Hodgkin lymphoma	85	4	0.5 (0.2 to 1.4)	0	—	2	1.0 (0.2 to 4.0)	0	—	2	0.6 (0.2 to 2.6)
C82–85, C96	Non-Hodgkin lymphoma	448	27	0.7 (0.5 to 1.0)	11	0.8 (0.4 to 1.5)	5	0.6 (0.3 to 1.5)	1	0.4 (0.1 to 2.6)	10	0.7 (0.4 to 1.3)

The letter 'n' denotes number of cases.

\*Statistically significant.

**Table 3** Characteristics of the oesophageal cancer cases found among male workers in four job categories in the upstream petroleum industry, Norway, 1981–2003

Job category	Worker	Localisation in oesophagus	Cell type	Year of first registered engagement	Year of diagnosis	Age at diagnosis	Time from first registered engagement to diagnosis (years)
Upstream operators	1	Lower third	Adenocarcinoma	1984	2003	49	19
	2	Lower third	Adenocarcinoma	1984	1991	47	7
	3	Lower third	Adenocarcinoma	1984	2002	61	18
	4	Unspecified	Squamous cell carcinoma	1984	2003	69	19
Drilling and well maintenance	1	Middle third	Other carcinomas	1981	2003	48	22
	2	Lower third	Squamous cell carcinoma	1982	1984	50	2
Other workers offshore	1	Upper third	Other carcinomas	1991	2003	53	12
	2	Lower third	Adenocarcinoma	1987	2003	52	16
	3	Lower third	Adenocarcinoma	1982	1991	55	9
	4	Lower third	Squamous cell carcinoma	1987	1995	59	8
	5	Lower third	Squamous cell carcinoma	1989	1999	55	10
Catering	1	Lower third	Squamous cell carcinoma	1989	1989	47	1

diagnosis was 57 years (range 47–69). The corresponding mean age for referents was 58 years (range 41–74). The groups did not differ significantly in age at diagnosis (data not shown).

Table 4 shows the rate ratios of overall mortality and broad categories of causes of death related to lifestyle factors among the job categories. Overall mortality was slightly higher for the offshore workers combined (RR 1.1, 95% CI 1.0 to 1.2, n=844). This excess risk was ascribed to increased mortality in the job categories 'catering personnel' (RR 1.4, 95% CI 1.1 to 1.7, n=91) and 'others offshore' (RR 1.3, 95% CI 1.2 to 1.5, n=381). 'Upstream operators' had a decreased overall mortality of borderline significance (RR 0.9, 95% CI 0.7 to 1.0, n=215), having no increased risk of any of the lifestyle-related causes of death investigated. The risk estimates for diabetes mellitus showed only minor differences when we also included diabetes mellitus as a contributory cause of death ('upstream operators': RR 1.1, 95% CI 0.4 to 2.9, n=4).

## DISCUSSION

Male offshore workers had an increased risk of oesophageal adenocarcinoma compared with the general male working population. The increased risk was mainly ascribed to an excess among workers in the job category 'upstream operators'. These workers had a lower overall mortality and did not differ significantly from the general working population as regards incidence of overall cancer (all sites), cancer of the respiratory system and colon, or mortality from any of the lifestyle-related diseases investigated. All four subjects with oesophageal cancer among 'upstream operators' had their first registered engagement prior to 1984 and had long engagements as 'upstream operators' ending only after cancer was diagnosed, corresponding to the low turnover reported for this industry.<sup>13</sup> The 'upstream operators' also had an excess risk of leukaemia and multiple myeloma, which in a previous report was thought to be associated with the workers' contact with crude oil and its derivatives.<sup>11</sup> These results suggest that the work environment is at least partly associated with the excess risk of oesophageal adenocarcinoma.

