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Respiratory symptoms, lung function, and occupational exposure among seafood industry workers

A study among employees at Norwegian salmon factories and Russian North-West trawl fleet (Arkhangelsk)

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LIST OF ABBREVIATIONS

APC	Antigen-presenting cells
ATS	American Thoracic Society
BHT	Bedrifthelsetjeneste (local occupational health services)
CI	Confidence interval
COPD	Chronic obstructive pulmonary disease
CRP	C reactive protein
FE_{NO}	Fractional exhaled nitric oxide concentration
FEV_1	Forced expiratory volume in one second
ELISA	Enzyme-linked immunosorbent assay
EU	Endotoxin units
FVC	Forced vital capacity
HMW	High molecular weight
IgE	Immunoglobulin E
IL	Interleukin
LAL	Limulus Amoebocyte Lysate
LMW	Low molecular weight
LOD	Limit of detection
NIOH	National Institute of Occupational Health (Oslo, Norway)
OA	Occupational asthma
OR	Odds ratio
PAR	Protease activated receptor
PTEF	Polytetrafluoroethylene
TCR	T cell receptor
Th	T helper cells
TLR	Toll-like reseptors
TNF-α	Tumor necrosis factor
TP	Total protein fraction
TWA	Time-weighted average

Definitions of concepts used in the thesis

1) attributable to respiratory terminology

Respiratory (health) variables/outcomes in the presented study are respiratory symptoms (general (not associated with work situation) and work-related (experienced during or shortly after work)), spirometric test results (absolute values of FVC and FEV_1 and FVC and FEV_1 % of predicted, fixed spirometric declines (FVC and FEV_1 < 80%, FEV1/FVC < 5th percentile of predicted value), levels of nitric oxide concentration in exhaled air (FE_{NO}), as well as cross-shift change of FEV_1 and acute respiratory symptoms emerged during a workshift.

By analysis of *respiratory (health) status* we mean analysis of respiratory variables measured in the study. Term of *impaired respiratory (health) status* [1] is meant to reflect increased prevalence/odds ratio of respiratory symptoms, as well as decreased spirometric test results among the studied workers.

2) attributable to occupational terminology

Seafood workers are workers whose tasks include work with seafood. *Seafood* is any form of sea life, and prominently includes fish and/or shellfish. The harvesting of wild seafood is known as *fishing* and the cultivation and farming of seafood is known as *aquaculture*, mariculture, or in the case of fish, fish farming.

The term *fish processing* refers to the processes associated with fish and fish products between the time fish are caught or harvested, and the time the final product is delivered to the customer. The term refers to fish harvested for commercial purposes, whether caught in wild fisheries or harvested from aquaculture or fish farming. Three main steps of fish processing at a processing plant include *slaughtering* (killing fish, degutting and deheading (as alternative)); *filleting* is often an alternative processing, and comprises cutting the fillets from the backbone and removing the collarbone, pin bones (trimming), fish fillets may also be skinned during filleting); and *packing.*

Two *types of workplace* in seafood industry are mentioned in the text, the first one is *onshore* and related to Norwegian salmon processing, the second one is *offshore* and related to Russian trawler fishing and onboard fish processing.

In the present study *salmon workers* are those who are involved in salmon processing at an onshore factory plant, while *trawler workers* are presented by workers, who are involved in processing of different types of fish at onboard processing facilities on a trawl vessel.

A term *worker group* is used in the text of the thesis to define either group of onshore salmon workers and offshore trawler workers (Paper IV), or salmon workers from the same department at a processing facility (Paper II) or group of trawler workers engaged in the same work tasks (Paper III).

3) attributable to exposure terminology

Bioaerosols are airborne particles that originate from living organisms (e.g., bacteria, plants, fungi, and animals), and can be formed from any process that involves biological materials [2, 3]. Most relevant constituents of bioaerosols in seafood industry are proteins, high molecular weight allergens, endotoxin, and microorganisms.

The term *biological agent* refers to any substance of biological origin that is capable of producing an effect on humans [2, 4].

4) attributable to mechanisms terminology

Tolerance takes place when a subject's reaction to a specific agent and concentration of the agent is reduced. Characteristics of tolerance: it is reversible, the rate depends on the particular agent, dosage and frequency, differential development occurs for different effects of the same agent. Tolerance occurs when a subject acquires a adaptation to the effects of an agent after repeated exposure.

LIST OF PUBLICATIONS

The thesis is based on the following papers, which will be referred to in the text by their Roman numerals:

I. Shiryaeva O, Aasmoe L, Straume B, Bang BE. Respiratory impairment in Norwegian salmon industry workers: a cross-sectional study. *J Occup Environ Med 2010; 52: 1167-72*

II. Shiryaeva O, Lisbeth Aasmoe, Bjørn Straume, Ann-Helen Olsen, Arild Øvrum, Eva Kramvik, Merethe Larsen, Anne Renstrøm, Anne-Sophie Merritt, Kari Kulvik Heldal, Berit Elisabeth Bang. Respiratory effects of bioaerosols: exposure-response study among salmon-processing workers. *Manuscript*.

III. Shiryaeva O, Aasmoe L, Straume B, Bang BE. An analysis of the respiratory health status among seafarers in the Russian trawler and merchant fleets. *Am J Ind Med 2011. 54(12): p. 971-9.*

IV. Shiryaeva O, Aasmoe L, Straume B, Bang BE. Respiratory symptoms, lung functions and exhaled nitric oxide (FE_{NO}) in two types of fish processing workers: Russian trawler fishermen and Norwegian salmon industry workers. *Manuscript*.

1. INTRODUCTION

1.1 Background of the study

During the last few decades increased consumption of seafood has been associated with a concomitant rise in fishing and aquaculture activities worldwide. This increase in processing of seafood has led to an increased awareness of respiratory health problems among workers engaged in seafood processing. Several international publications have shown elevated prevalence of airway symptoms, asthma and allergy in processors of seafood. [5-23].

The Department of Occupational and Environmental Medicine at the University Hospital North Norway works to increase the knowledge of relations between health and environmental factors with special emphasis on workplace environments. Researchers at the department attempt to have a regional profile by addressing challenges that are of special importance to northern populations.

In 2001 a study on workers involved in white fish, salmon (only from slaughtery), as well as shrimp and herring processing in Norway, was undertaken. It was found that processing workers reported respiratory symptoms and exhibited decreased lung function more often compared to a control population of administration workers in the same factories [21]. The main limitation of the study was a lack of linkage between exposure data and health outcome data.

