Leif Åge Strand

Epidemiological Studies Among Royal Norwegian Navy Servicemen

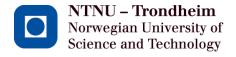
Cohort Establishment, Cancer Incidence and Cause-Specific Mortality



Thesis for the degree of Philosophiae Doctor

Trondheim, January 2011

Norwegian University of Science and Technology Faculty of Medicine Department of Public Health and General Practice





NTNU

Norwegian University of Science and Technology

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Epidemiologiske studier blant offiserer og vervet personell i Sjøforsvaret. Kohortetablering, kreftforekomst og årsaksspesifikk dødelighet

Avhandlingen omhandler etablering og kvalitetskontroller av kohorter (studiegrupper) bestående av sivilt og militært personell som har tjenestegjort i Sjøforsvaret (Marinen, Kystvakta og Kystartilleriet) etter 1950, samt to epidemiologiske studier blant mannlige militære. Tidsperioden karakteriseres av gjenoppbygging etter den andre verdenskrig, hvor Sjøforsvaret tilpasses "den kalde krigen" og designes for invasjonsforsvar i kystfarvann, og Sovjetunionens fall i 1991 med påfølgende omorganisering og nedbygging.

Arbeidet startet i 2002 med etablering av kohorter. Kilde til personopplysninger var Forsvarets Personelldatabase og rulleblader på papir. Inkludert i den sivile kohorten var alle sivilt ansatte, mens den militære kohorten ble begrenset til offiserer og vervete. Registreringsarbeidet resulterte i en militær kohort bestående av 29 056 personer, hvorav 2,5% kvinner, med gjennomsnitt tjenestetid i Sjøforsvaret på 6 år. Den sivile kohorten bestod av 8341 personer (39% kvinner) med 11 års tjeneste i snitt. Kohortene ble vurdert å være nær komplette.

Observerte antall krefttilfeller og dødsfall blant Sjøforsvarspersonellet ble sammenlignet med tilsvarende tall for den mannlige norske befolkning. Det ble også foretatt interne sammenligninger mellom ulike avdelinger i Sjøforsvaret.

Den første kohortstudien omhandlet asbestrelatert kreft. Asbest har vært brukt i skipsbygging som varme- og støyisolasjon og som brannsikring, og ble fjernet ved utskifting og overhaling av fartøyene i løpet av 1980-tallet. Rundt 11 500 besetningsmedlemmer kan ha vært eksponerte. Asbest er den eneste kjente miljøfaktor som kan forårsake mesoteliom (brysthinnekreft), og andre asbestrelaterte kreftformer (kreft i lunge, svelg, strupe, mage, og i tykk- og endetarm) ble evaluert i lys av tjenestested og forekomst av mesoteliom. Økt risiko for mesoteliom ble kun funnet blant maskinromsbesetninger.

Den andre kohortstudien dreide seg om kreft og dødsårsaker. Militær karriere betyr tilpasning til et rigid disiplinært system, håndtering av våpen og potensielt farlig maskineri, samt tjeneste på fjerne steder, atskilt fra familie. Et stort potensiale for ulykker, samt rapporter om høyt alkoholforbruk i utenlandske mariner, medførte fokus på voldsomme dødsfall samt dødsfall grunnet alkoholrelaterte sykdommer som skrumplever og alkoholpsykoser, og forekomst av alkoholrelatert kreft. For kohorten under ett var dødeligheten 16% lavere enn i den generelle norske mannlige befolkning. Dette kan forklares med seleksjoner på fysisk og mental helse ved opptak til militærtjeneste (sesjon) og befalsutdanning, samt regelmessige fysiske tester og helsekontroller under tjenesten. Kreftforekomsten var 6% forhøyet, først og fremst grunnet økt forekomst av prostatakreft og hudkreft. Voldsomme dødsfall (ulykker, selvmord) var 36% lavere enn forventet. Generelt var dødelighet og kreftforekomst høyere blant fartøybesetninger enn landbasert personell. Ingen økt risiko for alkoholbetinget dødsfall eller kreft ble observert for kohorten under ett, men høyere risiko ble funnet for fartøybesetningene sammenliknet med landpersonell.

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SUMMARY

The thesis covers the establishment and quality controls of two cohorts of civilian and military personnel serving in the Royal Norwegian Navy (RNoN) after January 1, 1950, and two studies among male members of the military cohort.

For the civilian cohort, the criterion for inclusion was all civilians who have served at any time during 1950–2005 in the Navy, while the military cohort was limited to officers and enlisted personnel. All branches of the Navy were covered, hereunder the Fleet, the Coast Guard and the Coastal Artillery. By 1950, the Norwegian Fleet was either destroyed during the Second World War (WWII) or out-dated. The rebuilding of the Navy was yet to begin, and Norway had just become a member of the North Atlantic Treaty Organisation (NATO) at the Treaty foundation in 1949. With its border with the Soviet Union in the north Norway became of strategic importance, and the Cold War shaped the design of the Norwegian Defence.

The present work started in 2002 with establishment of the cohorts. The registration work resulted in a military cohort of 29 056 persons (2.5% women) with an average of 6.2 years service in the Navy. The cohort of 8 378 civilians (39% women) had an average of 11 years in the Navy. Both cohorts were regarded as virtually complete.

The first cohort study dealt with asbestos related cancers among Navy vessels crews. Asbestos has been commonly used in shipbuilding for heat and sound insulation, and for fireproofing. Until 1987, asbestos aboard the Navy vessels potentially caused exposure to 11 500 crew members. Engine room crews were considered to experience higher exposure intensity than other crews aboard. Asbestos is the only environmental factor known to cause malignant mesothelioma, and an elevated incidence of this disease served as an indicator of asbestos exposure. The incidence of other potentially asbestos related cancers (lung, laryngeal, pharyngeal, stomach and colorectal cancers) was evaluated according to duty station and mesothelioma incidence. Elevated incidence of mesothelioma was found among engine room crews only, and the time from first exposure to date of diagnosis ranged from 28 to 48 years (median 41). The mesothelioma incidence offered no consistent explanation to the variation in incidence of other potentially asbestos-related cancers.

The second cohort study examined the cause-specific mortality and cancer incidence compared to the national rates. Internal comparisons between vessel crews and landbased personnel were performed. A military career implies adaptation to a rigid disciplinary system, handling of weaponry, and a life at remote locations causing separation from family members. In foreign navies, a higher than average alcohol consumption with a negative impact on occupational efficiency and adverse health outcome, has been reported. Special attention was thus given towards deaths from violent causes, alcohol related diseases (mental and behavioural disorders due to use of alcohol, liver cirrhosis) and incidence of alcohol-related cancers (mouth, pharynx, larynx, oesophagus and liver cancer). For the cohort as a whole, the overall mortality was 16% lower than in the general Norwegian male population. The physical and psychological screenings for military service and the demand for "keeping up" during service imply that the Navy personnel were highly selected and expected to be healthier than the general population. This phenomenon has been termed "healthy soldier effect". Overall cancer incidence was 6% higher, mostly due to excess prostate cancer and malignant melanoma and non-melanoma skin cancers. Death from violent causes (accidents and suicide) was 36% lower than expected. Both overall mortality and cancer were higher among sailors than among land-based personnel. No increased risk of alcohol related cancers or mortality was found for the cohort as a whole, but a higher risk was found among those serving aboard the vessels than for land based personnel.

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2. ABBREVIATIONS

CI Confidence interval

HDCN Headquarters Defence Command Norway

HSE Navy Health, Safety and Work Environment in the Royal Norwegian

Navy

IARC International Agency for Research on Cancer

ICD International Classification of Diseases

RN Royal Navy (UK)

RNoN Royal Norwegian Navy

RR Relative risk

SIR Standardised Incidence Ratio (of cancer)

SMR Standardised Mortality Ratio

UADT Upper aerodigestive tract

UK United Kingdom

US United States of America (USA)

WHO World Health Organisation

WWII Second World War

3. LIST OF PAPERS

- Strand LA, Koefoed VF, Oraug TM, Grimsrud TK. 2008. Establishment of the Royal Norwegian Navy personnel cohorts for cancer incidence and mortality studies. Mil Med. 173(8):785-91.
- II. Strand LA, Martinsen JI, Koefoed VF, Sommerfelt-Pettersen J, Grimsrud TK. 2010. Asbestos related cancers among 28,300 military servicemen in the Royal Norwegian Navy. Am J Ind Med 53(1):64-71.
- III. Strand LA, Martinsen JI, Koefoed VF, Sommerfelt-Pettersen J, Grimsrud TK.2010. Cause-specific mortality and cancer incidence among 28,300 RoyalNorwegian Navy servicemen followed through more than 50 years.(Submitted manuscript. Accepted for publication in a revised form)

4. BACKGROUND AND AIMS

4.1 Background

After Gulf War I (1991), possible health hazards among military personnel have come into focus, in Norway and internationally. Military operations during the United Nation (UN) missions in the Balkans, in which Norway participated, led to reports on health problems among the personnel. Putative health hazards like stress, vaccinations, environmental pollution, bad hygiene, risk of infection and exposure to ammunition made of depleted uranium have been discussed in United Kingdom (UK), Denmark, Sweden and Italy. In the United States of America (US), a wide range of health problems such as tiredness, headache, numbness and limb weakness, loss of concentration, memory problems and low mood have been reported among veterans from Gulf War I, often referred to as "The Gulf War Syndrome". An increase in multi-symptom conditions, injury, and mental health diagnoses among veterans has been demonstrated (Gray et al. 2004).

In Norway, focus has been directed towards health problems among civilian and military personnel in the Royal Norwegian Navy (RNoN). Examples of media enquiries were congenital anomalies in offspring of personnel who served aboard a missile torpedo boat, deaths among former submarine officers, asbestos exposure aboard the vessels and at the naval shipyards, and cancer incidence among civilians who worked at the coastal forts in northern Norway. In 2001, the Chief of the Naval Staff decided to investigate the alleged health problems, and started the research programme "Health, Safety and Work Environment in the Royal Norwegian Navy" (HSE Navy), a joint venture project between the University of Bergen and the Cancer Registry of Norway.

The project was organised and led by the Navy Medical Service, which also provided access to personnel files. The tasks of the University of Bergen were assessment of possible hazards in the workplace environment and to conduct cross-sectional surveys among present and former naval staff. The Cancer Registry was responsible for the establishing of cohorts of military and civilian personnel who served in the navy after 1950, and to perform research on cancer incidence and mortality among military

servicemen. The cohorts were established during 2002–2006, and the work on the thesis started in 2006.

4.2 The aims of the thesis

 The overall aim was to investigate cancer incidence and cause-specific mortality among military servicemen (officers and enlisted personnel) who served in the RNoN during the years 1950–2004.

• Specified aims were;

- to describe the establishment and quality controls of historical cohorts of civilian and military Navy personnel
- to investigate the risk of potentially asbestos related cancers (malignant mesothelioma, lung cancer, laryngeal, pharyngeal, stomach and colorectal cancers) in Navy vessel crews
- to investigate risk of all cancers, and cause-specific mortality among military servicemen, violent deaths and deaths from alcohol abuse and alcohol related diseases, and incidence of alcohol related cancers
- to compare health outcome between different exposure groups within the RNoN (land-based personnel, vessel crews hereunder engine room crews and non-engine room crews)

5. INTRODUCTION

5.1 After Second World War: the shaping of the modern Royal Norwegian Navy

Although the present studies cover the period from 1950 to present, the naval history spans more than 1000 years. In this section, an historic overlook of the Navy during the study period is presented, starting with the Second World War (WWII). During the occupation by Nazi Germany (1940–1945), Norway was fortified as a part of the Atlantic Wall, a protection against Allied invasion. The fortification ("Festung Norwegen") included strengthening of the Coast Artillery by modernization and the building of new coastal forts. When the war ended, Norway was left with 310 modern Coast Artillery facilities but a strongly reduced Fleet.

Norway became a founding member of the North Atlantic Treaty Organisation (NATO) in 1949 as a response to the up-coming Cold War. Norway's geo-strategic location made its territory important for monitoring enemy military activities, for denying the Soviet North Fleet access to the North Atlantic, and for projecting power against Soviet military bases and installations (Tamnes 2004). During the 1960s, 50 vessels were built, equipped and manned (Pettersen 1990). The Coast Artillery was updated, providing fortified batteries with anti-ship artillery and torpedoes, and controlled minefields. The forts were equipped with anti-aircraft artillery and surface-to-air missile systems (Gjelsten 1986). The Navy became designed for invasion defence in coastal waters.

During 1960–1990, the Fleet and the Coast Guard had 85–100 vessels operative simultaneously. In 1986, the inventory was 7 escort vessels, 14 diesel-electric submarines, 10 coast guard vessels, 38 motor/missile torpedo boats (MTBs), 12 mine sweepers and -layers, 7 landing crafts and 1 tender (Gjelsten 1986), and the number of military personnel (officers and enlisted personnel) reached a peak of approximately 5 000 during the 1980s. When the Cold War ended with the collapse of the Soviet Union in 1991, the need for personnel decreased. Most of the coastal forts were closed down during the subsequent years, and were in part replaced with small combat boats with light missile batteries (Bye 2004).

5.2 The military milieu

The choice of a military career implies adaptation to a rigid disciplinary system, service at remote locations, separation from family members, and handling of weapons and complex machinery. Theoretically, personality traits, lifestyle and chemical exposure might influence cancer incidence and mortality cause patterns that differ from that of the general population. The Navy work places are diverse. Many are similar to civilian work places, like offices, workshops, transport, and surface vessels. But there are work places rather specific to the military, in the Navy those include underground forts, submarines, and jobs involving handling of weaponry like mines, torpedoes, missiles, and gun batteries.

The demand for mental and physical fitness and overall good health at recruitment means that personnel seeking a military career were highly selected and expected to be healthier than the general population.

5.3 Epidemiological cohort studies among military navy personnel

The number of cohort studies aimed to investigate cancer incidence and cancer mortality in military navy personnel before the start of the thesis (2006) was limited. A search on Medline/PubMed using the words "cohort", "navy" and "cancer" in titleand abstract fields gave 7 hits, whereof only 4 among military personnel. Using the search word "military" instead of "navy" the result was 32 studies, but two of these where listed in the previous search result and four where limited to civilians or to women. There seems to be even fewer articles available on mortality from nonneoplastic diseases and violent causes on Medline/PubMed. Searching for titles containing the words "cohort", "navy" and "mortality" but excluding the word "cancer", only one article was found. Replacement of the word "navy" with "military" resulted in 37 articles, but the number was reduced to 29 after excluding articles on non-military personnel and women. Most of studies on cancer and mortality among Navy personnel have been conducted in the US Navy, but also in the British Royal Navy (RN) and in the Brazilian Navy. After 2006, two studies of high relevance for the thesis have been published. One is a review by McLaughlin et al. (2008) on quantifying the "healthy soldier effect", including 12 cohort studies on all-cause

mortality and cancer mortality, the other is the large census-based cohort study on occupational cancer risk in the five Nordic countries, inclusive of that of military personnel (Pukkala et al. 2009).