## OCCUPATIONAL EXPOSURE TO CHEMICAL AGENTS

At present there is no evidence indicating a causal relationship between occupational chemical exposure and any type of oesophageal cancer, but suggested agents include asbestos,<sup>9 10 14</sup> silica dust,<sup>15 16</sup> various types of organic solvents including chlorinated hydrocarbons,<sup>8 10 17–19</sup> volatile sulphur compounds,<sup>10</sup> combustion

by-products containing polycyclic aromatic hydrocarbons (PAH)<sup>20–23</sup> and mineral oils.<sup>24 25</sup> The few studies that have differentiated between the two subtypes of oesophageal cancer reported an association between the adenocarcinoma type and chlorinated hydrocarbon solvents,<sup>8 10</sup> asbestos<sup>9</sup> and volatile sulphur compounds.<sup>10</sup> In contrast, in a study assessing lifetime exposure to many of the above-mentioned occupational agents, it was concluded that specific airborne occupational exposures are not of major importance in the aetiology of adenocarcinoma,<sup>26</sup> while in two other studies no relationship was found between oesophageal cancer and occupational exposure to exhaust from diesel or gasoline engines.<sup>10 27</sup>

A retrospective exposure assessment performed in Norway's petroleum industry offshore concluded that offshore workers have been potentially exposed to most of the carcinogenic agents mentioned above either through their contact with the petroleum stream (crude oil, PAHs and volatile sulphur compounds) or agents used in the production process (asbestos, silica dust, chlorinated hydrocarbons and various synthetic and mineral oil-based fluids).<sup>12</sup> However, in the same study it is concluded that information about exposure levels is scarce. The main exposures for the job category 'upstream operators' are the different phases of the petroleum stream, a large number of synthetic and mineral oil-based fluids, and until the early 1990s chlorinated hydrocarbons used as metal-degreasing agents.<sup>12</sup>

Except for a few studies reporting an excess risk of oesophageal cancer (all subtypes) among oil refinery workers<sup>28</sup> and filling station attendants,<sup>29</sup> most studies performed in the petroleum industry that have included oesophageal cancer as a distinct cancer type have not shown significantly increased risk.<sup>30–34</sup> In one of these studies a deficit of oesophageal cancer (n=18) was found among 24 000 crude oil production workers.<sup>30</sup> However, as none of these studies differentiated between the two subtypes of oesophageal cancer, a possible association for the adenocarcinoma type might have been underestimated. Further, a healthy worker effect is a potential limitation of previous studies in the petroleum industry generally reporting a significantly lower overall mortality and overall cancer incidence compared with the general population. We aimed at reducing this effect by using a historical prospective design and selecting our referents from the general working population and from the same registry as the subjects 'at risk'. In our study, the overall incidence of cancer (all sites) among the offshore workers did not differ significantly from that of the general working population in any job category. However, the mortality ratio was significantly below unity for



**Table 4** Rate ratios (RR) with 95% CIs for all causes of death and broad categories of causes of death related to lifestyle factors among male workers in the different job categories in the upstream petroleum industry offshore versus referents from the general working population, Norway, 1981–2003, adjusted for age at inclusion in the cohort, year of first exposure and education using the Cox proportional hazards model

Cause of death	ICD-10	Referents		Offshore workers (all combined)		Upstream operators		Oil drilling		Catering personnel		Others offshore	
		n	RR (95% CI)	n	RR (95% CI)	n	RR (95% CI)	n	RR (95% CI)	n	RR (95% CI)	n	RR (95% CI)
All causes of death		8930	1.1 (1.0 to 1.2)*	844	1.1 (1.0 to 1.2)*	215	0.9 (0.7 to 1.0)*	157	1.1 (0.9 to 1.3)	91	1.4 (1.1 to 1.7)*	381	1.3 (1.2 to 1.5)*
Diabetes mellitus	E10–E14	111	0.6 (0.3 to 1.4)	6	0.6 (0.3 to 1.4)	3	1.0 (0.3 to 3.1)	1	0.5 (0.1 to 3.9)	0	—	2	0.5 (0.1 to 2.1)
Diseases of the circulatory system	I00–I99	2684	1.1 (0.9 to 1.2)	227	1.1 (0.9 to 1.2)	63	0.9 (0.7 to 1.1)	38	1.0 (0.7 to 1.3)	28	1.3 (0.9 to 1.9)	98	1.2 (1.0 to 1.5)
Ischaemic heart disease	I20–I25	1817	1.0 (0.8 to 1.2)	143	1.0 (0.8 to 1.2)	42	0.9 (0.6 to 1.2)	24	0.9 (0.6 to 1.3)	12	0.8 (0.4 to 1.4)	65	1.2 (0.9 to 1.5)
Cerebrovascular disease	I60–I69	374	1.3 (0.9 to 1.8)	38	1.3 (0.9 to 1.8)	14	1.4 (0.8 to 2.5)	5	1.0 (0.4 to 2.3)	5	1.8 (0.7 to 4.3)	14	1.1 (0.7 to 2.0)
Diseases of the respiratory system	J00–J99	279	1.5 (1.0 to 2.1)	30	1.5 (1.0 to 2.1)	9	1.5 (0.8 to 2.9)	6	1.5 (0.6 to 3.6)	5	2.2 (0.9 to 5.4)	10	1.2 (0.7 to 2.3)
Alcoholic liver disease	K70	130	1.3 (0.8 to 2.3)	14	1.3 (0.8 to 2.3)	5	1.4 (0.6 to 3.4)	2	1.0 (0.2 to 3.9)	2	2.0 (0.5 to 8.3)	5	1.2 (0.5 to 3.0)
Alcoholic psychosis or chronic alcohol abuse	F10	161	2.1 (1.4 to 3.1)*	29	2.1 (1.4 to 3.1)*	7	1.6 (0.7 to 3.3)	5	1.8 (0.7 to 4.4)	7	5.7 (2.7 to 12.2)*	10	1.9 (1.0 to 3.6)