Five years later the project leaders from the department visited Central Seamen Polyclinic that serves merchant and trawler seamen in Arkhangelsk, Russia. During a discussion with physicians performing examinations it was revealed that trawler workers involved in seafood processing experience respiratory symptoms.

Taking into account limitations from the first study conducted in Norway, the gap in research among workers involved in onboard seafood processing, and the lack of international publications on Russian worker populations, we decided to perform the study on seafood workers from both nations.

To further explore respiratory heath and risk factors in a rapid growing and economical important industry, we concentrated on salmon industry in Norway in the first part of the present study. Workers involved in onboard fish processing comprised the study population in the Russian part of the study.

1.2 Norwegian aquaculture industry and Russian trawl fishing

Norwegian aquaculture industry

Norway has fishing traditions dating back thousands of years. Norway's coastline extends to a length of more than 83,000 km, including islands. More than 200 different species of fish and shellfish inhabit Norway's coastal waters. Thanks to the Gulf Stream and other favorable natural conditions, Norwegian seafood has always been an important food source and economic resource that has contributed significantly to Norwegian prosperity. The seafood industry is a major industry in Norway besides the oil/gas industry and energy-intensive chemical industry.

The Norwegian seafood production consists of many different branches and has a great variety both in technology, production methods and profitability. Traditional fishing methods remain in use, while at the same time new technologies and modern methods have been introduced. Nowadays, many fish species are not caught exclusively 'in the wild' but are also bred in aquaculture operations. The development of commercial aquaculture in Norway began around 1970, since that time aquaculture has developed into a major industry in coastal areas [24]. The Norwegian export of farmed seafood are now much bigger than the wild caught seafood (62 /38 percent) [25].

Aquaculture has offered many Norwegians promising employment opportunities. Of 12,000 people employed in the fish industry, 5,100 are employed at fish farms (Directorate of Fisheries 2011).

Atlantic salmon is by far the most important farmed species in Norway. Production of salmon has shot up from 410,000 tons in 2001 to 1 059, 958 tons in 2011 [26].

Aquaculture facilities for salmon

The aquaculture facilities consists of mobile elements, the bag-like nets in which salmon swim, feeding devices and various monitoring equipment [27]. The floating element and the net together are called a cage (Figure 1). The nets are fastened to the floating elements and can be up to 40-50 meters deep and 60-160 meters in circumference. In the most modern facilities feeding is done by one automatic device per cage, or from a single central feeding plant, and is controlled on the basis of the fish's appetite [27].

When salmon have reached slaughter size, they are relocated, alive, to processing facilities where salmon prepared for the market. The bulk of the Norwegian salmon is sold as fresh degutted fish, but some are sold as fillets or are sent for other kinds of processing [26].

Figure 1. The floating element and the net in a salmon farm

Salmon processing

In a processing plant salmon are anaesthetized normally by CO2 and/or icy water and then slaughtered. In the slaughter departments salmon are degutted and washed and often deheaded (depends on a final product). Slaughtering of salmon is relying on a combination of manual handling and automated processes. The next alternative step in the process is filleting, which is normally done by mechanical filleting machines followed by manual trimming of fillets (Figure 2).

The filleting department is often separated from the slaughter area to prevent workers and goods passing from the non-sterile pretreatment area to the sterile filleting area. The filleting machines comprise pairs of mechanically operated knives, which cut the fillets from the backbone and remove the collarbone. Some fish fillets may also be skinned at this stage. During a trimming, pin bones are removed and operators inspect the fillets, removing defects and any parts that are of inferior quality.

Figure 2. Trimming of salmon

Offcuts are collected and minced (Figure 3). A final step is packaging. Fresh products are packed in boxes with ice. Products for freezing (whole degutted salmon/fillet/pieces) can be packed in a number of ways (individually frozen or wrapped in plastic) and kept in cold storage. Quality control checks are done along the whole production line in order to ensure a product standard.

Figure 3. Offcuts collecting

Work schedule
Workers involved in salmon processing normally have a 5-day, 8-hours work shift schedule from Monday through Friday. The day shift is scheduled from 6 or 7 a.m. to 2 or 3 p.m., with possibility of a shorter work shift on Fridays.

Russian fish industry

The coastline of the Russian Federation is the fourth longest in the world after the coastlines of Canada, Greenland, and Indonesia. The Russian fishing industry has an exclusive economic zone of 7.6 million km^2 [28]. It plays a significant role in the Russian economy. With access to the substantial resources of Arctic, Atlantic and Pacific oceans, marine fishing is particularly well developed, and Russia's fleet of factory ships can process huge catches at remote locations. The main European ocean fishing ports are Kaliningrad and St. Petersburg, and Murmansk and Arkhangelsk in the far north [29, 30].

Russia produces about one-third of all canned fish and some one-fourth of the world's total fresh and frozen fish. In 2011 the Russian fishing industry harvested 4.3 million tonnes of fish from wild fisheries [31].

The Russian fishery harvest includes about 170 species of finfish and more than 100 commercial species of invertebrates. Especially important catches are cod, pollock, and herring. Russia's earnings from the export of fish are steadily larger than from grain export. [30].
The fishing industry in Russia is a big source of employment. More than 800,000 Russians rely on fishing as a source of income [28, 32].
The majority of the industry is marine fishing, which makes up about 60%. The remaining 40% is inland fishing which takes advantage of Russia's numerous ponds, rivers, lakes, reservoirs and aquaculture [32].

Trawl fishing
The offshore marine fleet comprises around 2500 fishing vessels [28]. The trawl still remains the principal fishing method in marine fishing. Fishing vessels vary, depending on equipment used, and include very modern to old-fashioned ships. The Russian fish processing – is both onshore and onboard, with 70% of the total fish processing capacity on board of vessels [32].
A factory ship is an ocean going fish processing vessel (Figure 4). It normally has facilities for processing and freezing of caught fish.

Figure 4. Fishing trawler

Processing of fish on board of trawler factories

Processing operations onboard the trawler fish factory are similar to those in onshore fish processing plants, however may have some adaptations due to narrow factory premises.

Fish processing on board are executed by automated machines and manually.

Firstly, fish are pretreated, and afterwards transferred to a processing plant. Departments in processing plants at trawler factory are often only partly separated due to narrow production spaces on board. In the slaughtery section catches are degutted, washed, and often deheaded (depends on a final product). Nowadays slaughtering of fish is performed mainly automatically but in some old-fashioned vessels slaughtering may be done manually.

If filleting takes place, this is done by simple filleting machines or by manual filleting which is labor-intensive and largely depends on the skills of the workers.