5.4 Possible health hazards associated with Navy service

Moen et al. (2005) made an overview on carcinogens and potential carcinogenic agents occurring in the Navy based on interviews and measurements from visits to 42 land-based facilities and vessels. The report addressed potential exposure to asbestos, metals (arsenic, copper, lead, cobalt, nickel, chromium), hydrocarbons (benzene, polycyclic aromatic hydrocarbons (PAH), exhaust), and radiation (radon, ionizing radiation, electromagnetic fields). Some of the agents, like metal compounds (in shipbottom paint containing antifouling components), have probably caused exposure only to civilian personnel at shipyards and workshops, and were regarded as not relevant as occupational exposures to military personnel. Exposure to and potential health effects from electromagnetic fields has been a topic for research by the University of Bergen, and is not part of the thesis. In the following paragraphs, focus is directed towards exposures that are known, or assumed to be encountered at military navy work places or to be associated with lifestyle.

5.4.1 Physical hazards (violent deaths)

The purpose of military organisations in peace time is preparation for war, and military service includes military exercises and manoeuvres. Handling of weaponry and potentially dangerous machinery in the military means a huge potential of accidents even in peace time, an effect which easily could be amplified by attraction of risk takers to military jobs. Studies have shown elevated risk of mortality by accidents in foreign military forces. Darby et al. (1990) found a standardised mortality ratio (SMR) of violent causes of 1.32 (p<0.001) in UK Royal Navy (RN) personnel compared with the national rates, hereunder drowning and water transport accidents (SMR = 2.37) and suicide (SMR = 1.39). Inskip (1997) observed a 15% increase bordering on statistical significance in deaths from violent causes in RN submariners, mainly due to drowning (SMR = 3.26) and motor vehicle traffic accidents (SMR = 1.18, not significant). In Finland, most accidents among permanent military personnel occurred during military exercises (57%) but the accident frequency for military work

was lower than for civilian work (Lehtomäki et al. 2005). The meta-analyses by McLaughlin et al. (2008), which included the study by Inskip (1997), found a non-significant lowered risk of deaths by violent causes (meta-SMR = 0.90) among deployed veterans, and a borderline significant lowered risk (meta-SMR of 0.80) among non-deployed veterans.

5.4.2 Asbestos

Military and civilian vessels have traditionally been packed with asbestos, due to the compound's excellent heat and sound insulation properties. The association between inhalation of asbestos fibres and malignant mesothelioma and lung cancer is well established (International Agency for Research on Cancer (IARC) 1977). The evidence that exposure to asbestos fibres is associated with laryngeal cancer is considered sufficient, but suggestive only for pharyngeal, stomach and colorectal cancers (Board on Population Health and Public Health Practices, 2006; Straif et al. 2009). In Norway, restrictions on use of asbestos aboard ships were introduced in 1978. Navy vessels built before that time had asbestos applied inside as well as outside the engine rooms. Vibrations during sailing, inspections and maintenance work involving removal and reapplication of insulation containing asbestos might have caused fibre release to the breathing atmosphere aboard, putting the crews at risk. Pukkala et al. (2009) showed an overall increased risk of mesothelioma of the pleura and peritoneum among Nordic seafarers on merchant vessels, and significant excess of both lung cancers and mesotheliomas among Finnish engine room crews was found by Saarni et al. (2002). As far as I know, no such study has been carried out among crews aboard military vessels. Navy ships may differ from civilian ships with respect of asbestos exposure among the crews, by having more powerful engines and target practice. Asbestos was gradually phased out from the work environment aboard Navy vessels during the 1980s by refitting or disposal of vessels (Moen et al. 2005).

5.4.3 Radon

Radon is a naturally occurring and radioactive uranium-decay gas that seeps out of soil and rocks. The rate of seepage shows great variation, partly because the amounts of uranium in the soil vary considerably. Radon decays into a series of short-lived radioisotopes that can be inhaled and cause lung cancer (Copes & Scott 2007;

National Research Council 1999). Radon is considered second only to smoking as a cause of lung cancer. According to a meta-analysis by Darby et al. (2005), radon in homes accounts for about 9% of the deaths from lung cancer and hence 2% of all cancer deaths in Europe. Concentrations of radon gas in Norwegian dwellings are claimed to be among the highest in the world (Geological Survey of Norway 2008). The land based branch of the Navy armed forces is the coastal artillery, whose duty stations were a few fortresses and some 70 forts along the coast. The forts are mostly situated underground, which might have caused exposure to radon gas.

5.4.4 Diesel-exhaust fumes

Except from a few of the older vessels being propelled by steam from oil boilers or by petrol, all engines aboard were diesel powered, inclusive that of the submarines. Being designed for shorter missions, all RNoN submarines were diesel-electric. The diesel engine was running during surface sailing and at snorkeling depth, charging the propulsion batteries for submerged sailing. The closed submarine environment might have led to exposure among all crews members. Aboard surface vessels, possible exhaust leaks would primarily be expected to affect engine room crews. Diesel exhaust may be associated with both bladder and lung cancer, although there is limited epidemiological evidence (IARC 1989).

5.4.5 Solar radiation

Military work is associated with both indoor and outdoor activities, and the latter potentially causing occupational exposure to sunlight. The ultraviolet (UV) radiation in sunlight is a causal factor of malignant melanoma of skin and non-melanoma skin cancers (IARC 1992), and in census studies, these forms of skin cancers were elevated by 17 and 29% in military men in the 4 Nordic countries (Pukkala et al. 2009). Some duty stations, such as underground forts, inside surface vessels and in submarines, are shaded from sunshine, but the personnel might be exposed to intentional tanning.

5.4.6 Alcohol drinking

Easy access to alcoholic beverages during military service, such as availability in officers' mess, has led to questions raised by the Navy Medical Service about high consumption among Navy personnel. Alcoholic beverages are carcinogenic (IARC

1988). During the days of sail, serving of alcohol was common aboard the Navy vessels (Olafsen 1973). A higher than average alcohol consumption has been reported among foreign navy personnel, and alcohol abuse has been suggested as an occupational risk factor of military life (Henderson et al. 2009). Seafarers have long been associated with alcohol drinking, and the concept of the "drunken sailor" is not only a myth. In the study by Pukkala et al. (2009), Norwegian seamen showed an elevated SIR of 1.84 for alcohol-related cancers (upper aerodigestive tract, UADT–i.e. tongue, mouth, pharynx, larynx, esophagus cancers–and liver cancer combined). In a Swedish study, seamen received a psychiatric diagnosis of alcohol- and drug abuse at conscription for military service markedly more often than other unskilled workers, and the authors raised the question "do drinkers sail or do sailors drink?" (Hemmingsson et al. 1997).

6. MATERIAL AND METHODS

6.1 The study cohort: criteria for inclusion

Included in the study cohort were military personnel who served in the Navy at any time between 1 January 1950 and 31 December 2004, and who fulfilled one of the following criteria:

- Conscripts who underwent military education to become commissioned officers
 (COs) or non-commissioned officers (NCOs)
- Enlisted personnel who attended Officer Candidate Schools and achieved a Chief Petty Officer's rank (quartermaster)
- Enlisted personnel known as Able Seamen and Engineer Assistants. During 3–6
 years of enlistment, they attended military or civilian schools for maritime or
 technical education.

Conscripts serving the initial (compulsory) service without achieving an officer's rank were not included in the cohort.

The sources of personnel information were the Norwegian Defence computer system at Headquarters Defence Command Norway (HDCN) and paper-based personnel records. Electronic personnel information was available from 1989, containing service history files for approximately 16 000 persons of relevance for our project when the registration started in 2002. In addition, some 31 000 paper-based personnel records for military Navy personnel were available and computerized by a team of 8 persons from a temporary staff recruitment agency.

The crude registration work lasted nearly for 3 years. In 2005, the available data were extracted and transferred to the Cancer Registry for quality controls. The extracts included career information from all branches of the Armed forces and consisted of some 32 000 persons. After removal of personnel who did not meet the inclusion criteria of the cohort (i.e., civilians, ordinary conscripts and non-navy personnel) the

cohort consisted of 29 056 officers and enlisted personnel who had served in the Navy at any time during 1950–2004.

Matching against 2 different and independent sources of Navy personnel was performed to evaluate the completeness of the cohort. These sources were an overview of flag- and staff officers in the Navy for the period of 1814–1997 by Omberg (1998) and yearly listings of Navy officers with a fixed salary. The oldest available list (1963), and one list from each of the three following decades (1971, 1981 and 1990), were used. Each of the lists contained some 1500–2000 officers.

6.2 Description of the study population and sources of outcome

Due to the small proportion of women (2.5%) in the Military Cohort, the epidemiological studies were limited to a total of 28 345 men. The years of birth spanned 1883–1984 with a median of 1953. Some 15 400 had ever served aboard a vessel. Average duration of service in the Navy was 6.2 years, while vessel crews served aboard for 3 years. Table I shows average duration of service for all personnel combined, and according to military branch and duty station. The distribution of personnel according to the highest rank or status achieved before 2004 was: COs (42%), NCOs and petty officers (33%), seamen, able seamen and (other) enlisted personnel: 25%.

Table I. Average duration of service during 1950–2004 for all military personnel, and for personnel groups according to duty station. Vessel crews are defined by personnel who ever served aboard; submariners are defined by vessel crews who ever served aboard submarines; and land-based personnel are personnel who never served aboard a vessel, during 1950–2004.

Personnel group	Military	Proportion of	Total years	Years aboard
N=28 345	branch	all personnel	of service,	(in submarine),
		(%)	average	average
All personnel	Any	100	7.2	1.6
All personnel	Navy	100	6.2	1.6
Land-based personnel	Navy	46	4.4	_
All vessel crews	Navy	54	7.8	3.0
Surface vessel crews	Navy	45	7.2	2.7
Submariners	Navy	9	10.6	4.4 (2.9)

Cancer diagnosis and date of diagnosis were obtained by linkage to the Cancer Registry of Norway, and date and underlying cause for all deaths were obtained by linkage to the Cause-of-Death Registry at Statistics Norway. Data on vital status and emigration were provided by the National Population Register, which is continuously updated for the whole Norwegian population. The linkage was based on 11-digit unique personal identification numbers given to all citizens of Norway alive in 1960 or born later. For those who died before 1960, linkage to registries was based on name and date of birth.

6.2.1 The Cancer Registry of Norway

The Cancer Registry of Norway has systematically collected notifications on cancer for the entire Norwegian population since 1952, and is considered to be virtually complete since the following year (Larsen et al. 2007). According to a directive from the Ministry of Health and Social Affairs in 1951 reporting of neoplasms is compulsory. The reporting is based on pathology and cytology reports, clinical reports and death certificates. The coding of cancer is based upon a modified version of International Classification of Diseases (ICD), 7th revision (World Health Organisation, WHO, 1957).

6.2.2 The Cause of Death Registry

The Cause of Death Registry contains information on causes of death for all registered residents in Norway at the time of death. The Registry contains information back to 1922, and is regarded as complete from 1951, due to compulsory reporting. Statistics Norway is responsible for the management of the Registry in collaboration with Norwegian Institute of Public Health. Deaths were classified according to ICD, 6th revision throughout 1957, 7th revision during 1958–1968, 8th revision during 1969–1986, 9th revision during 1986–1995, and 10th revision during 1996–2007.

6.3 Follow-up

In the cancer incidence studies the cohort members were followed-up for cancer from the first date of entering service in the Navy, but no earlier than 1 January 1953, until date of death, date of emigration, but no later than 31 December 2007 (Paper II) or 31 December 2008 (Paper III). In the mortality study (Paper III) the cohort members

were followed from the date of entering the Navy, but no earlier than 1 January 1951, until date of death, date of emigration, or 31 December 2007, whichever came first.

By the end of follow-up all cohort members were either known to be alive and resident in Norway, to have died, or to have emigrated.

6.4 Statistical analyses

External comparisons: The analyses were based on comparison of observed numbers of deaths or cancer cases with those expected, computed from the national five-year age-specific and five-year period-specific rates among all Norwegian men. Standardised mortality ratios (SMRs) and standardised incidence ratios (SIRs) were calculated.

Internal comparisons: Poisson regression analyses were used to compare rates according to duty station, with observation period and age at risk included in the models. Relative risks expressed as rate ratios (RR) were calculated for engine-room crews with reference to non-engine room crews aboard the vessels (Paper II), and vessel crews with reference to land-based personnel (Paper III).

A p-value smaller than 0.05 was taken to indicate statistical significance. Ninety five percent confidence intervals (95% CI) were computed on the assumption of a Poisson distribution of the cases.

Epicure statistical software package (Preston 1993) was used in Paper II and III. In addition, Stata statistical software packages v. 10 and v. 11 were used in Paper II and III, respectively (Stata Corporation 2007; 2009).

6.5 Ethics

Full freedom of publication was granted by the RNoN to the Cancer Registry of Norway. The Norwegian Data Inspectorate, the Norwegian Directorate of Health and the Regional Committee for Medical Research Ethics approved the study.

7. SUMMARY OF RESULTS

7.1 Paper I

Establishment of the Royal Norwegian Navy personnel cohorts for cancer incidence and mortality studies

Cohorts of military and civilian personnel who served in the RNoN during 1950–2004 were established. Sources of service history files were the Norwegian Defence personnel database, and nearly 40 000 paper-based records stored at HDCN, the naval bases and the National Archives of Norway. The registration work started in 2002 and lasted 3 years. The result was the Military Cohort consisting of 29 056 officers and enlisted personnel (2.5% women), and the Civilian Cohort of 8 381 persons, 5 146 men and 3 235 women. Military personnel had shorter average service in the Navy (6.2 years) than had civilian personnel (10.8 years), and the median year of birth was 1954, compared to a median of 1942 among civilians. For quality control of the Military Cohort, two independent external lists of officers were available. Of a total of 3 760 officers on fixed salary listings during 1963–1990, 98% was retrieved in the cohort. Matching against the list of Flag- and Staff officers revealed a substantial lack of records for officers born before 1900. A variation in the number of personnel in service throughout the period, with peaks during the 1960s and 1980s was seen in both cohorts.