The letter 'r' denotes number of cases.

\*Statistically significant.

the job category 'upstream operators offshore', indicating that a healthy worker effect still might have been present in this specific work category.

## LIFESTYLE FACTORS

A major limitation of our study is the lack of data on other risk factors for oesophageal adenocarcinoma, such as prevalence of gastro-oesophageal reflux and the lifestyle factors BMI, smoking and alcohol consumption. However, an important finding in the present study is that the job category 'upstream operators' did not have an increased risk of cancer of the colon, rectum or anus, or any excess mortality from lifestyle-related diseases such as cardiovascular diseases or diabetes mellitus, which would have been expected if these workers had a higher BMI than the referents. This gives little support to BMI being the main cause for the increased cancer risk found in this job category.

Smoking is one of the primary risk factors for squamous cell carcinoma of the oesophagus and is, to a lesser degree, a risk factor for adenocarcinoma.<sup>5</sup> We do not have any information on smoking in our study population. However, in our analysis, the risk estimates were adjusted for level of education. Education might be used as a surrogate measure of smoking, with smoking increasing as educational level decreases.<sup>35</sup> In our study, educational level was inversely correlated with the risk of the squamous cell carcinoma type among offshore workers, which is compatible with smoking being a strong risk factor for this subtype. No such correlation was found for the adenocarcinoma type, arguing against smoking being a major causative agent of oesophageal adenocarcinoma. Further, the 'upstream operators' had only a modest and non-significantly increased risk of cancer of the lung, bronchus and trachea and mortality caused by diseases of the respiratory system, and no excess mortality from cardiovascular diseases. Again, these results indicate that smoking cannot alone explain the excess risk of oesophageal adenocarcinoma.

Alcohol consumption has mainly been associated with squamous cell carcinoma of the oesophagus<sup>3</sup> and not oesophageal adenocarcinoma. 'Upstream operators' did not have a significantly increased mortality associated with abuse of alcohol, such as alcoholic liver disease or chronic alcohol abuse.

The cohort used in this study was designed to investigate the relationship between being an upstream petroleum worker and risk of haematopoietic malignancies. In the present study we report the cancer incidence of all major cancer types, and when interpreting the finding of an excess risk of oesophageal cancer among upstream petroleum workers, one should consider that there might be a multiple testing problem. Nevertheless, the risk was markedly increased and found in two of the job categories investigated, arguing against this observation being a chance finding.

The job category 'drilling and well maintenance' did not have an excess risk of any of the cancer types investigated, while workers belonging to the heterogenous job category 'others offshore' had an elevated risk of cancer of the larynx, lung and prostate. A marked finding in our study is the increased risk of cancer and mortality related to lifestyle factors in the subgroup 'catering personnel'. This group of workers is not exposed to the chemical hazards specific to offshore installations. More focus should be given to this group of workers.

In conclusion, despite the small number of cases, we found a significant fourfold excess of oesophageal adenocarcinoma among workers assumed to have had the most extensive contact with different phases of crude oil. Our study lacked detailed data on occupational exposure and lifestyle factors. Nevertheless,

given the low risk of lifestyle-related cancers and causes of death in this working group, the results add to the observations in other low-powered studies on oesophageal cancer, further suggesting that factors related to the petroleum stream or carcinogenic agents used in the production process might be associated with the risk of oesophageal adenocarcinoma. Still, caution should be used in interpreting the results, since the study does not allow us to identify specific causative agents for the observed increased risk of oesophageal adenocarcinoma.