After processing operations fillet/or degutted fish is frozen. Fish products are packed in boxes with ice and relocated into a freezer section. Many modern trawlers offer also wrapped in plastic whole degutted fish or fillet.

Work template (Russian North-West trawl fleet)

Workers engaged in fish processing on board of trawl vessels are normally offshore 4-6 months and have normally one of three 8-hours workshifts in 24 hours.

Health surveillance of employees in Norwegian salmon industry and Russian trawl fishing

Workers at salmon factories (Norway)

Salmon factories are associated with local occupational health services (OHS) for the employees. The main tasks of OHS are:

- preventive measures (advising, consultations)
- individual medical consultations
- vaccination
- treatment and follow-up.

Workers in trawl fishing (Russia)

Fishermen regularly undergo medical examination and receive health certificates, according to the national regulations. Medical examinations are implemented throughout a year. All workers are obliged to medical examinations once per year.

1.3 Characteristics of exposure in seafood industry

There is a great variation in processing procedures for the different types of seafood. Processing plants vary in the levels of technology, with some of the smaller workplaces relying to a great extent on manual handling of the seafood and larger companies using modern highly automated processes [33]. Despite the use of industrial technologies in workplaces in seafood industry, workers may still be exposed to a wide variety of factors. Many processes in the seafood industry involve extensive use of water, and the production areas are often characterized by a moist environment and high relative humidity. Wet aerosols generated from production machines or washing procedures are spread to the breathing zones of the workers. The aerosols may contain biological materials from the raw material itself or from microbiological organisms in the environment [34, 35]. The moist environment may facilitate the growth of mold and other microorganisms in certain areas. Dry particles may also be generated from some processes. Air jets used for shell removal in the shrimp industry, salt particles from salt spreading machines, and exhaust particles from forklift engines may be sources of dry aerosols. Water jets commonly used to rinse floors and equipment during ongoing production and cleaning procedures as well as water nozzles rinsing the fish along the production line, may lead to development of wet aerosols containing organic matter [2, 33].

Bioaerosols are defined as small droplets or particulate matter of microbial, animal or plant origin suspended in the air [2, 3]. Work at seafood industry may involve inhalation exposure to a number of bioaerosol components, depending on the processes performed and seafood tissues exposed to [33, 35]. Bioaerosols in seafood industry may comprise proteins, high molecular weight allergens, endotoxin, microorganisms etc.

The transport and the ultimate settling of bioaerosols are affected by its physical properties: size, density, and shape of droplets or particles, the environmental factors include magnitude of air currents, relative humidity and temperature, which determine the capacity to be airborne [2]. Bioaerosols generated from liquid suspensions undergo desiccation, whereas those generated as dusts or powders partially rehydrate.

In general, particles in bioaerosols are 0.3 to 100 μm in diameter; however, the respirable size fraction of < 10 μm is of primary concern [2]. Bioaerosols ranging in size up to 5.0 μm generally remain in the air, whereas larger particles tend to settle out of the air quite quickly due to gravitational forces.

A limited number of studies have been conducted to assess exposure to various bioaerosol components in seafood processing plants. Results of these studies are summarized in Table 1.

Table 1. Bioaerosols exposure characteristics in seafood industry.

Seafood industry	Protein levels (mg/m^3)	Allergen levels (µg/m^3)	Particulate concentration (mg/m^3)	Endotoxin levels EU/m^3	Reference
Bony fish					
Pollock	ND	ND	0.004	ND	[36]
Pilchard	LOD-0.006	0.01-0.89	LOD-2,95	49.0 (GM)	[35]
Cod	ND	3.80-5.10	ND	0.9-59.0	[21]
Salmon	ND	0.10-1,00	0.04-3,57	ND	[9]
	ND	0.4-1.60	ND	0.9-36.0	[21]
	ND	0.02-0.186	ND	1.6-7.1 (GM)	[23]
Herring	ND	0.30-1.90	ND	0.5-1,350	[21]
Anchovy (fishmeal)	LOD-0.004	0.07-75,74	LOD-11,29	136.0 (GM)	[35]
Crustaceans					
Crab	0.001-6,40	0.001-5,06	0.001-0.68	32.6 (GM)	[36, 37]
	ND	0.079-21,09	ND	ND	[22]
Prawn	ND	ND	0.10-3,30	ND	[10]
Shrimp	ND	1.50-6.26	ND	0.2-100.0	[21]
Rock lobster	LOD-0.002	ND	LOD-0.66	ND	[35]
Scampi	ND	0.047-1,04	ND	ND	[38]

ND- not done, LOD- limit of detection, GM-geometric mean. Modified and adapted from Jeebhay M. [39]

These studies present a wide range of allergen, protein, endotoxin levels as well as particulate concentrations measured in processing facilities from different types of seafood industry. Following processes were revealed to cause bioaerosol production: degutting, deheading, filleting of fish; washing and scrubbing of shellfish; cleaning and brushing of crabs/lobsters; cleaning of the processing line with water hoses [33].

Levels of airborne agents is often higher in seafood processing facilities with more advanced technologies, compared to older factories using much manual technology, because new machine processing often produce more aerosols.

It has been shown that allergen levels may reach higher levels on the processing plants on boards of vessels than in land-based processing facilities, due to narrow facilities and lack of ventilation systems [22, 37]. Processes that generate dry aerosols such as prawn blowing operations using compressed air and fishmeal loading and bagging appear to generate higher concentrations of particulate than wet processes.

Comparisons between studies are difficult because exposure levels besides the type of fish processed are also likely to be attributable to factors such as factory size, handling procedures of fish, ventilation, amount of fish processed, and equipment used. Sampling and laboratory methods for bioaerosol exposure assessment in the studies could be also different.

Besides seafood itself, processing workers may be exposed to non-seafood contaminants and factors encountered in fish processing.

Exposure to Anisakis simplex

Parasites such as *Anisakis simplex* have been often found in seafood [40, 41] and cause exposure either through inhalation or direct contact with infested fish [42-45]. As consequence, a potential occupational risk was suggested in fishermen and workers assigned to fish processing [46].

Exposure to disinfectants

Seafood workers may also be exposed to disinfectants, which are used during cleaning procedures in production areas. Chlorine compounds, quaternary ammonium compounds and peroxygen compounds are commonly used disinfecting agents [47], often in the form of foams that are sprayed over the total production area prior to washing/rinsing by high pressure water. The workers themselves may be involved in cleaning procedures and may, therefore, be directly exposed to disinfectants. In big seafood factories the cleaning process is normally done by special cleaning personnel using respiratory protective equipment, but seafood processing workers may still be exposed to remains of the chemical agents in workplace air.