7.2 Paper II

Asbestos related cancers among 28 300 military servicemen in the Royal Norwegian Navy

The study investigated the incidence of potentially asbestos related cancers among 28 345 officers and enlisted servicemen in the RNoN. Asbestos was used for heat and sound insulation and for fireproofing in Navy vessels until it was gradually phased out during the 1980s. By 1987, all vessels were regarded as free of asbestos. Some 11 500 crew members served aboard before 1987 and were considered exposed. Follow-up period was 1953–2007. SIRs for malignant mesothelioma, lung cancer, and laryngeal, pharyngeal, stomach and colorectal cancers were calculated according to service aboard between 1950 and 1987 and in other Navy personnel. An increased risk of mesothelioma among engine room crews was observed, with SIR = 6.23 (95% CI = 2.51–12.8) for personnel who served less than 2 years and SIR = 6.49 (95% CI =

2.11-15.1) for those with longer service. No elevated risk was seen in other personnel groups. Lung cancer was nearly 20% higher than expected among both engine crews and non-engine crews, and 23% lower than expected among land-based personnel and personnel who served aboard after 1987 (SIR = 0.77, 95% CI = 0.64–0.92). An excess of colorectal cancer bordering on statistical significance was seen among non-engine crews (SIR = 1.14, 95% CI = 0.98–1.32). No elevated risk of laryngeal, pharyngeal or stomach cancers was found. Among engine room crews, the latency time (i.e., the time period between start of work in engine rooms to date of diagnosis) ranged from 28 to 48 years, with a median of 41 years.

7.3 Paper III

Cause-specific mortality and cancer incidence among 28 300 Royal Norwegian Navy servicemen followed for more than 50 years

The objective of this study was to examine mortality and cancer incidence in the cohort of 28 300 RNoN servicemen, whereof 15 400 who had served aboard the Navy vessels. Special attention was directed towards all-cause mortality, deaths from violent causes, and mortality and cancer incidence related to alcohol drinking. Mortality for all Navy personnel was lower than expected for all causes combined (SMR = 0.84, 95% CI = 0.81-0.87) and for selected groups of diseases, but not for cancer mortality (SMR = 1.02). Mortality from violent causes was 0.64 of expected (95% CI = 0.58-0.71). The SMRs for vessel crews were consistently higher than that of land-based personnel but still lower than or equal to the national rates. Internal comparisons showed a difference in the same direction for mortality from violent causes (RR = 1.36, 95% CI = 1.11-1.36), for alcohol abuse and non-neoplastic alcohol related diseases (bordering on statistical significance; RR = 1.56, 95% CI = 0.96–2.52), for the incidence of alcohol-related cancers (RR = 1.58, 95% CI = 1.12– 2.52), and for lung cancer (RR = 1.65, 95% CI = 1.33-2.04). The cohort as a whole had a slightly elevated SIR for all cancers combined (SIR = 1.06, 95% CI = 1.02– 1.09), mainly caused by prostate cancer (SIR = 1.12, 95% CI = 1.04-1.20), malignant melanoma (SIR = 1.18, 95% CI = 1.03–1.35) and non-melanoma skin cancer (SIR = 1.37, 95% CI = 1.18–1.59). An excess of bladder cancer was observed among submariners (SIR = 1.53, 95% CI = 1.01-2.23).

8. DISCUSSION

8.1 General remarks

The aims of this thesis were to establish cohorts of military and civilian personnel, and to perform cancer incidence and mortality studies among servicemen in the military cohort. The cohorts were established from relevant available sources. Lack of records for officers born before 1900 was regarded as of minor importance. The variation in the annual number of personnel at work during 1950–2004 showed the same pattern in both cohorts and was taken to reflect the activity in the Navy and the availability of work force. Both cohorts were regarded as virtually complete.

Compared to the general Norwegian male population, military servicemen were found to have a slightly elevated overall cancer incidence; cancer mortality in line with that of the general population; and a reduced overall mortality and mortality from nonneoplastic diseases. With reference to land-based personnel, vessel crews had higher rates for total cancer, hereunder lung cancer and alcohol-related cancers, and higher overall mortality, including deaths due to diseases of the circulatory system, and deaths from violent causes. Excess malignant mesothelioma was only seen among engine room crews aboard.

The large size of the cohort, the long follow-up and linkage to virtually complete national registers by means of unique personal identification numbers strengthen the studies. Lack of quantitative information about occupational exposures, no information about occupations outside the military, and lack of individual data on smoking, alcohol drinking and diet were limiting factors for interpretation of the results.

The incidence of some forms of cancers was taken as results of specific exposure or even as indicators of exposure. At the group level, incidence of malignant mesothelioma was taken as an indicator of presence of asbestos fibres in the breathing atmosphere, which is plausible, since asbestos is the only environmental factor known to cause the disease. Lung cancer is strongly associated with tobacco smoking, and the variation in incidence across subgroups was mainly ascribed to different smoking habits. Still, lung cancer may be caused by occupational exposures, such as asbestos,

and the lack of exposure data hampered the possibility of making precise conclusions. Cancers of the UADT and the liver are known to increase as a result of heavy alcohol drinking, but the UADT-cancers are also linked to tobacco smoking. The variation of mortality from alcohol-related (non-neoplastic) diseases (mental and behavioural disorders and cirrhosis of liver) across the subgroups was pointing in the same direction as the alcohol-related cancers, suggesting that confounding from smoking would be a minor problem. Both the cancers and the non-neoplastic mortality were taken to reflect variation in alcohol consumption.

8.2 Methodological considerations

8.2.1 Study design, selection bias and representativeness

Longitudinal (cohort) studies are commonly regarded as the best epidemiological tool. A group of persons with a certain exposure (the cohort) is established and followed forward in time during which diseases are accumulated. Breslow & Day (1987) outline two ways to conduct the follow-up: A cohort can be established in the present and followed into the future (a prospective cohort study), or assembled from historical records and followed forward in time from a start-point in the past (a historical prospective cohort study). The present work consists of two cohort studies of historical prospective design. The cohort is regarded as virtually complete and should by definition representative for Navy personnel during the observation period. Unbiased results should additionally be ensured by linkage to virtually complete disease or death registries by a unique personal identification number.

8.2.2 Exposures

The cancer incidence and mortality rates were evaluated according to Navy work place (duty station) (and in Paper II: duration of vessel service). In Paper II, personnel were classified into groups of personnel who ever served in engine rooms aboard during 1950–1987 (engine room crews) and those who served aboard but never in the engine rooms during the same period (non-engine room crews), with sub-categories of those who served inside and outside engine rooms aboard submarines. Land-based personnel and personnel who served aboard after 1987 were regarded as a separate group. In Paper III, personnel was classified into groups of personnel who never served aboard a vessel (land based personnel), personnel who ever served aboard

(vessel crews), and a subgroup of vessel crews who ever served aboard the submarines (submariners). The "ever-never" definition of personnel groups means that personnel with only one day of service in a given category are good for classification as such. This might weaken the results, as persons with very short exposure (to vessel service or engine room service) were counted as exposed. In both studies, each individual was followed according to land-based service, (all) vessel service or submarine service from the first day in the Navy, as vessel crews normally start their service aboard during the first three months of initial service. In Paper II, duration of service aboard vessels and in engine rooms with a cut-point of 2 years was used to assess the effect of long-term exposure. All crews starting with any particular service was followed according to the lowest category (shortest duration) until they qualified for a higher one. Those who never qualified for a higher category were followed according to the lower one throughout their entire follow-up time.

8.2.3 Misclassification of exposure

In Paper II, risk of asbestos-related cancers was analysed according to duty station aboard the vessels during 1950–1987. Engine room crews were considered to experience higher levels of asbestos exposure than other crew members, while personnel who did not serve aboard during the same period were regarded as unexposed to asbestos. Due to the German occupation of Norway during WWII, historical service files before 1950 were incomplete or missing, and service history before 1950 was not registered. Personnel with only land-based service after 1950, who had vessel service prior to that time, would be misclassified as unexposed. Likewise, personnel who served aboard before 1987 but aboard vessels which already had the asbestos removed (or build after 1980 with no asbestos applied), would represent unexposed personnel in the exposed group (the year of 1987 was chosen as the year when virtually all vessels were free of asbestos due to disposal or refitting). The possible "leak" of exposed personnel into the unexposed group and vice versa, was a potential source of misclassification and would have biased the risk estimates towards unity. In Paper III, where cancer incidence and cause-specific mortality was evaluated for vessel crews with reference to that of land-based personnel during 1950–2004, unknown service before 1950 was a possible source of misclassification.

8.2.4 Confounding

Confounding can be defined as the distortion of the exposure—outcome association by an uneven distribution of other factors that may affect the outcome. Tobacco smoking and inhalation of asbestos fibres are both causal factors for development of lung cancer. When differences in smoking across subgroups of personnel were discussed in light of lung cancer incidence, asbestos exposure could be a potential confounder. No individual or quantitative data on asbestos exposure were available, and the estimated ratio between asbestos-related lung cancer and mesothelioma suggested by Darnton et al. (2006) was used to adjust for asbestos exposure (8.3.1). When variation in incidence of UADT-cancers between personnel groups was used to discuss alcohol consumption, smoking might act as a confounder as it too is a causal factor for the same cancers.

8.2.5 Loss to follow-up

Individuals left the cohort either by death or through emigration. Loss to follow-up occurs when individuals leave the observable cohort unnoticed and continue to contribute to the person-years at risk, without contributing to the event of interest. The risk estimates will be biased downwards (Breslow & Day 1987). The National Population Register is continuously updated with residential and vital status for all Norwegian citizens, and linkage with the cohort should ensure virtually no loss to follow-up.

8.3 Interpretation of results

8.3.1 Asbestos related cancers

In Paper II, no elevated risk of malignant mesothelioma was found among personnel who did not serve aboard the vessels during 1950–1987, or among personnel who served aboard but never in the engine room. Engine room service was associated with a 6-fold increase compared to the national rates, and a 7-fold increase compared to non-engine crews aboard. Inhalation of asbestos fibres is the only recognised cause of mesothelioma, and Dreyer et al. (1997) estimated the proportion attributable to asbestos to be 83% in Norwegian men. Asbestos was applied almost everywhere aboard, but it seemed that the concentration of asbestos fibres in the breathing atmosphere only was high enough to cause elevated risk of the disease in the engine

room. There was probably more asbestos applied in the engine room than elsewhere aboard due to the noise and heat production from the ship's engine. Also, inspection and maintenance involve removal and re-application of insulation containing asbestos. Vibrations causing fibre release were probably more intense in the engine room, since most vibrations aboard were caused by the engine itself. The risk did not seem to increase with increasing length of service in the engine room. Short duration of exposure has been reported to be sufficient to cause mesotheliomas. In a study among British asbestos factory workers, Browne and Smither (1983) found that 45% of the pleural mesothelioma cases followed exposure lasting less than 2 years. Another plausible explanation to our finding is asbestos exposure outside the Navy, which might have obscured the effect of service length in the Navy.

In fact, 5 of the 7 cases with less than 2 years of service in engine rooms were enlisted personnel, while only one of the 5 cases with longer service was enlisted. A typical contract period for enlisted personnel was 3 years, which included 1-2 years of maritime and technical education, followed by obligatory vessel service. Optionally, it was possible to sign up for a second 3-year period. Enlisted personnel were not obliged to compulsory service and mobilization, and had no further obligations with respect to military duty after fulfilling their contracts. The intention of enlistment might have been to sign on to civilian vessels, rather than having a military career. For the 12 mesothelioma cases in engine room crews, the latency period ranged from 28 to 48. Latency time for mesotheliomas as long as > 70 years have been reported (Bianchi & Bianchi 2009) and an extended follow-up might display latency periods longer than 48 years. Ideally, the cohort should be subjected to a life-time follow-up before median and range were calculated. The risk of lung cancer was some 20% elevated in both engine room crews and in non-engine crews. Taking excess mesotheliomas as an indicator of asbestos exposure, we would expect to find asbestos-related lung cancer risk among engine room crews. Based on the assumption of the ratio of asbestos-related lung cancer to mesothelioma deaths to be somewhere between two thirds and unity (Darnton et al. 2006), all excess lung cancers among engine room crews could be ascribed to asbestos exposure. This item was not discussed in Paper II. In Paper III, however, it was estimated that 5–8% of lung cancers in vessel crews could be caused by asbestos exposure.

When mesothelioma incidence was used as an indicator of the presence or absence of asbestos exposure, the data did not suggest an effect on laryngeal, pharyngeal, stomach or colorectal cancers. Maybe the exposure to personnel who do not handle asbestos was too low to have detectable effects.

8.3.2 All-cause mortality and non-neoplastic diseases (other than alcohol-related) In Paper III, all-cause mortality for the cohort as a whole was 16% lower than the national rates. This is in accordance with one of the most consistent findings in epidemiological studies on military personnel, a phenomenon termed a "healthy soldier effect", as a military equivalent to the "healthy worker effect". In Norway, all military personnel were selected through psychological and physical screening for the initial compulsory military service, thereby excluding individuals with chronic diseases or simply physically unfit or unable to adjust to military discipline. Further selection occurred due to high mental and physical demands during Officer Candidate Schools and Military Academies. In addition, officers are required to stay fit during service, and to pass physical and medical tests at regular intervals. Socioeconomic factors have been associated with mortality, and military officers have traditionally been regarded as a high-status group with safe employment and steady income. Among Norwegian men, mortality has been shown to decrease with increasing level of education and income (Zahl et al. 2003). The magnitude of the "healthy soldier effect" showed a wide variation within 12 studies (whereof 9 among US military personnel) included in a meta-analysis by McLaughlin et al. (2008). The combined SMR was around 0.75, compared to the SMR of 0.84 in the RNoN. The difference might be due to more stringent selection and lower mortality among military personnel in countries like US, who are trained for offensive warfare around the world. Generally, the magnitude is also depending upon the mortality of the reference population. In countries with greater social differences and/or lower standard of medical care provided to the general public, the "healthy soldier effect" will probably be stronger. The lower magnitude of the "healthy soldier effect" in our study might be due to less stringent selection of military personnel, and a generally low mortality in the reference population as a consequence of the egalitarian Norwegian society with social security, medical services provided by the state to all citizens and fairly equal living conditions across the population.

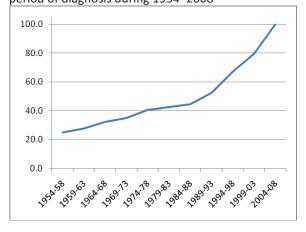
Navy personnel had a lower than expected mortality from circulatory, respiratory, digestive and infectious diseases. When lung cancer incidence was used as an indicator, the level of tobacco smoking in the cohort seemed to be similar to that of the general Norwegian male population, and other factors may have contributed to the low mortality. In addition to the effect from selection by employment, such factors might include higher level of physical activity, fewer hazardous occupational exposures, and healthier diet compared to the reference population.