**Funding** This study was funded by EXTRA funds from the Norwegian Foundation for Health and Rehabilitation (Karl Johans gt. 23 B, 0159 Oslo, Norway), the Norwegian Cancer Society (PO Box 4, Sentrum, 0101 Oslo), the Research Council of Norway (PO Box 2700, St. Hanshaugen, 0131 Oslo, Norway) and the Department of Health of UNIFOB AS (PO Box 7800, 5020 Bergen, Norway).

**Competing interests** None.

**Ethics approval** This study was conducted with the approval of the Regional Committee for Medical Research Ethics of Western Norway, the Norwegian Data Inspectorate and the Norwegian Directorate of Health.

**Contributors** JK and TR designed the study, analysed the data and prepared the manuscript. TB scrutinised all oesophageal cases blinded to exposure and contributed to discussions and the writing of all sections of the text. MB, BEM and DCC contributed to discussions, interpretations and the writing of all sections of the text.

**Provenance and peer review** Not commissioned; externally peer reviewed.

## REFERENCES

1. **Bosetti C**, Levi F, Ferlay J, *et al.* Trends in oesophageal cancer incidence and mortality in Europe. *Int J Cancer* 2008;**122**:1118–29.
2. **Trivers KF**, Sabatino SA, Stewart SL. Trends in esophageal cancer incidence by histology, United States, 1998–2003. *Int J Cancer* 2008;**123**:1422–8.
3. **Enzinger PC**, Mayer RJ. Esophageal cancer. *N Engl J Med* 2003;**349**:2241–52.
4. **Cook MB**, Wild CP, Everett SM, *et al.* Risk of mortality and cancer incidence in Barrett's esophagus. *Cancer Epidemiol Biomarkers Prev* 2007;**16**:2090–6.
5. **Lagergren J**, Bergström R, Lindgren A, *et al.* Symptomatic gastroesophageal reflux as a risk factor for esophageal adenocarcinoma. *N Engl J Med* 1999;**340**:825–31.
6. **Engeland A**, Tretli S, Bjørge T. Height and body mass index in relation to esophageal cancer; 23 year follow-up of two million Norwegian men and women. *Cancer Causes Control* 2004;**15**:837–43.
7. **Merry AHH**, Schouten LL, Goldbohm RA, *et al.* Body mass index, height and risk of adenocarcinoma of the oesophagus and gastric cardia: a prospective cohort study. *Gut* 2007;**56**:1503–11.
8. **Raaschou-Nielsen O**, Hansen J, McLaughlin JK, *et al.* Cancer risk among workers at Danish companies using trichloroethylene: a cohort study. *Am J Epidemiol* 2003;**158**:1182–92.
9. **Jansson C**, Johansson ALV, Bergdahl IA, *et al.* Occupational exposures and risk of esophageal and gastric cardia cancers among male Swedish construction workers. *Cancer Causes Control* 2005;**16**:755–64.
10. **Santibanez M**, Vioque J, Alguacil J, *et al.* PANESOES Study Group. Occupational exposures and risk of esophageal cancer by histological type: a case-control study in eastern Spain. *Occup Environ Med* 2008;**65**:774–81.
11. **Kirkeleit J**, Riise T, Bråtveit M, *et al.* Increased risk of acute myelogenous leukemia and multiple myeloma in a historical cohort of upstream petroleum workers offshore. *Cancer Causes Control* 2008;**19**:13–23.
12. **Steinsvåg K**, Bråtveit M, Moen BE. Exposure to carcinogens for defined job categories in Norway's offshore petroleum industry, 1970 to 2005. *Occup Environ Med* 2007;**64**:250–8.
13. **Mehlum IS**, Kjuus H. *Omfang og konsekvenser av arbeidskader og arbeidsbetinget sykdom på norsk kontinentalsokkel* (In Norwegian) [The extent and consequences of work related injuries and diseases on Norway's continental shelf]. Oslo: National Institute of Occupational Health, 2005, vol. 4. <http://asp.bibits.no/stami/filestore/STAMI-rapp/2005/05nr.4.pdf> (accessed 01 October 2009). ISSN 1502-0932.