Exposure to low ambient temperature

The ambient temperatures in the processing facilities are often low due to open gates to unloading and loading areas, cold surfaces, water spills, and insufficient heating systems. The seafood itself is held at a low temperature to ensure high quality of the products, and causes additional cold exposure.

The production areas of onshore and offshore seafood processing facilities are normally above 0, but often below 10 degrees Celsius. While onshore workers are working in a relatively stable thermal environment [48], offshore workers are more exposed to thermal variations with influence from harsh outdoor climate through open hatchways during loading/unloading activities and occasional outdoor work tasks. Therefore, thermal conditions are expected to offer greater challenges for workers involved in processing of seafood on board of vessels than in land-based facilities.

Physical strain

The activity levels among workers may vary considerably from sitting or standing with only minimal hand/arm movements to high activity with use of large muscle groups. Physical strain may also increase uptake of bioaerosols and contribute to more pronounced exposure to cold due to increased pulmonary ventilation.

1.4 Effects from the respiratory system associated with processing of seafood

It has been suggested that aerosolization of the seafood during manual or automated processing and inhalation of airborne particles by workers are associated with effects from the respiratory system [5-23, 49].

Respiratory symptoms

Workers involved in seafood processing may experience a wide range of general and work-related respiratory symptoms. A questionnaire has been the main tool in the studies assessing a presence of respiratory symptoms among seafood workers. Symptoms from upper and lower airways have been reported by seafood workers. Prevalence of the symptoms was shown to be relatively high irrespective of types of seafood processed. Some studies relate presence of symptoms to results from immunologic tests, which allows making a suggestion on possible mechanisms of symptoms development. Higher percentage of allergic respiratory symptoms was found among seafood workers involved in crustaceans (crab and shrimp) processing compared to workers processing bony fish [34, 50]. Table 2 summarizes the results of several published studies on seafood processing workers.

Rhinitis and conjunctivitis

Symptoms of rhinitis and conjunctivitis are often reported by seafood processing workers (Table 2). Nasal symptoms might appear due to allergy or non-allergic irritation. It has been suggested that rhinitis and conjunctivitis are often associated and may precede the development of asthma symptoms [14, 51, 52], therefore can be regarded as useful early risk markers for occupational asthma among workers exposed to seafood-derived agents. Exposure to cold was also revealed to trigger nasal symptoms, and it has been also shown that the most common short- term respiratory effects of cold are rhinorrhea, nasal congestion, and rhinoconjunctivitis [53, 54].

Occupational asthma

Occupational asthma is the most frequent work-related respiratory disease reported in the seafood industry, with the prevalence varying from 2 to 36% [50]. Symptoms of asthma may develop after only few weeks or after several years, being normally worse at work, improving on weekends or holidays [51]. Improvement of occupational asthma symptoms after removal from exposure is, on average, 2 years, although part of affected individuals continue to have signs of asthma even longer [55, 56].

Occupational COPD

Symptoms suggestive of COPD have been less reported and were often associated with high percentage of smokers among seafood workers. Prevalence of self-reported doctor-diagnosed COPD in our previous study was shown to range up to 4.3% among workers processing different types of seafood (non-smokers), while COPD-like symptoms among these workers were shown to range up to 13.7% [21]. Results from other study revealed 3 % of workers involved in fish processing with symptoms suggestive of chronic bronchitis [20].

Table 2. Studies and case reports on processing workers in seafood industry

Type of seafood processed	**Number of study subjects**	**Symptoms experienced by workers**	**Prevalence of occupational asthma (%)**	**Skin prick test positive (%)**	**Other immunological tests (%)**	**Reference**
Trout	8	Rhino-conjunctivitis	5 of 8 workers	NA	100% had positive RAST against contaminated water contained 1 microgram endotoxin/ml	[5]
Pilchard, anchovy	594	Work-related nasal symptoms, asthma symptoms	1.8%	7% to fish species	Atopy prevalence 36% Specific IgE to anchovy (5/15), to pilchard (4/15)	[20]
Salmon	291	Rhino-conjunctivitis	8.2%	NA	Specific IgE against salmon 9%	[9]
Salmon	211 total number, 50 participated in clin.tests	General and work-related respiratory symptoms	NA	NA	Total IgE≥100 kU/L in 19% of workers, 0% had specific IgE to salmon, 6.5% had specific IgE to shrimp	[21]
Salmon	26 and three index cases	Respiratory symptoms at work	10.3	NA	10.3% IgE to salmon, 10 of 26 were atopic	[23]
Cod, sardines, shrimp, spiny lobster, crabs, salmon, mussels, and trout	64	Rhino-conjunctivitis, conjunctivitis, work-related asthma symptoms	NA	To shrimp 12.5%, to lobster 10.9%, to mussels 7.8%, to crab 3.1%, to cod 3.1%, to trout 1.6%	Specific IgE to same species as SPT	[57]
White fish (haddock, Pollock, cod)	387 total number, 115 participated in clin.tests	Work-related respiratory symptoms	NA	NA	Total IgE≥100 kU/L in 24.8%, Specific IgE to cod 2.7%, to shrimp 8.2%, to herring 1.4%	[21]

Shrimp	162 total number, 60 participated in clin.tests	General and work-related respiratory symptoms	NA	NA	Total IgE≥100 kU/L in 13.6%, specific IgE to shrimp in 20.3%	[21]
Shrimp	1	Urticaria, anaphylaxis	NA	To herring, shrimp	Specific IgE to herring, sardine, shrimp, swordfish	[58]
King crab	825	NA	1.5 % (incid ence)	NA	NA	[17]
Snow crab	303	Rhino-conjunctivitis, conjunctivitis, skin rash	NA	NA	NA	[59]
Snow Crab	215	Rhino-conjunctivitis, conjunctivitis, rash	15.8%	To crab 30/164 tested (18.3%)	Specific IgE to crab 28/196 tested (14.3%)	[60]
Snow crab and atlantic shrimp	20	Symptoms suggestive of asthma, work-related symptoms of skin rash, rhinitis, and/or conjunctivitis	Probable OA 11%	40% to snow crab, 20% to shrimp	21% IgE to snow crab, 10% had elevated total IgE	[6]
Queen scallop	1	Urticaria	NA	NA	Specific IgE to queen scallop	[61]
Octopus	1	Rhino-conjunctivitis, conjunctivitis	NA	To octopus, squid, shrimp	Specific IgE to octopus, squid, shrimp	[62]
Prawn	135	Respiratory symptoms, dermatitis	NA	NA	To prawn 16/52 tested (64%)	[10]

NA- not available. Adopted and modified from Jebbhay M. [39]

Pathophysiological mechanisms related to respiratory effects in seafood workers

Individual reactions associated with seafood processing could be due to allergic or non-allergic reactions to seafood agents and contaminants as well as to other non-seafood factors [63]. The allergic reactions are commonly mediated by specific IgE antibodies in response to a seafood allergen or associated agent present in the seafood. Many asthma cases in seafood industry were shown to have specific sensitization to offending allergen, which suggest that asthmatic reactions are predominantly IgE-mediated. The prevalence of IgE sensitization among asthmatic workers exposed to crustaceans were shown to be very high and varied up to 60% and less among asthmatic workers exposed to bony fish (up to 23%) [50].