8.3.3 Cancer incidence and cancer mortality

The 6% higher than expected incidence of all cancers combined in the cohort seems to contrast the low mortality from non-neoplastic causes and the general "healthy soldier effect". Screening and improvements in medical diagnostics may contribute to a low overall mortality, and may also increase the reported cancer incidence. One such cancer is prostate cancer, which was elevated by 12% and thus a major contributor to the elevated overall cancer incidence. A similar SIR of 1.10 was found among military personnel in four Nordic countries (Pukkala et al. 2009). There are few known carcinogens associated with prostate cancer. A plausible explanation of the elevated incidence is higher diagnostic intensity during regular health controls among active-duty and retired servicemen, compared to the reference population. Following the introduction during the late 1980s of prostate specific antigen (PSA) tests

provided to asymptomatic men, a marked increase in prostate cancer incidence was observed (fig. 8.1) (Kvåle et al. 2007; Hernes et al. 2010). Variation in the distribution of the test across population groups will lead to differences of prostate cancer incidence. Among US military men, Zhu et al. (2009) observed a doubled incidence and regarded free access to medical

Figure 8.1: Age-adjusted incidence rate per 100 000 person years for prostate cancer in Norway by 5-year period of diagnosis during 1954–2008



care and greater likelihood to undergo prostate cancer screening as the most plausible explanation. Also in the pre-PSA era, increased diagnostic intensity among military men might have lead to a higher incidence of prostate cancer, and thereby a higher

number of deaths attributed to the disease, as suggested by Feuer et al. (1999). Darby et al. (1990) found a 56% increased prostate mortality among UK military personnel who served abroad in the 1950s and 1960s, and Logan (1982) observed tripled SMRs for prostate cancer among UK armed forces servicemen in occupational mortality analyses in 1961 and 1971.

The increased risk of both malignant melanoma and non-melanoma skin cancer in the cohort as a whole is in accordance with that among military men in four Nordic countries (Pukkala et al. 2009). The major causal factor involved in development of skin cancers is exposure to ultraviolet (UV) radiation from sunlight (IARC 1992). Navy service is associated with both indoor and outdoor activities, but the elevated skin cancer risk might be due to intentional (leisure) tanning as well as be of occupational nature. The high risk of non-melanoma skin cancer among vessel crews was also seen in the subgroup of submariners, which strongly support the idea of off-duty tanning. In the study by Pukkala et al. (2009), typical outdoor occupational groups like farmers, forestry workers, gardeners and fishermen, as well as indoor labour groups like factory workers and craftsmen showed lowered risk of melanoma and non-melanoma skin cancers. Elevated risk was seen among highly educated professions including medical doctors, dentists, administrators, teachers and religious workers, indicating a social gradient and leisure-time exposure as more important than occupational exposure for the incidence of skin cancers.

In spite of an elevated overall cancer incidence, the cancer mortality was in par with that of the general population. This might in part be explained by screening which might have lead to early diagnosis and improved survival rates, and overdiagnosis. Further, that the main contribution to the elevated cancer incidence (prostate cancer, malignant melanoma and non-melanoma skin cancer) was cancers with relatively low mortality rates.

8.3.4 Violent deaths

The very low rate of death from external causes, including transport accidents, other accidents and suicide, is remarkable for an organisation designed for military activity, where the personnel by routine are handling potentially dangerous weapons and machinery. The result can possibly be explained by a culture of safety in the Navy,

involving selection of personnel, proper training, regulations, and a psychosocial environment with emphasis on personal control. These factors might even have outbalanced a possible attraction of risk takers to military jobs.

8.3.5 Alcohol-related diseases

For the cohort as a whole, deaths from alcohol abuse and non-neoplastic alcohol-related diseases (including liver cirrhosis) were less frequent than in the general male population, while the incidence of alcohol related cancers did not differ from the reference population. Our observation is in line with the results from Pukkala et al. (2009), where military men showed a lower than expected mortality from liver diseases (SMR 0.80), and an incidence of alcohol-related cancers similar to that of non-military men. For the Navy cohort as a whole, the results are pointing towards alcohol consumption slightly lower than or similar to that of Norwegian males in general, a result supported by surveys including data on alcohol consumption in the Norwegian Navy (Baste et al. 2006).

8.3.6 Sea and land – two different cultures?

In general, vessel crews had higher mortality rates and cancer incidence rates compared to those of land-based personnel, inclusive of deaths from violent causes, deaths from non-neoplastic alcohol related diseases, incidence of alcohol-related cancers, and incidence of lung cancer.

Even if the rates of alcohol-related deaths and cancers were higher among vessel crews, these rates were not elevated compared to the general population. This contrasts the findings in foreign navies. A doubled age-adjusted proportionate mortality ratio (PMR) for alcohol related liver disease was observed among Brazilian Navy servicemen, compared to the reference population of males in the State of Rio de Janeiro (Silva & Santana 2004). Darby et al. (1990) reported high alcohol-related mortality among British RN servicemen, and deaths from alcohol related diseases (other than cancer) were nearly 7 times higher than that of the Army and the Royal Air force (RAF) combined. This might be due to the old tradition of alcohol drinking aboard. In the RN, the tradition of sailor's rum rations originated some 360 years ago because of the need for preservation of drinking supplies during the long overseas voyages. The rum tradition was abolished as late as in 1970 (Pack 1982), whereas the

Norwegian tradition of distributing rations of distilled spirits aboard navy vessels was abandoned more than 80 years earlier, when spirits was replaced by hot beverages like tea and coffee (Olafsen 1973).

A proportion of the difference in mortality and cancer incidence between vessel crews and land-based personnel is likely attributable to a higher prevalence of smoking among vessel crews. An estimated 5–8% of lung cancers in vessel crews could be ascribed to asbestos exposure, leaving a lung cancer excess of 12–15% probably explained by tobacco smoking (see 8.3.1.). The largest land-based branch of the Navy is the Coastal Artillery, which operated the coastal forts. The forts were mostly located in mountain halls, where personnel on duty used to live around the clock. Smoking was prohibited, at least in areas where ammunition was stored, and smokers would probably not apply for this type of service. According to self-reported data on smoking among 1 500 cohort members in active service in 2002, 27% of those who ever served aboard a vessel were present-day smokers, in contrast to 20% of the landbased group (data from Magerøy et al. 2006). The difference was statistically significant (p<0.005). According to Ezzati & Lopez (2004) the leading causes of death from smoking in industrialized regions in the year 2000 were cardiovascular diseases, lung cancer, and chronic obstructive pulmonary disease (COPD). It is therefore plausible that the lower mortality from circulatory and respiratory diseases observed in land-based personnel compared to vessel crews, at least in part, can be explained by less tobacco smoking. The low incidence of lung cancer among landbased personnel (SIR = 0.75) gave by itself no support to the idea of radon exposure in the underground Coastal Artillery facilities, although a potential effect could be masked by lower smoking rates.

An elevated risk of bladder cancer among submariners was observed. Relevant exposure to diesel exhaust could have occurred from diesel powered engines, but the evidence of a causal link to lung cancer is limited, and still weaker for bladder cancer (IARC 1989). Smoking is an established risk factor for cancers of bladder and lung, but lung cancer incidence was not elevated in submariners. The cause of the elevated risk of bladder cancer remains unexplained, but the SIR of 1.53 was based on 27 cases which gave a wide CI close to borderline, statistically (1.01–2.23).

Navy vessel crews experienced more deaths from external causes than land-based personnel, which might be caused by a higher potential risk of accidents aboard a vessel, and/or related to alcohol drinking. Similarly, in a census-based study on mortality among occupational groups in Norway, Borgan (2009) reported a higher risk of death by external causes among Norwegian seamen compared to land-based personnel.

9. CONCLUSIONS

Overall, Royal Norwegian Navy servicemen were found to have lower all-cause mortality inclusive of mortality from circulatory, respiratory, digestive and infectious diseases, in line with a "healthy soldier effect". Selection of physically and mentally fit persons, requirement of passing physical and medical tests at regular intervals during service, and high socioeconomic status are factors which may have contributed to this pattern. The very low rates of deaths from external causes, including transport accidents, other accidents and suicide, may be achieved by a culture of safety in the Navy and thorough selection of personnel.

An elevated overall cancer incidence was mostly caused by excess cancers of the skin and prostate gland, the latter probably due to increased diagnostic intensity in present or former navy personnel. An increased incidence of skin cancers is seen among other occupational groups with long education and high income, and a potential effect of occupational UV exposure is difficult to sort out.

Mortality from alcohol abuse and alcohol related diseases, and incidence of alcohol related cancers, was higher among vessel crews than among land-based personnel, but the none of the rates were higher than in the general population. The incidence of lung cancer in vessel crews and in the land-based group differed in the same direction. This suggests a cultural difference between sea and land: Vessel crews tend to drink and smoke more than land based personnel. A higher prevalence of smoking among vessel crews might explain the higher mortality rates for circulatory and respiratory diseases. The higher risk of deaths from violent causes among seamen might be caused by a higher potential for accidents at sea, or, possibly, related to consumption of alcohol.

In spite of being applied also outside engine rooms, only engine room crews showed increased risk of malignant mesothelioma. The latency time for cases among engine room crews ranged from 28 to 48 years, with a median of 41 years. An effect on other potentially asbestos-related cancers was not found.

10. LITERATURE

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Cause-specific mortality and cancer incidence among 28,300 Royal Norwegian Navy servicemen followed through more than 50 years

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ABSTRACT

Objectives: To examine mortality and cancer incidence in a cohort of 28,300 military servicemen known from personnel files to have served in the Royal Norwegian Navy during 1950–2004.

Methods: The cohort was followed from 1951 through 2007 for mortality, and from 1953 through 2008 for cancer. Standardized mortality ratios (SMR) and incidence ratios for cancer (SIR) were calculated from national rates. Internal comparisons (rate ratios, RR) were made using Poisson regression.

Results: Mortality for all Navy personnel was lower than expected for all causes combined (SMR 0.84), for most disease groups and violent causes, but not for cancer mortality (SMR 1.02). Vessel crews had consistently higher SMRs than had land-based personnel, still on the low side of—or close to—the national rates. Vessel crews differed in the same direction with respect to mortality from alcohol abuse and non-malignant alcohol-related diseases (RR 1.56), and for the incidence of alcohol-related cancers (RR 1.58) and lung cancer (RR 1.65). An overall small excess of all cancers combined (SIR 1.06) was caused by prostate cancer, malignant melanoma and non-melanoma skin cancer. An excess of bladder cancer was observed among submariners (SIR 1.53) based on 9 excess cases.

Conclusion: The low all-cause mortality was in line with a —healthy soldier effect". Navy personnel had a lower than expected mortality from accidents and suicide. Alcohol-related diseases were more frequent among vessel crews than among land based personnel, but largely similar to the rates in all Norwegian men.

Keywords: Navy, vessel crews, mortality, cancer, alcohol, violent deaths, cohort study

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INTRODUCTION

The aim of our study was to investigate cause-specific mortality and cancer incidence according to duty station (land-based, all vessels, submarines) among officers and enlisted military personnel serving in the Royal Norwegian Navy during 1950–2004 (1). The investigation was a part of the research program —Health, Safety and Work Environment in the Royal Norwegian Navy", initiated after claims that a number of health hazards were associated with service in the navy. The incidence of potentially asbestos related cancers (malignant mesothelioma, and cancers of the lung, larynx, pharynx, stomach, and colorectal cancer) in the cohort has been presented in a previous paper, showing a 6-fold increased risk of malignant mesothelioma in marine engine crews with service aboard before 1987, when asbestos was removed from the vessels. Lung cancer incidence was nearly 20% higher than expected among both engine crews and non-engine crews during the same period, while all land-based personnel and personnel who served aboard after 1987 had lung cancer incidence 23% lower than expected (2). In the present study we investigated cause-specific mortality, with a special focus on preventable diseases and external causes, as well as the incidence of cancer.

Regular physical and psychological screening for service, and the requirement to maintain physical fitness implies that personnel pursuing a military career are highly selected throughout their service. As a consequence, they would be expected to experience lower mortality than the general population, and perhaps lower mortality than occupationally active groups without repeated health examinations. This phenomenon has been observed and termed a —healthy soldier bias" in Bross & Bross (3), later denoted —healthy soldier effect", as a military equivalent to the healthy worker effect. A review by McLaughlin *et al.* (4) found lower mortality rates for all-causes (meta-SMR 0.76, 95% CI 0.65–0.89) and cancer mortality (meta-SMR 0.78, 95% CI 0.63–0.98) among deployed military personnel compared to the general population. We therefore expected a general —hælthy soldier effect" in our study, although it might vary across different subgroups of personnel.

A number of factors might put military personnel at elevated risk for accidents and violent deaths: A service that includes handling of weaponry, explosives, and potentially dangerous machinery, might also attract risk takers. The essence of military activity is violence, force and destruction, and military exercise includes simulation of war. Darby *et al.* (5) found a SMR of accidents and violence of 1.32 (p<0.001) in RN personnel compared with the national rates. In Finland, most accidents among permanent military personnel occurred during military exercises (57%) but the accident frequency for military work was lower than for civilian work (6). Alcohol drinking might increase this risk. Among male U.S. army soldiers in active duty, Bell *et al.* (7) noted that alcohol use was associated with a 10-fold increase in reckless behavior (OR 9.6, 95% CI 4.5–20.7).

Several studies report evidence of a higher than average alcohol consumption among military personnel, especially in the naval forces. Alcohol abuse has been suggested as an occupational hazard of military life (8). Alcohol consumption in the navies could be seen as a result of drinking traditions, readily available of alcoholic beverages, and a life isolated from family members. Daily rations of alcoholic beverages became tradition in the early days of sail, the most famous example is the naval rum introduced in the British Royal Navy (RN) after the capture of Jamaica in 1655. Rum rations were known as —grog" and —Nelson's blood" (9). Military servicemen in the RN have shown a higher alcohol consumption and more frequent binge drinking than that expected from the general population (8). The causal relationship between alcohol consumption and risk of cancers of the upper aerodigestive tract

(UADT) (tongue, mouth, pharynx, larynx, esophagus) and of liver is well established (10), and a high consumption might also lead other potentially life threatening diseases, such as liver cirrhosis and mental and behavioral disorders.

Elevated death rates ascribed to alcohol intake has been reported in navy personnel. Silva & Santana (11) found increased PMR for liver diseases in the Brazilian Navy. Among UK servicemen with service in tropical or desert areas, Darby *et al.* (5) found excess deaths in RN personnel from alcohol related cancers (SMR 1.81) and other alcohol related diseases (SMR 2.29) compared with national rates. British submariners had elevated risk of deaths from liver cirrhosis (SMR 2.21) (12).