14. **Hein MJ**, Stayner LT, Lehman E, *et al.* Follow-up study of chrysotile textile workers: cohort mortality and exposure-response. *Occup Environ Med* 2007;**64**:616–25.
15. **Yu ITS**, Tse LA, Wong TW, *et al.* Further evidence for a link between silica dust and esophageal cancer. *Int J Cancer* 2005;**114**:479–83.
16. **Wernli KJ**, Fitzgibbons ED, Ray RM, *et al.* Occupational risk factors for esophageal and stomach cancers among female textile workers in Shanghai, China. *Am J Epidemiol* 2006;**163**:717–25.
17. **Hansen J**, Raaschou-Nielsen O, Christensen JM, *et al.* Cancer incidence among Danish workers exposed to trichloroethylene. *J Occup Environ Med* 2001;**43**:133–9.
18. **Ruder AM**, Ward EM, Brown DP. Mortality in dry-cleaning workers: an update. *Am J Ind Med* 2001;**39**:121–32.
19. **Blair A**, Petralia SA, Stewart PA. Extended mortality follow-up of a cohort of dry cleaners. *Ann Epidemiol* 2003;**13**:50–6.
20. **Norell S**, Ahlbom A, Lipping H, *et al.* Oesophageal cancer and vulcanisation work. *Lancet* 1983;**1**:462–3.
21. **Evanoff BA**, Gustavsson P, Hogstedt C. Mortality and incidence of cancer in a cohort of Swedish chimney sweeps: an extended follow up study. *Br J Ind Med* 1993;**50**:450–9.
22. **Gustavsson P**, Evanoff B, Högstedt C. Increased risk of esophageal cancer among workers exposed to combustion products. *Arch Environ Health* 1993;**48**:243–5.
23. **Gustavsson P**, Jakobsson R, Johansson H, *et al.* Occupational exposures and squamous cell carcinoma of the oral cavity, pharynx, larynx, and oesophagus: a case-control study in Sweden. *Occup Environ Med* 1998;**55**:393–400.
24. **Zhao Y**, Krishnadasan A, Kennedy N, *et al.* Estimated effects of solvents and mineral oils on cancer incidence and mortality in a cohort of aerospace workers. *Am J Ind Med* 2005;**48**:249–58.
25. **Sullivan P**, Eisen EA, Woskie SR, *et al.* Mortality studies of metalworking fluid exposure in the automobile industry: VI. A case control study of esophageal cancer. *Am J Ind Med* 1998;**34**:36–48.
26. **Jansson C**, Plato N, Johansson ALV, *et al.* Airborne occupational exposures and risk of oesophageal and cardia adenocarcinoma. *Occup Environ Med* 2006;**63**:107–12.
27. **Guo J**, Kauppinen T, Kyrrönen P, *et al.* Risk of esophageal, ovarian, testicular, kidney and bladder cancers and leukemia among Finnish workers exposed to diesel or gasoline engine exhaust. *Int J Cancer* 2004;**111**:286–92.
28. **Hanis NM**, Stavrakys KM, Fowler JL. Cancer mortality in oil refinery workers. *J Occup Med* 1979;**21**:167–74.
29. **Lagorio S**, Forastiere F, Iavarone I, *et al.* Mortality of filling station attendants. *Scand J Work Environ Health* 1994;**20**:331–8.
30. **Divine BJ**, Hartman CM. Update of a study of crude oil production workers 1946–94. *Occup Environ Med* 2000;**57**:411–17.
31. **Satin KP**, Bailey WJ, Newton KL, *et al.* Updated epidemiological study of workers at two California petroleum refineries, 1950–95. *Occup Environ Med* 2002;**59**:248–56.
32. **Lewis RJ**, Schnatter AR, Drummond I, *et al.* Mortality and cancer morbidity in a cohort of Canadian petroleum workers. *Occup Environ Med* 2003;**60**:918–28.
33. **Gun RT**, Pratt N, Ryan P, *et al.* Update of mortality and cancer incidence in the Australian petroleum industry cohort. *Occup Environ Med* 2006;**63**:476–81.
34. **Sorahan T**. Mortality of UK oil refinery and petroleum distribution workers, 1951–2003. *Occup Med (Lond)* 2007;**57**:177–85.
35. **Jha P**, Peto R, Zatonski W, *et al.* Social inequalities in male mortality, and in male mortality from smoking: indirect estimation from national death rates in England and Wales, Poland, and North America. *Lancet* 2006;**368**:367–70.