It has also been shown that seafood-processing workers may exhibit respiratory symptoms and have impaired lung function without specific sensitization [21, 23]. Respiratory symptoms in these workers may be induced by agents that do not act as allergens.

Allergic mechanisms

Seafood contains a wide variety of proteins [63-65], and some of them are allergens, which may trigger acquired immune response and cause typical IgE-mediated symptoms in individuals who have been sensitized through inhalation in occupational settings after a "latency period". The underlying immune mechanisms of IgE-mediated symptoms correspond to type I Allergy; antigen recognition and processing by antigen-presenting cells (APC), induction of the Th2 immune response resulting in the production of antigen-specific IgE antibodies, and finally release and generation of bronchospastic and inflammatory mediators by mast and other cells [66].

Besides seafood allergens, occupational exposure to parasites *Anisakis simplex* has been implicated in causing respiratory symptoms and allergic asthma in seafood processing workers through an allergic mechanisms [41, 44, 67, 68].

Non-allergic mechanisms

The type of non-allergic response is often called "irritant-induced" airway response. The common features of this response are shown to be an activation of innate immune mechanisms rather than IgE-mediated activation of acquired immunity. In contrast to allergic airway response, previously unexposed subjects can develop symptoms and (reversible) airflow obstruction without any prior sensitisation or latency period. The underlying inflammation is one in which neutrophils dominate [69]. It has been suggested that the initial irritant exposure may cause epithelial damage. This damage can lead to release of relaxing factors, along with non-specific macrophages and mast cell activation, which release proinflammatory cytokines (IL-1, IL-6, IL-8), tumour necrosis factor (TNF)-a, and the subsequent massive infiltration and activation of neutrophils in the lower and upper airways, resulting in epithelial cell desquamation, smooth muscle cell hypertrophy and matrix degranulation [70, 71].

Less is known about agents, which may induce irritative type of respiratory response in seafood workers compared to agents, which trigger allergic respiratory response.

It has been suggested that exposure to agents from bioaerosols may itrigger airways symptoms through non-allergic reactions [72-74]. Studies performed on occupational groups exposed to organic dust have showed that endotoxin may induce nasal neutrophil influx and proinflammatory cytokine production [75, 76].

Besides aerosolization of the seafood, other factors may play a role of irritative agents. It has been shown that airway effects of exposure to cold may include bronchoconstriction, secretions, and decreased mucociliary clearance [77, 78]. Cold may also trigger cough and asthmatic attacks. Results of our previous study revealed that the thermal climate may be a significant contributing factor to the increased frequency of airway symptoms among seafood industry workers [48].

The use of disinfection chemicals has been linked to irritative airway effects. They can provoke acute and transient narrowing of the airways, and may do so through a variety of non-immunological mechanisms such as mast cell mediator release, and interaction with sensory nerve endings in bronchial epithelium or receptors in smooth muscle. A dose-response relation was found between acute irritant symptoms (eye, nasal, and throat) and exposure levels to chloramines and aldehydes [79]. It has been also shown that use of disinfectants is an important aetiological factor of chronic respiratory health [80], as well as atopic sensitization and symptoms consistent with asthma [81]. Irritation power of disinfectants was confirmed in a toxicological study [82].

Host factors

Host factors such as atopy and smoking may play a role in the development of respiratory reactions in seafood workers [49]. Atopy is a predisposing factor for respiratory symptoms and asthma caused by high molecular weight agents and defined as the tendency to produce

specific IgE antibodies to environmental and occupational allergens [83-86]. However, the probability of developing of asthma in non-atopic subjects is approximately 30% [87, 88].
Smoking has been shown to increase the risk of developing respiratory symptoms and asthma due to exposure to HMW agents [59] as well as LMW agents [89, 90].

Exposure--response relationships

Several studies on seafood workers have indicated exposure–response relationships between the levels of exposure to biological agents and the development of asthma, respiratory symptoms and sensitization. It has been demonstrated in one study from South Africa that workers who have been exposed to pilchard-antigen concentrations above 30 ng/m^3 have a two-fold increased risk of work-related asthma symptoms [20]. Douglas et al. reported that changing the ventilation system over the gutting machines in a salmon processing facility reduced airborne aerosol levels from a mean of 3.14 mg/m^3 to less than 0.01 mg/m^3. Since then, no new cases of occupational asthma occurred over 24 months versus an initial incidence of 8% over an 18-month period [9]. Gaddie et al. reported that workers in a prawn processing plant experienced relief of symptoms including asthma symptoms when compressed air jets used to extrude prawns from their carapace were replaced by cold water jets, leading to a reduction in airborne particles. The wet weight of material filtered in the air decreased from 1.8–3.3 mg/m^3 to 0.1–0.3 mg/m^3 [10]. It has been shown that cumulative exposure to snow crab allergens is positively associated with occupational asthma and allergy in a dose–response manner [60].
But overall, studies of exposure-response-relationships in seafood workers are still very sparse.

2. GAPS IN KNOWLEDGE

A number of epidemiological studies have been performed to evaluate respiratory health outcomes among seafood industry worker populations. However, very few studies included reference populations without occupational exposure to seafood. Most of the existing reports are on land-based fish processing factories. Data from vessels, with or without onboard seafood processing facilities, are very limited. Despite the risky nature of the occupation of workers engaged in fish processing on board of factory vessels, very little research has been conducted on their health. Unusual working patterns, involving long periods of time at sea and only short periods of time on shore make seafarers difficult to contact and thus a challenging population to recruit for research. There is a need for detailed epidemiological studies of workers involved in fish processing on board of vessels.

The technology level varies greatly in different sectors of seafood industry as well as between developing countries and industrialized countries. How new technology affects bioaerosol levels and other work environmental factors, should be subject to researchers attention. The use of aquaculture to breed seafood resources for exploitation is increasing and leads to gross changes in worker conditions compared to traditional open water fishing. Research on occupational health in workplaces related to aquaculture is sparse.