Submarines as work places are specific for the Navy, and the crew must undergo special training in a submarine-escape training tank. The Norwegian Navy operated diesel-electric submarines, with the potential to expose the crews to diesel exhaust and battery acid fumes. The land-based branch of the Navy's armed forces is the Coastal Artillery, whose duty stations are forts and fortresses along the coast. These forts are mostly located underground.

MATERIAL AND METHODS

Study population

A historical cohort of 28,345 officers and enlisted servicemen who served in the Royal Norwegian Navy between 1950 and 2004 had been established. The cohort covers all branches of the Navy, inclusive of the Fleet, the Coast Guard and the Coastal Artillery, and is believed to comprise virtually all active military personnel in the Navy for the period (1). The inventory during our study period was 7 naval bases, 70 coastal forts, 3-4 fortresses and around 300 vessels. Some 15,400 persons (54% of the cohort members) had ever served aboard a vessel, whereof 2665 aboard submarines. The distribution of personnel according to the highest rank or status achieved during this period was: commissioned officers (42%), noncommissioned officers and petty officers (33%), seamen, able seamen and (other) enlisted personnel: 25%. Women were not included in our study due to small numbers. Conscripts in compulsory service that did not achieve an officer's rank were not included. The birth years of the cohort members span the period 1883–1984 with a median of 1953. Average total service length in the Navy was 6.2 years, and for vessel crews, average service aboard the vessels was 3 years. Individual data on tobacco smoking was available only for a limited number (1500) of cohort members, who participated in a survey among Navy personnel in active service in 2002 (data from Magerøy et al. (13)). No individual data was available for alcohol drinking, diet and occupational exposure, which, together with tobacco smoking, are factors that might have a large impact on mortality and cancer incidence.

Case identification and follow-up

The cohort members were followed with respect to the event of death from the first date he entered service in the Navy, but no earlier than 1st of January 1951, until date of death, date of emigration, or 31 December 2007, whichever came first. By the end of follow-up, all cohort members were either known to be alive and resident in Norway, known to have died, or known to have emigrated. Data on residence, vital status and emigration was provided by the National Population Register, which is continuously updated for the whole Norwegian

population. We obtained date and underlying cause for all deaths by linkage to the Cause-of-Death Registry at Statistics Norway, which eventually receives the death certificates for all Norwegian citizens. The linkage was based on 11-digit unique personal identification numbers given to all citizens of Norway alive in 1960 or born later. For those who died before 1960, linkage was based on name and date of birth. Deaths were classified according to the International Classification of Diseases (ICD), 6th revision throughout 1957, 7th revision during 1958–1968, 8th revision during 1969–1986, 9th revision during 1986–1995, and 10th revision during 1996–2007.

All cohort members were followed for incident cancers from the first date he entered service in the Navy, but no earlier than 1st of January 1953, until date of death, date of emigration, or 31 December 2008, whichever came first. Cancer diagnosis and date of diagnosis were obtained by linkage to the Cancer Registry of Norway, which, due to compulsory reporting, is virtually complete (14). Cancer was classified according to ICD, 7th revision, as registered by the Cancer Registry of Norway. More than one cancer diagnosis could be counted in each individual.

Alcohol-related diseases and cancers

Deaths by alcohol related diseases other than cancer were defined as caused by —Mental and behavioral disorders due to use of alcohol" (ICD-10 code F10) and liver cirrhosis (ICD-10 code K70). Alcohol related cancers were defined by cancers of the upper aerodigestive tract (UADT) which includes tongue (ICD-7 code 141), mouth (ICD-7 codes 143–144), pharynx (ICD-7 codes 145–148), esophagus (ICD-7 code 150) and larynx (ICD-7 code 161), and of liver cancer (ICD-7 code 155) combined, a definition also used by Pukkala *et al.* (15) in a census-based study on occupational cancer risk in the five Nordic countries.

Statistical analysis and duty stations

The analysis was based on a comparison of the observed numbers of deaths or cancer cases with those expected, computed from the national five-year age-specific and five-year period-specific rates among all Norwegian men. The standardized mortality and incidence ratios (SMRs and SIRs) were calculated, and ninety-five percent confidence intervals (95% CI) were computed on the assumption of a Poisson distribution of the observed numbers.

The results for mortality and cancer incidence are presented for the whole cohort and for 3 subsets: personnel who never served aboard a vessel (land based personnel), personnel who ever served aboard (vessel crews), and for an additional subgroup of vessel crews who ever served aboard the submarines (submariners). Personnel within the subsets are followed equally (from the first day in the Navy but no earlier than 1 January 1951 for mortality and 1 January 1953 for cancer) as vessel crews normally start their service aboard within the first few weeks of initial service. Poisson regression analysis was used to compare rates according to duty station, with observation period and age at risk included in the models. Relative risks, expressed as rate ratios (RR) were calculated for vessel crews with reference to land-based personnel. Epicure (Hirosoft International Corp, Seattle, WA, USA) and Stata (StataCorp LP, College Station, TX, USA) software packages were used for statistical analysis. We chose a p value smaller than 0.05 to indicate statistical significance.

Seventy eight deaths (2%), whereof 36 occurring during 2000–2007, were classified as having an –unknown cause". According to Statistics Norway, most of these deaths probably occurred abroad. The number of Norwegians dying abroad increased by 20% during 2000–2007, and 90% of all deaths abroad in 2007 were of unknown cause (16). Individuals with unknown cause of death were excluded from all SMR and Poisson analyses.

Death within 31 days after end of last recorded service was regarded as service-related, but we still could not discriminate between active-duty and off-duty deaths.

RESULTS

Total mortality

There were 3650 deaths of known cause during 1951–2007. Average follow-up time was 31.5 years. All-cause mortality was 16% lower than expected, and it was stable throughout the last four decades (data not shown). Table 1 shows the mortality from all causes combined and from selected causes for the cohort as a whole. Mortality by duty station is presented in Table 2, and mortality rate ratios derived by Poisson regression are shown in Table 3, where the risks for vessel crews are compared to land-based personnel. All-cause mortality was lower than expected for vessel crews as well as land-based personnel (table 2) but the Poisson analysis showed a significantly higher mortality among vessel crews when the two groups were compared (RR 1.15) (table 3).

Alcohol-related deaths and cancers

Deaths from alcohol abuse and non-malignant alcohol related diseases were two thirds of that expected from all Norwegian men. Cirrhosis of the liver constituted half the number of these deaths, giving a SMR of 0.73 (35 deaths, borderline significance, data not shown). The incidence of alcohol related cancer was similar to that of the reference population (Table 4). Compared to land-based personnel, vessel crews had between 50 and 60 % higher risk of dying from non-malignant alcohol related diseases, and of being diagnosed with an alcohol related cancer (Tables 3 and 6).

Deaths from violent causes

Among all personnel, a lower than expected mortality was seen for external causes of injury and poisoning combined (SMR 0.64) and for the selected sub-categories in this group: transport accidents (SMR 0.78), other accidents (SMR 0.63) and suicide (SMR 0.53) (table 1). For injury and poisoning combined, the mortality was lower than expected among both land-based personnel (SMR 0.53) and vessel crews (SMR 0.73), although the Poisson regression analysis confirmed a 36% higher mortality in the latter (vessel crews) when the two groups were compared (Table 3). Mortality from transport accidents was significantly lower than expected in land-based personnel, but not convincingly so in vessel crews (Table 2). Suicide occurred at nearly half the expected rate for both personnel groups. A total of 206 service-related deaths (i.e., deaths within one month after end of last recorded service) were observed,

whereof 47 deaths of violent causes. Violent causes counted for 26% of service-related deaths in vessel crews and 17% in land-based personnel.

Deaths from other causes

The most common cause of death in the cohort was diseases of the circulatory system (1315 cases), which was 14% lower than expected. Ischaemic heart disease and cerebrovascular diseases counted for 819 and 200 of these cases, giving SMRs of 0.86 and 0.77, respectively. Except from cancer mortality, which was similar to that of the general population, the mortality from all other selected groups of diseases was lower than expected for the cohort as a whole. The Poisson regression analyses suggested a 10 to 20 percent higher risk of death from diseases of the circulatory, respiratory, and digestive system in vessel crews compared with land-based personnel (table 3).

Cancer incidence

There were a total of 3362 cancer cases in the cohort during follow-up. Average follow-up time was 32.2 years. The risk for selected forms of cancer is presented for the cohort as a whole in table 4, and for personnel according to duty station in table 5. Relative risks for vessel crews compared to land-based personnel are presented in table 6. The overall cancer risk among all personnel was slightly elevated, with 179 excess cases. Melanoma of the skin (SIR 1.18), other skin cancers (SIR 1.37), and prostate cancer (SIR 1.12) counted for 88% of the excess number of cancers. The total incidence of lung cancer was close to that expected for the general population, but it was elevated by 21% among vessel crews and lowered by 25% in the land-based personnel group (Table 5). This contrast was confirmed in the Poisson regressions (Table 6). Vessel crews also showed higher incidence of all cancers combined (RR 1.16). Submarine service was associated with an excess of bladder cancer (SIR 1.53). Prostate cancer was elevated in both vessel crews and land-based personnel.

DISCUSSION

For navy servicemen, our study showed a lower than expected all-cause mortality and a lower than expected mortality from most selected causes of death. For cancer, we found a slightly elevated standardized incidence ratio (SIR) for the cohort as a whole, mainly caused by prostate and skin cancers (melanoma and non-melanoma). In general, vessel crews had higher mortality rates and cancer incidence rates compared to those of land-based personnel, inclusive of deaths from non-malignant alcohol related diseases, incidence of alcohol-related cancers, and incidence of lung cancer. Deaths from violent causes were lower than expected for all personnel, but, again, higher among vessel crews than in land-based personnel.

The strengths of this study were the quality and the completeness of the outcome derived from independent sources, despite a slight deficit of deaths from unknown cause (2% of all, excluded from analyses, see Material and methods section). There was no loss to follow-up except emigrations at specified dates. Accurate Navy service history (duration, occupation and work places) and unique personal identity numbers secured a complete and unbiased linkage. Weaknesses were a relatively short duration of service in the Navy and a lack of

information about other (non-military) occupations. We had no access to occupational exposures in the Navy and lacked data on lifestyle for more than a minor part of the cohort (see below).

Total mortality

The low mortality is in accordance with a —healthy soldier effect", as described by Kang and Bullman (17) and in a review by McLaughlin *et al.* (4) In Norway, navy personnel are selected through screening at the initial compulsory military service, excluding individuals that were physically unfit or unable to adjust to military discipline. Further selection occurs due to high mental and physical demands during Officer Candidate Schools and Military Academies. In addition, officers are required to stay fit during service, and to pass physical and medical tests at regular intervals.

Socioeconomic factors have been associated with mortality. In Britain, life expectancy for men in the period 1992–1996 was 9.5 years shorter for the bottom social class, compared to that of the top social class (18). In Norway, mortality decreases with increasing level of education and income, more pronounced in men than in women (19). Traditionally, military officers have been regarded as a high-status group, but our cohort consists of individuals from different social strata. Income is highly correlated with rank and length of service. Most personnel with a short career in the Navy were able seamen and other enlisted personnel, who had maritime or technical education during their enlistment period. The intention of enlistment was often to attain a career aboard civilian vessels.

The magnitude of the —healthy soldier effect" vary between cohorts in the review of McLaughlin *et al.* (4), with meta-SMRs for deployed and non-deployed personnel around 0.75. The deviation is not only dependent on the mortality in the cohort under study, but also on that of the reference population. In countries with greater social differences and/or lower standard of medical care provided to the general public, the difference might be bigger. Our data suggests a —healthy soldier effect" of a modest magnitude, possibly caused by the egalitarian Norwegian society with generally high standard of living, social security and health services provided by the State to all citizens, those are factors which contribute to low mortality in the general population.

Alcohol-related deaths and cancers

For the cohort as a whole, deaths from alcohol abuse and non-malignant alcohol-related diseases (including liver cirrhosis) were less frequent than in the general male population, while the incidence of alcohol related cancers did not differ from the reference. Our observation is in line with the results from a cohort study based on employed populations in one or more censuses in the Nordic countries, where military men showed a lower than expected mortality from liver diseases (SMR 0.80), and an incidence of alcohol cancers similar to, that of non-military men (15). Our results indicate an alcohol consumption similar to or lower than that of Norwegian males in general, a finding which is supported by surveys including data on alcohol consumption in the Norwegian Navy (20).

Vessel crews had higher risk of death from alcohol abuse and alcohol-related diseases and higher incidence of alcohol cancers than land-based personnel. Compared to the general

population, a 14% higher than expected risk of alcohol-related cancers was seen (not statistically significant). Pukkala *et al.*(15) showed an 84% increase among Norwegian civilian seamen, and there is a possibility that our observation of more alcohol-related diseases in vessel crews can be explained by post-military service in the merchant fleet. Our results do indeed contrast the high alcohol-related mortality reported among British RN servicemen (5). In UK, the rum tradition was abolished as late as 1970 (9, 21), while the Norwegian tradition of distributing rations of distilled spirits aboard navy vessels was abandoned more than 80 years earlier, spirits being replaced by hot beverages like tea and coffee (22).

Deaths from external causes

The death rates of external causes, including transport accidents, other accidents and suicide, were very low. Navy vessel crews experienced more deaths from external causes than land-based personnel, possibly due to a higher risk of accidents aboard a vessel compared to land-based activity, and higher consumption of alcohol. Similarly, in a census-based study on mortality among occupational groups in Norway, Borgan (23) reported a higher risk of death by external causes among Norwegian seamen compared to land-based personnel. Our result are remarkable for an organization designed for military activity and it might reflect—in addition to the obvious absence of real warfare—a culture of safety, involving selection of personnel, proper training, regulations, and a psychosocial environment with emphasis on personal control. These factors might even have outbalanced a possible attraction of risk takers by military jobs.

Deaths from other causes

Navy personnel had a lower than expected mortality from circulatory, respiratory, digestive and infectious diseases. Judged by the lung cancer incidence, it seems fair to assume that the historical smoking habits in the cohort have been compatible with those of the general population. This may be taken to suggest that factors other than smoking, such as selection by employment, diet, physical activity, occupational exposures, indoor or outdoor air quality, may have had a positive impact on the incidence and prevalence of these diseases.

Differences in mortality across the personnel groups: explained by tobacco smoking?