More studies aiming to characterize the bioactive constituents of the bioaerosols in different work environments are needed. Conditions favouring the liberation of allergens, enzymes, microbes, toxins, etc, to the air should be explored in relation to processes and work tasks. The effects and mechanisms of bioactive agents, whether present as single exposures or in combinations, should be investigated. Increasing the knowledge of bioaerosol components will form the basis for detailed dose-response studies aimed to assess the relative contribution of the various bioaerosol components to respiratory effects.

The data so far points to the existence of both atopic and non-atopic asthma among seafood industry workers. Still little is known about the relative importance of allergic and non-allergic pathways in the respiratory response. The role of host factors on respiratory outcomes among seafood workers were covered to at a limited degree in the literature, however may be of importance in the development of the health outcomes. The linkage between working with seafood and short term respiratory effects is poorly described. To our knowledge studies exploring cross-shift and cross-week changes in respiratory outcomes among seafood workers have not been undertaken previously.

3. HYPOTHESIS AND AIMS OF THE STUDY

Based on the available literature, identified gaps in knowledge and the results of previous investigations performed by the staff of the Department of Occupational and Environmental Medicine, we hypothesized that workers involved in seafood processing at Norwegian salmon factories and in the Russian North-West trawl fleet, exhibit increased prevalence of respiratory symptoms and decreased lung function values compared to control populations not exposed to seafood at work. We also hypothesized that an exposure-response relationship existed between bioactive agents present in the bioaerosols and respiratory health outcomes. Finally, we expected to find variations in work-environmental factors between the two seafood worker populations that could be reflected in differences of respiratory health outcomes.

Accordingly the aim of the present study was to gain deeper knowledge of respiratory symptoms and lung function in relation to bioaerosol exposure, other work environmental and host-associated factors in the two populations of seafood processing workers.
To achieve this goal we set out to:

- characterize respiratory health status of onshore Norwegian salmon-processing workers and offshore Russian trawler fishermen by comparing self-reported respiratory symptoms and diagnoses, spirometric test results, FE_{NO} values and host-associated factors with the same parameters in control populations

- characterize personal bioaerosol exposure levels in salmon processing workers with respect to total proteins, allergens, and endotoxin; and find possible determinants of bioaerosol exposure

- investigate the association between exposure to bioaerosols in salmon industry, respiratory symptoms and spirometric test results measured repeatedly during a workweek

- compare respiratory symptoms, spirometric test values, FE_{NO} levels, host-associated and work environmental factors between Norwegian salmon-processing workers and Russian trawler fishermen.

4. MATERIALS AND METHODS

4.1 Organization and design of the study

The present study was carried out on two seafood industry worker populations: Norwegian salmon workers and Russian trawler fishermen. There were two main reasons for including two ethnical populations:

1. A previous project conducted in 2001 by the researchers at the department of occupational medicine, University Hospital of Northern Norway (UNN) showed high prevalence of respiratory symptoms and decreased lung function among Norwegian seafood workers [21]. The referred study involved workers from salmon slaughtery departments in addition to white fish industry, shrimp industry and herring industry. The study had important limitations, lacking a linkage between exposure data and health outcome data, impeding proper exposure-response considerations. Thus, to further explore respiratory heath outcomes and associated risk factors in a rapid growing and economical important industry, we chose to concentrate on salmon industry plants (Norway) in the first part of the present study.

2. Additional funding allowed us to further extend our research and include Russian fishermen. Since 1991 there has been a continuous ongoing collaboration between University of Tromsø, University Hospital of North Norway and Northern State Medical University and local hospitals in Arkhangelsk, Russia. In 2006 the project leaders of the present project visited Central Seamen Polyclinic (CSP) that serves as the base for annual medical examinations of merchant and trawler seamen. During the discussion with physicians performing examinations it became clear that there are observations of increased respiratory symptoms in seafood processing workers on ships. Initial agreements to perform the study on the mentioned population were achieved during this visit and the Russian study was accordingly implemented in the overall research protocol. The choice of workers at fish factory ships was partly motivated by an expectation to find high exposure levels of bioaerosols in the confined fish factories aboard trawl vessels. We, thus, expected the trawler fishermen to be representatives of a high-exposure population, expressing exposure-dependent airway effects even clearer. However, strict legal regulations and logistic difficulties hindered

us in performing the originally planned exposure measurements under production aboard trawl vessels, and thus exposure-response analyses were not possible to include in this part of the study. The lack of international publications on Russian worker populations in general and in seafood industry in particular, motivated us to perform the presented study despite the described limitations.

The study of Norwegian salmon industry workers

Study design

The study was conducted in the period between November 2007 and April 2008 and was designed as cross-sectional study with repeated measurements performed over a workweek period.

Recruitment of the study subjects

1) Exposed study population

To find potential salmon factories the following main criteria were applied:

- number of employees above 50
- two main departments (slaughtery and fillet department)

The Register of Business Enterprises (Brønnøysundregistrene) was used to find salmon factories with the mentioned criteria, as well as communication with occupational health services (bedrifthelsetjenester). Initially there were 20 potential salmon factories found. Upon communication with management of the factories we discovered that 5 of 20 had less than 50 workers, and 3 lacked either slaughtery or filleting department. Of the remaining 12 factories, seven denied participation due to one of the pointed reasons: reorganization projects, reconstructions, or time pressure.

The project leaders visited the remaining 5 salmon factories in spring 2007. During these visits planning of the project as well as practical aspects of the study were discussed. At each of the factories a contact person was chosen, who was responsible for distribution of the information of the project, consent papers and general questionnaires among employees. Consent papers (Appendix A and B) and general questionnaires (Appendix F) were sent to the factories one month before the planned visit. Deadline for posting a consent paper and filling in the questionnaire and was two weeks. An excess of questionnaires were sent to the contact persons of the factories.

Due to the lack on information on how many workers were asked for the participation in the study by the contact persons at the factories, we were not able to calculate a response rate. Although information on precise number of workers involved in salmon processing at five factories (n=469) and number of general questionnaires filled out by workers (n=139) enabled us to calculate "participation" rate in the study (29.6%). Table 3 gives more detailed information on "participation" rate from each of five factories.

Table 3. Number of employees at five salmon factories and participation rate of the study

Factory	**Time visit**	**Total number of employees**	**Number of employees involved in salmon processing**	**Number of employees participated in the study***	**Participation rate† (%)**
Factory 1	27.10-01.11, 2007	91	53	18	34.0
Factory 2	17.11-22.11, 2007	115	100	32	32.0
Factory 3	1) 26.01-31.01, 2008 2) 05.04-10.04, 2008	215	169	37	21.9
Factory 4	08.03-13.03, 2008	125	115	31	27.0
Factory 5	04.01-9.01, 2008	76	59	21	35.6
Total	27.10.2007-10.04.2008	622	469	139	29.6

* Number of employees who signed a consent paper and filled out a general questionnaire
†calculates as number of employees participated in the study x 100/ number of employees involved in salmon processing.

Not all workers who agreed to answer a general questionnaire were enrolled in repeated health examinations and exposure measurements. This was due to limitations in the number of exposure measurements pumps or other technical equipment, as well as the time limitations for pre and post-shift health examinations.

The planned number of subjects chosen for health and exposure measurements was 12 at four factories, while 24 at the biggest factory (Factory 3), which was visited twice. Therefore, the total expected number of workers participated in repeated health/exposure measurements was 72. Some of the production workers were not able to participate in all of the repeated measurements because of production activity or absence from work. The number of subjects with complete repeated measurements data was 66, while the number of participants with incomplete data was 4 (number of repeated measurements =3). They were included in the analysis as well. Therefore, total number of subjects involved in the analysis of repeated measures health and exposure data was 70.

Besides these 70 subjects, a part of the salmon workers participated in physiological/laboratory tests only once (up to 19) , therefore were not included in the analysis of repeated measured data, but were involved in comparative analysis with controls (Paper I) and trawl workers (Paper IV).

2) Non-exposed study population

Employees at local municipalities were invited to participate in the study as a control population. Similarly to the salmon worker population, one month before our visits consent forms were sent (Appendix C and D) with general questionnaires (Appendix F) to a contact person at each municipality who distributed these to employees. The deadline was two weeks. Analogically, an excess of questionnaires were sent to the contacts. Lacking the data of how many employees actually were asked, we were not able to calculate an exact response rate among controls. Not all workers who answered the questionnaire agreed or had the possibility to leave work to participate in health examinations. The number of completed questionnaires sent to us was 214, while the number of subjects who participated in health examinations was 151.

Inclusion and exclusion criteria for exposed/non-exposed study populations

Contact persons from salmon factories and municipalities were asked to select participants according to the below described criteria with the best of their knowledge.

1) Salmon workers, the whole group

Inclusion criteria for study subjects were work in indoor fish-processing facilities at salmon factories more than 50% of work hours, age above 18 years and employment at salmon factory as a full time job.

Exclusion criteria were age below 18 years, work outside production area more than 50 %, work with wrapped salmon more than 50 %, work mainly outside at the salmon breeding facilities, work as forklift driver.

2) Salmon workers participating in repeated health and exposure measurements

The salmon workers, who participated in extended health and exposure assessments should work in the production area of the factory more than 80% of work shifts. 12 workers meeting these criteria were picked by our contact, where possible 6 of the workers should work mainly in the filleting part of the production area and 6 from the slaughtery part of the production area. The contact person was instructed to choose randomly among the workers who met these criteria and agreed to participate.

3) Non-exposed study population

Similarly to the exposed study group, the inclusion criteria for the Norwegian control group were age above 18 years and at least 80 % work employment. An exclusion criterion was previous work in fish industry.

Ethical considerations

We conducted the Norwegian part of the study with the approval of the Regional Committee for Medical Research Ethics in Northern Norway and the Norwegian Data Inspectorate.

Written informed consent was obtained from all participants of the study.

Through information given in consent papers the participants were informed that given answers would not be forwarded to their employers or any other persons besides the trusted project assistants.

The study of Russian trawler workers

Study design

The study was performed in December 2009 - January 2010 and designed as a cross-sectional study.

Recruitment of the study subjects (exposed/non-exposed study populations)

During the initial visit of the project leaders to CSP, the possible ways to recruit the study subjects were discussed. Since seamen are a difficult group to get into contact with, the decision was taken to link the project-specific health examinations to routine medical health examinations, which are performed throughout the year at CSP. As the highest frequency of seamen examinations at CSP were in wintertime, the study was conducted in the winter months.

Participants were invited to take part in the study immediately after regular medical health examinations at CSP. The consent papers with the information about the project (Appendix E) were presented in a paper form in the hall where employees were waiting for their visit and issuing of health certificate. In order to minimize possible selection bias, participation was confirmed by participants after the issue of health certificate. Those workers, who were interested in participation, signed a consent form, filled out the questionnaire (Appendix G) and were invited to a separate examination room where lung function test and measurements of FE_{NO} were performed.

Medical check-ups at CSP are given to two main groups of employees: merchant and trawl fleet workers. We chose the merchant seafarers as *non-exposed* controls to the trawl fleet workers who comprised our *exposed* study group, involved in fish processing on board of factory trawlers catching various fish species (mainly in the Barents Sea). The total number of participants was a compromise between the desire of large and representative study and control groups and the practical and economical limitations due to the fact that the researcher had to stay in Archangelsk during the data-gathering phase.

Total number of workers visiting CSP during period December 2009 - January 2010 was 247, while the number of workers participated in our study was 245, resulting in a participation rate of 99%.

Inclusion and exclusion criteria for exposed/non-exposed study populations

Inclusion criteria were age above 18 years, employment in either trawler (engagement in on-board fish processing) for exposed study group or merchant fleet for non-exposed study group as a full time job. *Potential exclusion criteria* from the analytical part of the study were trawler workers not involved in onboard fish processing. An *exclusion criterion* for controls was previous work in trawler fishing industry.

Ethical considerations

The study was approved by the Regional Committee for Medical Research Ethics at Northern State Medical University, Arkhangelsk, Russia and by Regional Committee for Medical Research Ethics in Northern Norway, Tromsø.

Written informed consent was obtained from all participants of the study.

Through information given in consent papers the participants were informed that given answers would not be forwarded to any persons besides the trusted project assistants.

4.2 Methodological approach in Papers I, III and IV

In Papers I and III we aimed to compare respiratory health status between workers engaged in fish processing and control subjects without the exposure of interest. In the Norwegian part of the study exposed workers were presented by 139 full-time employees comprising the workforce at five large seafood factories processing Atlantic salmon, and non-exposed by 214 workers from municipal organizations, respectively. In the Russian part of the study the exposed study population comprised 127 trawler workers engaged in onboard fish processing, while 118 merchant seafarers composed a reference group.

In Paper IV we aimed to compare respiratory variables between 139 Norwegian salmon workers and 127 Russian trawler workers, and find putative factors associated with respiratory outcomes in two populations.