A proportion of the difference in mortality and cancer incidence between vessel crews and land-based personnel is likely attributable to a higher prevalence of smoking among vessel crews. An excess of mesotheliomas was observed in vessel crews by Strand *et al.* (2), and based on an estimated ratio of asbestos-related lung cancer to mesothelioma deaths to be somewhere between two thirds an unity—suggested from UK data by Darnton *et al.* (24)—some 5–8% of lung cancers in vessel crews could be ascribed to asbestos exposure. This still leaves room for a higher lung cancer rate attributable to smoking among vessel crews compared to land-based personnel. According to self-reported data on smoking among 1500 cohort members in active service in 2002, 27% of those who ever served aboard a vessel were present-day smokers, in contrast to 20% of the land-based group (data from Magerøy *et al.* (13)). Although a modest difference, the observation was statistically significant (p<0.005)

and it would be in line with a historical difference in the same direction. According to Ezzati & Lopez (25), the leading causes of death from smoking in industrialized regions in the year 2000 were cardiovascular diseases, lung cancer, and chronic obstructive pulmonary disease (COPD). We therefore assume that lower mortality from circulatory and respiratory diseases observed in land-based personnel compared to vessel crews, at least in part, can be explained by less tobacco smoking.

Other cancers

The 6% higher than expected incidence of all cancers combined in the cohort seems to contrast the low mortality from non-neoplastic causes and the —healthy soldier effect". It is, however, well known that screening and improvements in medical diagnostic may increase the reported cancer incidence.

Prostate cancer incidence was elevated for land-based personnel as well as for vessel crews. A similar SIR of 1.10 was found among military personnel in a census-based study in four Nordic countries (15). There are few known carcinogens associated with prostate cancer. The steep increase in prostate cancer incidence in Norway since 1990 is attributed to the increasing use of prostate specific antigen (PSA) tests in asymptomatic men (26, 27). The most plausible explanation of our finding is a difference in diagnostic intensity compared to the reference population, possibly taking place in regular health examinations among active or retired personnel. In line with our assumption, Zhu *et al.* (28) regarded screening as the most plausible explanation to the doubled incidence seen among US military men. Interestingly, Darby *et al.* (5) found a 56% increased prostate mortality among British military personnel based on 29 deaths. Even in the pre-PSA era, an increased diagnostic intensity might lead to a higher incidence of prostate cancer, and subsequently to a higher number of deaths attributed to the disease, as suggested by Feuer *et al.* (29).

The increased risk of non-melanoma skin cancer was more marked than that of malignant melanoma. Our finding is in accordance with that among military men in four Nordic countries (15). The major causal factor involved in development of skin cancers is exposure to ultraviolet (UV) radiation from sunlight (30). Vessel crews might be more exposed to occupational sunlight than land-based personnel. The elevated risk of non-melanoma skin cancer in vessel crews was also seen in the subgroup of submariners, whose submarine service counts for less than one third of their total Navy employment. We find it reasonable to assume that the excess is linked to intentional tanning although some exposure may take place during work hours in land-based or surface activity. In the study by Pukkala et al. (15), elevated risk of skin cancers was seen among highly educated professions including medical doctors, dentists, administrators, teachers and religious workers, while typical outdoor workers like farmers, forestry workers, gardeners and fishermen showed lowered risk, indicating that a social gradient and leisure-time exposure could be more important than occupational exposure for the incidence of skin cancers. A certain correlation between skin cancer and social gradient might also exist in our cohort, as military rank is linked to duration of service, and vessel crews have a longer average duration of service compared to land-based personnel, 7.8 years against 4.5 years, respectively.

There was sign of an increased risk of bladder cancer among submariners. Relevant exposure to diesel exhaust could have occurred from diesel powered engines, but the evidence of a causal link to bladder cancer is even weaker than that for lung cancer (31).

CONCLUSION

All-cause mortality and most of the selected causes of mortality were significantly lower than expected, in line with a —healthy soldier effect". An elevated overall cancer incidence was mostly due to excess cancers of the skin and prostate gland. Mortality from alcohol abuse and alcohol related diseases, and incidence of alcohol related cancers, were higher among vessel crews than land based personnel, but not higher than in the reference population. The risk of death from violent causes was lower than expected, although vessel crews experienced a higher mortality from external causes than did land-based personnel. Lung cancer incidence was 65% higher among vessel crews than in land-based personnel, with some of the difference probably explained by asbestos and most of it by contrasts in tobacco smoking. The smoking patterns may also explain the higher mortality from circulatory and respiratory diseases in vessel crews compared to land-based personnel.

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Ethics approval

The study was approved by the Norwegian Data Inspectorate, the Regional Ethics Committee and the Norwegian Directorate of Health.

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Table 1 All-cause mortality and selected causes of death among 28,265 Royal Norwegian Navy servicemen followed between 1951 and 2007; 890,771 person-years

ICD-10*	Obs.†	Exp.‡	SMR§	95% CI¶
A00-Y99	3648	4339.4	0.84	0.81-0.87
#	73	108.6	0.67	0.53-0.85
A00-B99	24	43.6	0.55	0.35-0.82
C00-C97	1208	1189.6	1.02	0.96-1.07
100-199	1315	1532.4	0.86	0.81-0.91
120-125	819	951.7	0.86	0.80-0.92
160-169	200	261.3	0.77	0.67-0.88
J00-J99	170	231.1	0.74	0.63-0.85
J40-J47	89	104.8	0.85	0.68-1.04
K00-K93	108	133.4	0.81	0.67-0.98
V01-X59	402	628.4	0.64	0.58-0.71
V01-V99	155	199.9	0.78	0.66-0.91
W00-19,X40-49	138	219.2	0.63	0.53-0.74
X60-84,Y87.0	101	189.6	0.53	0.44-0.65
	A00-Y99 # A00-B99 C00-C97 I00-I99 I20-I25 I60-I69 J00-J99 J40-J47 K00-K93 V01-X59 V01-V99	A00-Y99 3648 # 73 A00-B99 24 C00-C97 1208 I00-I99 1315 I20-I25 819 I60-I69 200 J00-J99 170 J40-J47 89 K00-K93 108 V01-X59 402 V01-V99 155 W00-19,X40-49 138	A00-Y99 3648 4339.4 # 73 108.6 A00-B99 24 43.6 C00-C97 1208 1189.6 I00-I99 1315 1532.4 I20-I25 819 951.7 I60-I69 200 261.3 J00-J99 170 231.1 J40-J47 89 104.8 K00-K93 108 133.4 V01-X59 402 628.4 V01-V99 155 199.9 W00-19,X40-49 138 219.2	A00-Y99 3648 4339.4 0.84 # 73 108.6 0.67 A00-B99 24 43.6 0.55 C00-C97 1208 1189.6 1.02 I00-I99 1315 1532.4 0.86 I20-I25 819 951.7 0.86 I60-I69 200 261.3 0.77 J00-J99 170 231.1 0.74 J40-J47 89 104.8 0.85 K00-K93 108 133.4 0.81 V01-X59 402 628.4 0.64 V01-V99 155 199.9 0.78 W00-19,X40-49 138 219.2 0.63

^{*} ICD, International Classification of Diseases

[†] Obs., Observed number of cases

[‡] Exp., Expected number of cases based on population rates

[§] SMR, Standardized Mortality Ratio

[¶] CI, Confidence Interval

[#] Mental and behavioural disorders due to use of alcohol (F10), liver cirrhosis (K70)

Table 2 All-cause mortality and deaths of selected causes among 28,265 Royal Norwegian Navy servicemen according to duty station: land-based personnel (never vessel, 401,493 person-years), all vessel crews (489,278 person-years), and a subgroup of the latter: submariners (86,815 person-years). Follow-up 1951–2007

Causes of death	ICD-10*	Duty station	Obs.†	Exp.‡	SMR§	95% CI¶
All causes	A00-Y99	Land-based	1535	1986.6	0.77	0.73-0.81
		All vessels	2113	2352.7	0.90	0.86-0.94
		- Submarines	303	354.4	0.85	0.76-0.96
Alcohol abuse and alcohol	#	Land-based	25	48.2	0.52	0.34-0.77
related diseases		All vessels	48	60.4	0.79	0.58-1.05
		- Submarines	4	10.3	0.39	0.11-1.00
Malignant neoplasms	C00-C97	Land-based	503	536.2	0.94	0.86-1.02
		All vessels	705	653.4	1.08	1.00-1.16
		- Submarines	108	100.3	1.08	0.89-1.30
Diseases of the circulatory system	100-199	Land-based	569	713.6	0.80	0.73-0.87
		All vessels	746	818.8	0.91	0.85-0.98
		- Submarines	110	114.3	0.96	0.80-1.16
Ischaemic heart disease	120-125	Land-based	344	438.7	0.78	0.71-0.87
		All vessels	475	513.0	0.93	0.85-1.01
		- Submarines	67	72.5	0.92	0.72-1.17
Cerebrovascular diseases	160–169	Land-based	94	125.9	0.75	0.60-0.91
		All vessels	106	135.4	0.78	0.65-0.95
		- Submarines	12	18.0	0.67	0.34-1.16
Diseases of the respiratory system	J00-J99	Land-based	71	106.9	0.66	0.52-0.84
		All vessels	99	124.2	0.80	0.65-0.97
		- Submarines	11	16.7	0.66	0.33-1.18
Diseases of the digestive system	K00-K93	Land-based	46	60.9	0.76	0.55-1.01
		All vessels	62	72.5	0.86	0.66-1.10
		- Submarines	7	11.1	0.63	0.25-1.29
External causes of injury	V01–X59	Land-based	151	282.6	0.53	0.46-0.63
and poisoning		All vessels	251	345.8	0.73	0.64-0.82
		- Submarines	39	59.7	0.65	0.46-0.89
Transport accidents	V01-V99	Land-based	54	88.7	0.61	0.46-0.79
		All vessels	101	111.3	0.91	0.75-1.10
		- Submarines	16	19.5	0.82	0.47-1.33
Other accidents	W00-19,X40-49	Land-based	48	98.9	0.49	0.36-0.65
		All vessels	90	120.3	0.75	0.61-0.93
		- Submarines	10	20.0	0.50	0.24-0.92
Suicide	X60-84,Y87.0	Land-based	47	86.1	0.55	0.40-0.73
		All vessels	54	103.5	0.52	0.39-0.68
		- Submarines	12	18.3	0.65	0.34-1.14

^{*} ICD, International Classification of Diseases

[†] Obs., Observed number of cases

[‡] Exp., Expected number of cases based on population rates

[§] SMR, Standardized Mortality Ratio

[¶] CI, Confidence Interval

[#] Mental and behavioural disorders due to use of alcohol (F10), liver cirrhosis (K70)

Table 3 Mortality rate ratios (RR) comparing vessel crews with land-based personnel in the Royal Norwegian Navy. Poisson regression analysis adjusted for observation period and age

Causes of death	ICD-10*	RR†	95% CI‡
All causes	A00-Y99	1.15	1.08-1.23
Alcohol abuse and alcohol related diseases	§	1.56	0.96-2.52
Diseases of the circulatory system	100-199	1.12	1.00-1.24
Diseases of the respiratory system	J00-J99	1.18	0.86-1.60
Diseases of the digestive system	K00-K93	1.14	0.78-1.67
External causes of injury and poisoning	V01-X59	1.36	1.11-1.66

^{*} ICD, International Classification of Diseases

Table 4 Cancer incidence among 28,345 Royal Norwegian Navy servicemen followed between 1953 and 2008; 912,527 person-years

Cancer site	ICD-7*	Obs.†	Exp.‡	SIR§	95% CI¶
All sites	140-204	3362	3183.0	1.06	1.02-1.09
Alcohol related cancers	#	147	153.3	0.96	0.82-1.13
Lip	140	14	20.3	0.69	0.38-1.16
Stomach	151	109	113.5	0.96	0.80-1.16
Colon	153	266	258.1	1.03	0.91-1.16
Rectum	154	159	152.8	1.04	0.89-1.22
Pancreas	157	82	78.1	1.05	0.83-1.30
Trachea, bronchus and lung	162	375	370.5	1.01	0.91-1.12
Prostate	177	777	696.7	1.12	1.04-1.20
Testis	178	117	107.7	1.09	0.91-1.30
Kidney, renal pelvis and urether	180	116	115.3	1.01	0.84-1.21
Bladder and other urinary organs	181	207	198.2	1.04	0.91-1.20
Melanoma of skin	190	217	183.8	1.18	1.03-1.35
Other skin	191	168	122.9	1.37	1.18-1.59
Brain, nervous system	193	126	122.9	1.03	0.86-1.22
Thyroid gland	194	14	21.4	0.66	0.36-1.10
Lymphomas	200-202	143	143.4	1.00	0.85-1.17
Multiple myeloma and leukemias	203-204	142	137.6	1.03	0.88-1.22

^{*} ICD, International Classification of Diseases

[†] RR, Rate Ratio

[‡] CI, Confidence Interval

[§] Mental and behavioural disorders due to use of alcohol (F10), liver cirrhosis (K70)

[†] Obs., Observed number of cases

[‡] Exp., Expected number of cases based on population rates

[§] SIR, Standardized Incidence Ratio

[¶] CI, Confidence Interval

[#] Tongue (141), mouth (143–144), pharynx (145–148), oesophagus (150), liver (155), larynx (161)

Table 5 Incidence of selected cancers among Royal Norwegian Navy servicemen according to duty station: land-based personnel (411,208 person-years), all vessel crews (501,319 person-years), and a subgroup of the latter: submariners (89,315 person-years). Follow-up 1953–2008

Cancer site	ICD-7*	Duty station	Obs.†	Exp.‡	SIR§	95% CI¶
All sites	140-204	Land-based	1382	1418.1	0.97	0.92-1.03
		All vessels	1980	1764.9	1.12	1.07-1.17
		- Submarines	332	288.6	1.15	1.03-1.28
Alcohol related cancers	#	Land-based	50	68.3	0.73	0.54-0.97
		All vessels	97	85.0	1.14	0.93-1.39
		- Submarines	18	14.1	1.28	0.76-2.02
Trachea, bronchus and lung	162	Land-based	123	163.0	0.75	0.63-0.90
		All vessels	252	207.5	1.21	1.07-1.37
		- Submarines	32	33.5	0.95	0.65-1.35
Prostate	177	Land-based	351	308.6	1.14	1.02-1.26
		All vessels	426	388.1	1.10	1.00-1.21
		- Submarines	69	62.6	1.10	0.86-1.40
Bladder and other urinary	181	Land-based	87	87.6	0.99	0.80-1.23
organs		All vessels	120	110.6	1.09	0.91-1.30
		- Submarines	27	17.6	1.53	1.01-2.23
Melanoma of skin	190	Land-based	97	82.0	1.18	0.96-1.44
		All vessels	120	101.8	1.18	0.99-1.41
		- Submarines	24	17.7	1.35	0.87-2.01
Other skin	191	Land-based	67	54.5	1.23	0.95-1.56
		All vessels	101	68.4	1.48	1.21-1.79
		- Submarines	20	10.8	1.85	1.13-2.86

^{*} ICD, International Classification of Diseases

Table 6 Incidence rate ratios (RR) for selected cancers among vessel crews with reference to land-based personnel in the Royal Norwegian Navy. Poisson regression analysis adjusted for observation period and age

Cancer site	ICD-7*	RR†	95% CI‡
All sites	140-204	1.16	1.08-1.24
Alcohol related cancers	§	1.58	1.12-2.22
Lung cancer	162	1.65	1.33-2.04
Other skin	191	1.20	0.88-1.63

^{*} ICD, International Classification of Diseases

[†] Obs., Observed number of cases

[‡] Exp., Expected number of cases based on population rates

[§] SIR, Standardized Incidence Ratio

[¶] CI, Confidence Interval

[#] Tongue (141), mouth (143-144), pharynx (145-148), oesophagus (150), liver (155), larynx (161)

[†] RR, Rate Ratio

[‡] CI, Confidence Interval

[§] Tongue (141), mouth (143–144), pharynx (145–148), oesophagus (150), liver (155), larynx (161)

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- 68. Trond Sand: THE EFFECTS OF CLICK POLARITY ON BRAINSTEM AUDITORY EVOKED POTENTIALS AMPLITUDE, DISPERSION, AND LATENCY VARIABLES.
- 69. Kjetil B. Åsbakk: STUDIES OF A PROTEIN FROM PSORIATIC SCALE, PSO P27, WITH RESPECT TO ITS POTENTIAL ROLE IN IMMUNE REACTIONS IN PSORIASIS.
- 70. Arnulf Hestnes: STUDIES ON DOWN'S SYNDROME.
- 71. Randi Nygaard: LONG-TERM SURVIVAL IN CHILDHOOD LEUKEMIA.
- 72. Bjørn Hagen: THIO-TEPA.
- 73. Svein Anda: EVALUATION OF THE HIP JOINT BY COMPUTED TOMOGRAMPHY AND ULTRASONOGRAPHY.

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- 74. Martin Svartberg: AN INVESTIGATION OF PROCESS AND OUTCOME OF SHORT-TERM PSYCHODYNAMIC PSYCHOTHERAPY.
- 75. Stig Arild Slørdahl: AORTIC REGURGITATION.
- 76. Harold C Sexton: STUDIES RELATING TO THE TREATMENT OF SYMPTOMATIC NON-PSYCHOTIC PATIENTS.
- 77. Maurice B. Vincent: VASOACTIVE PEPTIDES IN THE OCULAR/FOREHEAD AREA.
- 78. Terje Johannessen: CONTROLLED TRIALS IN SINGLE SUBJECTS.
- 79. Turid Nilsen: PYROPHOSPHATE IN HEPATOCYTE IRON METABOLISM.
- 80. Olav Haraldseth: NMR SPECTROSCOPY OF CEREBRAL ISCHEMIA AND REPERFUSION IN RAT.
- 81. Eiliv Brenna: REGULATION OF FUNCTION AND GROWTH OF THE OXYNTIC MUCOSA.

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- 82. Gunnar Bovim: CERVICOGENIC HEADACHE.
- 83. Jarl Arne Kahn: ASSISTED PROCREATION.
- 84. Bjørn Naume: IMMUNOREGULATORY EFFECTS OF CYTOKINES ON NK CELLS.
- 85. Rune Wiseth: AORTIC VALVE REPLACEMENT.
- 86. Jie Ming Shen: BLOOD FLOW VELOCITY AND RESPIRATORY STUDIES.
- 87. Piotr Kruszewski: SUNCT SYNDROME WITH SPECIAL REFERENCE TO THE AUTONOMIC NERVOUS SYSTEM.
- 88. Mette Haase Moen: ENDOMETRIOSIS.
- 89. Anne Vik: VASCULAR GAS EMBOLISM DURING AIR INFUSION AND AFTER DECOMPRESSION IN PIGS.
- 90. Lars Jacob Stovner: THE CHIARI TYPE I MALFORMATION.
- 91. Kjell Å. Salvesen: ROUTINE ULTRASONOGRAPHY IN UTERO AND DEVELOPMENT IN CHILDHOOD.

- 92. Nina-Beate Liabakk: DEVELOPMENT OF IMMUNOASSAYS FOR TNF AND ITS SOLUBLE RECEPTORS.
- 93. Sverre Helge Torp: erbB ONCOGENES IN HUMAN GLIOMAS AND MENINGIOMAS.
- 94. Olav M. Linaker: MENTAL RETARDATION AND PSYCHIATRY. Past and present.
- 95. Per Oscar Feet: INCREASED ANTIDEPRESSANT AND ANTIPANIC EFFECT IN COMBINED TREATMENT WITH DIXYRAZINE AND TRICYCLIC ANTIDEPRESSANTS.
- 96. Stein Olav Samstad: CROSS SECTIONAL FLOW VELOCITY PROFILES FROM TWO-DIMENSIONAL DOPPLER ULTRASOUND: Studies on early mitral blood flow.
- 97. Bjørn Backe: STUDIES IN ANTENATAL CARE.
- 98. Gerd Inger Ringdal: QUALITY OF LIFE IN CANCER PATIENTS.
- 99. Torvid Kiserud: THE DUCTUS VENOSUS IN THE HUMAN FETUS.
- 100. Hans E. Fjøsne: HORMONAL REGULATION OF PROSTATIC METABOLISM.
- 101. Eylert Brodtkorb: CLINICAL ASPECTS OF EPILEPSY IN THE MENTALLY RETARDED.

102.Roar Juul: PEPTIDERGIC MECHANISMS IN HUMAN SUBARACHNOID HEMORRHAGE.

103. Unni Syversen: CHROMOGRANIN A. Phsysiological and Clinical Role.

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- 104.Odd Gunnar Brakstad: THERMOSTABLE NUCLEASE AND THE *nuc* GENE IN THE DIAGNOSIS OF *Staphylococcus aureus* INFECTIONS.
- 105.Terje Engan: NUCLEAR MAGNETIC RESONANCE (NMR) SPECTROSCOPY OF PLASMA IN MALIGNANT DISEASE.
- 106.Kirsten Rasmussen: VIOLENCE IN THE MENTALLY DISORDERED.
- 107. Finn Egil Skjeldestad: INDUCED ABORTION: Timetrends and Determinants.
- 108.Roar Stenseth: THORACIC EPIDURAL ANALGESIA IN AORTOCORONARY BYPASS SURGERY
- 109. Arild Faxvaag: STUDIES OF IMMUNE CELL FUNCTION in mice infected with MURINE RETROVIRUS.

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- 110.Svend Aakhus: NONINVASIVE COMPUTERIZED ASSESSMENT OF LEFT VENTRICULAR FUNCTION AND SYSTEMIC ARTERIAL PROPERTIES. Methodology and some clinical applications.
- 111.Klaus-Dieter Bolz: INTRAVASCULAR ULTRASONOGRAPHY.
- 112.Petter Aadahl: CARDIOVASCULAR EFFECTS OF THORACIC AORTIC CROSS-CLAMPING.
- 113. Sigurd Steinshamn: CYTOKINE MEDIATORS DURING GRANULOCYTOPENIC INFECTIONS.
- 114. Hans Stifoss-Hanssen: SEEKING MEANING OR HAPPINESS?
- 115. Anne Kvikstad: LIFE CHANGE EVENTS AND MARITAL STATUS IN RELATION TO RISK AND PROGNOSIS OF CANCER.
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- 118.Jan Schjøtt: MYOCARDIAL PROTECTION: Functional and Metabolic Characteristics of Two Endogenous Protective Principles.
- 119.Marit Martinussen: STUDIES OF INTESTINAL BLOOD FLOW AND ITS RELATION TO TRANSITIONAL CIRCULATORY ADAPATION IN NEWBORN INFANTS.
- 120. Tomm B. Müller: MAGNETIC RESONANCE IMAGING IN FOCAL CEREBRAL ISCHEMIA.
- 121.Rune Haaverstad: OEDEMA FORMATION OF THE LOWER EXTREMITIES.
- 122. Magne Børset: THE ROLE OF CYTOKINES IN MULTIPLE MYELOMA, WITH SPECIAL REFERENCE TO HEPATOCYTE GROWTH FACTOR.
- 123.Geir Smedslund: A THEORETICAL AND EMPIRICAL INVESTIGATION OF SMOKING, STRESS AND DISEASE: RESULTS FROM A POPULATION SURVEY.

- 124.Torstein Vik: GROWTH, MORBIDITY, AND PSYCHOMOTOR DEVELOPMENT IN INFANTS WHO WERE GROWTH RETARDED *IN UTERO*.
- 125.Siri Forsmo: ASPECTS AND CONSEQUENCES OF OPPORTUNISTIC SCREENING FOR CERVICAL CANCER. Results based on data from three Norwegian counties.
- 126.Jon S. Skranes: CEREBRAL MRI AND NEURODEVELOPMENTAL OUTCOME IN VERY LOW BIRTH WEIGHT (VLBW) CHILDREN. A follow-up study of a geographically based year cohort of VLBW children at ages one and six years.
- 127.Knut Bjørnstad: COMPUTERIZED ECHOCARDIOGRAPHY FOR EVALUTION OF CORONARY ARTERY DISEASE.
- 128.Grethe Elisabeth Borchgrevink: DIAGNOSIS AND TREATMENT OF WHIPLASH/NECK SPRAIN INJURIES CAUSED BY CAR ACCIDENTS.
- 129. Tor Elsås: NEUROPEPTIDES AND NITRIC OXIDE SYNTHASE IN OCULAR AUTONOMIC AND SENSORY NERVES.
- 130.Rolf W. Gråwe: EPIDEMIOLOGICAL AND NEUROPSYCHOLOGICAL PERSPECTIVES ON SCHIZOPHRENIA.
- 131. Tonje Strømholm: CEREBRAL HAEMODYNAMICS DURING THORACIC AORTIC CROSSCLAMPING. An experimental study in pigs.

- 132.Martinus Bråten: STUDIES ON SOME PROBLEMS REALTED TO INTRAMEDULLARY NAILING OF FEMORAL FRACTURES.
- 133. Ståle Nordgård: PROLIFERATIVE ACTIVITY AND DNA CONTENT AS PROGNOSTIC INDICATORS IN ADENOID CYSTIC CARCINOMA OF THE HEAD AND NECK.
- 134.Egil Lien: SOLUBLE RECEPTORS FOR TNF AND LPS: RELEASE PATTERN AND POSSIBLE SIGNIFICANCE IN DISEASE.
- 135.Marit Bjørgaas: HYPOGLYCAEMIA IN CHILDREN WITH DIABETES MELLITUS
- 136.Frank Skorpen: GENETIC AND FUNCTIONAL ANALYSES OF DNA REPAIR IN HUMAN CELLS.
- 137. Juan A. Pareja: SUNCT SYNDROME. ON THE CLINICAL PICTURE. ITS DISTINCTION FROM OTHER, SIMILAR HEADACHES.
- 138. Anders Angelsen: NEUROENDOCRINE CELLS IN HUMAN PROSTATIC CARCINOMAS AND THE PROSTATIC COMPLEX OF RAT, GUINEA PIG, CAT AND DOG.
- 139.Fabio Antonaci: CHRONIC PAROXYSMAL HEMICRANIA AND HEMICRANIA CONTINUA: TWO DIFFERENT ENTITIES?
- 140.Sven M. Carlsen: ENDOCRINE AND METABOLIC EFFECTS OF METFORMIN WITH SPECIAL EMPHASIS ON CARDIOVASCULAR RISK FACTORES.

- 141.Terje A. Murberg: DEPRESSIVE SYMPTOMS AND COPING AMONG PATIENTS WITH CONGESTIVE HEART FAILURE.
- 142.Harm-Gerd Karl Blaas: THE EMBRYONIC EXAMINATION. Ultrasound studies on the development of the human embryo.
- 143. Noèmi Becser Andersen: THE CEPHALIC SENSORY NERVES IN UNILATERAL HEADACHES. Anatomical background and neurophysiological evaluation.
- 144.Eli-Janne Fiskerstrand: LASER TREATMENT OF PORT WINE STAINS. A study of the efficacy and limitations of the pulsed dye laser. Clinical and morfological analyses aimed at improving the therapeutic outcome.
- 145.Bård Kulseng: A STUDY OF ALGINATE CAPSULE PROPERTIES AND CYTOKINES IN RELATION TO INSULIN DEPENDENT DIABETES MELLITUS.
- 146. Terje Haug: STRUCTURE AND REGULATION OF THE HUMAN UNG GENE ENCODING URACIL-DNA GLYCOSYLASE.
- 147. Heidi Brurok: MANGANESE AND THE HEART. A Magic Metal with Diagnostic and Therapeutic Possibilites.
- 148.Agnes Kathrine Lie: DIAGNOSIS AND PREVALENCE OF HUMAN PAPILLOMAVIRUS INFECTION IN CERVICAL INTRAEPITELIAL NEOPLASIA. Relationship to Cell Cycle Regulatory Proteins and HLA DQBI Genes.
- 149.Ronald Mårvik: PHARMACOLOGICAL, PHYSIOLOGICAL AND PATHOPHYSIOLOGICAL STUDIES ON ISOLATED STOMACS.
- 150.Ketil Jarl Holen: THE ROLE OF ULTRASONOGRAPHY IN THE DIAGNOSIS AND TREATMENT OF HIP DYSPLASIA IN NEWBORNS.
- 151.Irene Hetlevik: THE ROLE OF CLINICAL GUIDELINES IN CARDIOVASCULAR RISK INTERVENTION IN GENERAL PRACTICE.
- 152.Katarina Tunòn: ULTRASOUND AND PREDICTION OF GESTATIONAL AGE.
- 153. Johannes Soma: INTERACTION BETWEEN THE LEFT VENTRICLE AND THE SYSTEMIC ARTERIES.
- 154.Arild Aamodt: DEVELOPMENT AND PRE-CLINICAL EVALUATION OF A CUSTOM-MADE FEMORAL STEM.
- 155.Agnar Tegnander: DIAGNOSIS AND FOLLOW-UP OF CHILDREN WITH SUSPECTED OR KNOWN HIP DYSPLASIA.
- 156.Bent Indredavik: STROKE UNIT TREATMENT: SHORT AND LONG-TERM EFFECTS
- 157. Jolanta Vanagaite Vingen: PHOTOPHOBIA AND PHONOPHOBIA IN PRIMARY HEADACHES

- 158.Ola Dalsegg Sæther: PATHOPHYSIOLOGY DURING PROXIMAL AORTIC CROSS-CLAMPING CLINICAL AND EXPERIMENTAL STUDIES
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- 160.Christina Vogt Isaksen: PRENATAL ULTRASOUND AND POSTMORTEM FINDINGS A TEN YEAR CORRELATIVE STUDY OF FETUSES AND INFANTS WITH DEVELOPMENTAL ANOMALIES.

- 161.Holger Seidel: HIGH-DOSE METHOTREXATE THERAPY IN CHILDREN WITH ACUTE LYMPHOCYTIC LEUKEMIA: DOSE, CONCENTRATION, AND EFFECT CONSIDERATIONS.
- 162. Stein Hallan: IMPLEMENTATION OF MODERN MEDICAL DECISION ANALYSIS INTO CLINICAL DIAGNOSIS AND TREATMENT.
- 163.Malcolm Sue-Chu: INVASIVE AND NON-INVASIVE STUDIES IN CROSS-COUNTRY SKIERS WITH ASTHMA-LIKE SYMPTOMS.
- 164.Ole-Lars Brekke: EFFECTS OF ANTIOXIDANTS AND FATTY ACIDS ON TUMOR NECROSIS FACTOR-INDUCED CYTOTOXICITY.
- 165.Jan Lundbom: AORTOCORONARY BYPASS SURGERY: CLINICAL ASPECTS, COST CONSIDERATIONS AND WORKING ABILITY.
- 166. John-Anker Zwart: LUMBAR NERVE ROOT COMPRESSION, BIOCHEMICAL AND NEUROPHYSIOLOGICAL ASPECTS.
- 167.Geir Falck: HYPEROSMOLALITY AND THE HEART.
- 168. Eirik Skogvoll: CARDIAC ARREST Incidence, Intervention and Outcome.
- 169. Dalius Bansevicius: SHOULDER-NECK REGION IN CERTAIN HEADACHES AND CHRONIC PAIN SYNDROMES.
- 170.Bettina Kinge: REFRACTIVE ERRORS AND BIOMETRIC CHANGES AMONG UNIVERSITY STUDENTS IN NORWAY.
- 171. Gunnar Qvigstad: CONSEQUENCES OF HYPERGASTRINEMIA IN MAN
- 172.Hanne Ellekjær: EPIDEMIOLOGICAL STUDIES OF STROKE IN A NORWEGIAN POPULATION. INCIDENCE, RISK FACTORS AND PROGNOSIS
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- 174. Astrid Hjelde: SURFACE TENSION AND COMPLEMENT ACTIVATION: Factors influencing bubble formation and bubble effects after decompression.
- 175. Kjell A. Kvistad: MR IN BREAST CANCER A CLINICAL STUDY.
- 176.Ivar Rossvoll: ELECTIVE ORTHOPAEDIC SURGERY IN A DEFINED POPULATION. Studies on demand, waiting time for treatment and incapacity for work.
- 177. Carina Seidel: PROGNOSTIC VALUE AND BIOLOGICAL EFFECTS OF HEPATOCYTE GROWTH FACTOR AND SYNDECAN-1 IN MULTIPLE MYELOMA.

- 178.Alexander Wahba: THE INFLUENCE OF CARDIOPULMONARY BYPASS ON PLATELET FUNCTION AND BLOOD COAGULATION DETERMINANTS AND CLINICAL CONSEQUENSES
- 179.Marcus Schmitt-Egenolf: THE RELEVANCE OF THE MAJOR hISTOCOMPATIBILITY COMPLEX FOR THE GENETICS OF PSORIASIS
- 180.Odrun Arna Gederaas: BIOLOGICAL MECHANISMS INVOLVED IN 5-AMINOLEVULINIC ACID BASED PHOTODYNAMIC THERAPY
- 181.Pål Richard Romundstad: CANCER INCIDENCE AMONG NORWEGIAN ALUMINIUM WORKERS
- 182.Henrik Hjorth-Hansen: NOVEL CYTOKINES IN GROWTH CONTROL AND BONE DISEASE OF MULTIPLE MYELOMA
- 183.Gunnar Morken: SEASONAL VARIATION OF HUMAN MOOD AND BEHAVIOUR
- 184.Bjørn Olav Haugen: MEASUREMENT OF CARDIAC OUTPUT AND STUDIES OF VELOCITY PROFILES IN AORTIC AND MITRAL FLOW USING TWO- AND THREE-DIMENSIONAL COLOUR FLOW IMAGING
- 185.Geir Bråthen: THE CLASSIFICATION AND CLINICAL DIAGNOSIS OF ALCOHOL-RELATED SEIZURES
- 186.Knut Ivar Aasarød: RENAL INVOLVEMENT IN INFLAMMATORY RHEUMATIC DISEASE. A Study of Renal Disease in Wegener's Granulomatosis and in Primary Sjögren's Syndrome
- 187.Trude Helen Flo: RESEPTORS INVOLVED IN CELL ACTIVATION BY DEFINED URONIC ACID POLYMERS AND BACTERIAL COMPONENTS
- 188.Bodil Kavli: HUMAN URACIL-DNA GLYCOSYLASES FROM THE UNG GENE: STRUCTRUAL BASIS FOR SUBSTRATE SPECIFICITY AND REPAIR
- 189.Liv Thommesen: MOLECULAR MECHANISMS INVOLVED IN TNF- AND GASTRIN-MEDIATED GENE REGULATION
- 190. Turid Lingaas Holmen: SMOKING AND HEALTH IN ADOLESCENCE; THE NORD-TRØNDELAG HEALTH STUDY, 1995-97

- 191.Øyvind Hjertner: MULTIPLE MYELOMA: INTERACTIONS BETWEEN MALIGNANT PLASMA CELLS AND THE BONE MICROENVIRONMENT
- 192.Asbjørn Støylen: STRAIN RATE IMAGING OF THE LEFT VENTRICLE BY ULTRASOUND. FEASIBILITY, CLINICAL VALIDATION AND PHYSIOLOGICAL ASPECTS
- 193.Kristian Midthjell: DIABETES IN ADULTS IN NORD-TRØNDELAG. PUBLIC HEALTH ASPECTS OF DIABETES MELLITUS IN A LARGE, NON-SELECTED NORWEGIAN POPULATION.
- 194. Guanglin Cui: FUNCTIONAL ASPECTS OF THE ECL CELL IN RODENTS
- 195.Ulrik Wisløff: CARDIAC EFFECTS OF AEROBIC ENDURANCE TRAINING: HYPERTROPHY, CONTRACTILITY AND CALCUIM HANDLING IN NORMAL AND FAILING HEART
- 196.Øyvind Halaas: MECHANISMS OF IMMUNOMODULATION AND CELL-MEDIATED CYTOTOXICITY INDUCED BY BACTERIAL PRODUCTS
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- 198. Nanna Kurtze: THE SIGNIFICANCE OF ANXIETY AND DEPRESSION IN FATIQUE AND PATTERNS OF PAIN AMONG INDIVIDUALS DIAGNOSED WITH FIBROMYALGIA: RELATIONS WITH QUALITY OF LIFE, FUNCTIONAL DISABILITY, LIFESTYLE, EMPLOYMENT STATUS, CO-MORBIDITY AND GENDER
- 199.Tom Ivar Lund Nilsen: PROSPECTIVE STUDIES OF CANCER RISK IN NORD-TRØNDELAG: THE HUNT STUDY. Associations with anthropometric, socioeconomic, and lifestyle risk factors
- 200. Asta Kristine Håberg: A NEW APPROACH TO THE STUDY OF MIDDLE CEREBRAL ARTERY OCCLUSION IN THE RAT USING MAGNETIC RESONANCE TECHNIQUES

- 201. Knut Jørgen Arntzen: PREGNANCY AND CYTOKINES
- 202. Henrik Døllner: INFLAMMATORY MEDIATORS IN PERINATAL INFECTIONS
- 203. Asta Bye: LOW FAT, LOW LACTOSE DIET USED AS PROPHYLACTIC TREATMENT OF ACUTE INTESTINAL REACTIONS DURING PELVIC RADIOTHERAPY. A PROSPECTIVE RANDOMISED STUDY.
- 204. Sylvester Moyo: STUDIES ON STREPTOCOCCUS AGALACTIAE (GROUP B STREPTOCOCCUS) SURFACE-ANCHORED MARKERS WITH EMPHASIS ON STRAINS AND HUMAN SERA FROM ZIMBABWE.
- 205.Knut Hagen: HEAD-HUNT: THE EPIDEMIOLOGY OF HEADACHE IN NORD-TRØNDELAG
- 206.Li Lixin: ON THE REGULATION AND ROLE OF UNCOUPLING PROTEIN-2 IN INSULIN PRODUCING β-CELLS
- 207. Anne Hildur Henriksen: SYMPTOMS OF ALLERGY AND ASTHMA VERSUS MARKERS OF LOWER AIRWAY INFLAMMATION AMONG ADOLESCENTS
- 208.Egil Andreas Fors: NON-MALIGNANT PAIN IN RELATION TO PSYCHOLOGICAL AND ENVIRONTENTAL FACTORS. EXPERIENTAL AND CLINICAL STUDES OF PAIN WITH FOCUS ON FIBROMYALGIA
- 209. Pål Klepstad: MORPHINE FOR CANCER PAIN
- 210.Ingunn Bakke: MECHANISMS AND CONSEQUENCES OF PEROXISOME PROLIFERATOR-INDUCED HYPERFUNCTION OF THE RAT GASTRIN PRODUCING CELL
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- 213. Johan Haux: STUDIES ON CYTOTOXICITY INDUCED BY HUMAN NATURAL KILLER CELLS AND DIGITOXIN
- 214. Turid Suzanne Berg-Nielsen: PARENTING PRACTICES AND MENTALLY DISORDERED ADOLESCENTS
- 215.Astrid Rydning: BLOOD FLOW AS A PROTECTIVE FACTOR FOR THE STOMACH MUCOSA. AN EXPERIMENTAL STUDY ON THE ROLE OF MAST CELLS AND SENSORY AFFERENT NEURONS

- 216. Jan Pål Loennechen: HEART FAILURE AFTER MYOCARDIAL INFARCTION. Regional Differences, Myocyte Function, Gene Expression, and Response to Cariporide, Losartan, and Exercise Training.
- 217.Elisabeth Qvigstad: EFFECTS OF FATTY ACIDS AND OVER-STIMULATION ON INSULIN SECRETION IN MAN
- 218.Arne Åsberg: EPIDEMIOLOGICAL STUDIES IN HEREDITARY HEMOCHROMATOSIS: PREVALENCE, MORBIDITY AND BENEFIT OF SCREENING.
- 219. Johan Fredrik Skomsvoll: REPRODUCTIVE OUTCOME IN WOMEN WITH RHEUMATIC DISEASE. A population registry based study of the effects of inflammatory rheumatic disease and connective tissue disease on reproductive outcome in Norwegian women in 1967-1995.
- 220.Siv Mørkved: URINARY INCONTINENCE DURING PREGNANCY AND AFTER DELIVERY: EFFECT OF PELVIC FLOOR MUSCLE TRAINING IN PREVENTION AND TREATMENT
- 221. Marit S. Jordhøy: THE IMPACT OF COMPREHENSIVE PALLIATIVE CARE
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- 234.Arne Wibe: RECTAL CANCER TREATMENT IN NORWAY STANDARDISATION OF SURGERY AND QUALITY ASSURANCE

- 235. Eivind Witsø: BONE GRAFT AS AN ANTIBIOTIC CARRIER
- 236.Anne Mari Sund: DEVELOPMENT OF DEPRESSIVE SYMPTOMS IN EARLY ADOLESCENCE
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- 241.Ingunn Dybedal: NEGATIVE REGULATORS OF HEMATOPOIETEC STEM AND PROGENITOR CELLS
- 242.Beate Sitter: TISSUE CHARACTERIZATION BY HIGH RESOLUTION MAGIC ANGLE SPINNING MR SPECTROSCOPY

- 243.Per Arne Aas: MACROMOLECULAR MAINTENANCE IN HUMAN CELLS REPAIR OF URACIL IN DNA AND METHYLATIONS IN DNA AND RNA
- 244. Anna Bofin: FINE NEEDLE ASPIRATION CYTOLOGY IN THE PRIMARY INVESTIGATION OF BREAST TUMOURS AND IN THE DETERMINATION OF TREATMENT STRATEGIES
- 245.Jim Aage Nøttestad: DEINSTITUTIONALIZATION AND MENTAL HEALTH CHANGES AMONG PEOPLE WITH MENTAL RETARDATION
- 246.Reidar Fossmark: GASTRIC CANCER IN JAPANESE COTTON RATS
- 247. Wibeke Nordhøy: MANGANESE AND THE HEART, INTRACELLULAR MR RELAXATION AND WATER EXCHANGE ACROSS THE CARDIAC CELL MEMBRANE 2005
 - 248.Sturla Molden: QUANTITATIVE ANALYSES OF SINGLE UNITS RECORDED FROM THE HIPPOCAMPUS AND ENTORHINAL CORTEX OF BEHAVING RATS
 - 249. Wenche Brenne Drøyvold: EPIDEMIOLOGICAL STUDIES ON WEIGHT CHANGE AND HEALTH IN A LARGE POPULATION. THE NORD-TRØNDELAG HEALTH STUDY (HUNT)
 - 250.Ragnhild Støen: ENDOTHELIUM-DEPENDENT VASODILATION IN THE FEMORAL ARTERY OF DEVELOPING PIGLETS
 - 251.Aslak Steinsbekk: HOMEOPATHY IN THE PREVENTION OF UPPER RESPIRATORY TRACT INFECTIONS IN CHILDREN
 - 252.Hill-Aina Steffenach: MEMORY IN HIPPOCAMPAL AND CORTICO-HIPPOCAMPAL CIRCUITS
 - 253.Eystein Stordal: ASPECTS OF THE EPIDEMIOLOGY OF DEPRESSIONS BASED ON SELF-RATING IN A LARGE GENERAL HEALTH STUDY (THE HUNT-2 STUDY)
 - 254. Viggo Pettersen: FROM MUSCLES TO SINGING: THE ACTIVITY OF ACCESSORY BREATHING MUSCLES AND THORAX MOVEMENT IN CLASSICAL SINGING
 - 255.Marianne Fyhn: SPATIAL MAPS IN THE HIPPOCAMPUS AND ENTORHINAL CORTEX
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 - 257.Erik Skaaheim Haug: INFRARENAL ABDOMINAL AORTIC ANEURYSMS COMORBIDITY AND RESULTS FOLLOWING OPEN SURGERY
 - 258.Daniel Kondziella: GLIAL-NEURONAL INTERACTIONS IN EXPERIMENTAL BRAIN DISORDERS
 - 259. Vegard Heimly Brun: ROUTES TO SPATIAL MEMORY IN HIPPOCAMPAL PLACE CELLS
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