The methodological approach in Paper I, III and IV involved analysis of:

- general questionnaire data
- lung function parameters
- levels of nitric oxide concentrations in exhaled air (FE_{NO})

In the Norwegian part of the study we also performed blood tests for the measurements of total and specific IgE, and C-reactive protein.

The following diagram (Figure 5) shows the included methods in the Papers I, III and IV and key information on outcomes in each of the method.

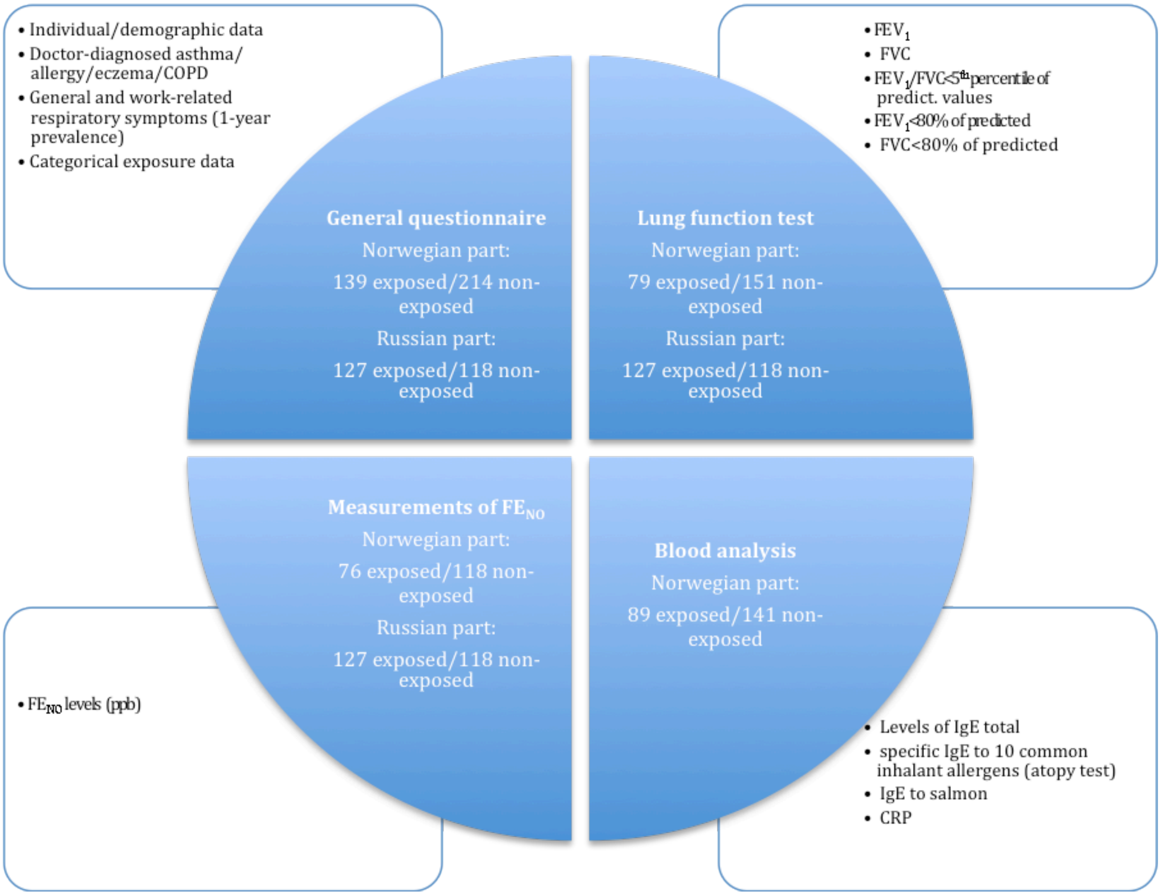

Figure 5. Diagram of the included methods in the Papers I, III and IV with key information on outcomes.

4.3 Methodological approach in Paper II

The aim of Paper II was to investigate the relationships between exposure to bioaerosol constituents, changes in FEV_1 and acute respiratory symptoms by repeated measures during a workweek among salmon workers. Of 139 study subjects 70 participated in repeated exposure and health measurements.

The following diagram (Figure 6) shows the included methods in Paper II and information on key outcomes in each of the method.

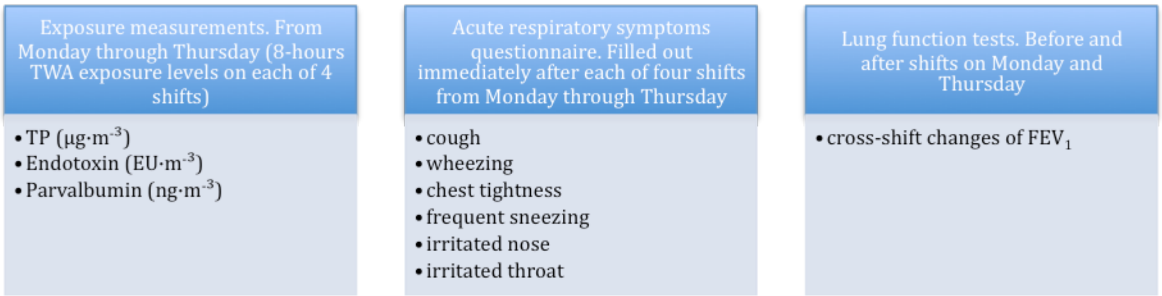

Figure 6. Diagram of the methods in the Paper II with key information on outcomes.

4.4 Methods used for data gathering

General questionnaire

The general questionnaire had two parts and was applied in Norwegian (Appendix F) and Russian (Appendix G) languages depending on the part of the study. The first part of the questionnaire included a modified version of a questionnaire developed by the British Medical Research Council [91] and comprised questions regarding general respiratory symptoms (wheezing, shortness of breath with wheezing, daily morning cough, daily morning phlegm, prolonged cough), personal and family history of respiratory and allergic diseases as well as demographic characteristics. The second part of the questionnaire asked for symptoms that the subjects attributed directly to their work (frequent sneezing, running nose, sore throat, dry cough, cough with phlegm, wheezing, shortness of breath, chest tightness.), and was derived from questionnaires previously used in Scandinavian studies on organic dust-related respiratory effects [92, 93].

All general and work-related respiratory symptoms were limited to the last 12 months. Asthma/allergy/eczema/COPD diagnoses were defined as adult-onset and doctor-diagnosed.

Categorical determinants of exposure

1) a dichotomy was used to identify *exposed* (salmon workers/trawler workers) and *non-exposed* (municipal workers/merchant seafarers). Category- exposed subjects was used as the basic of exposure surrogates in relevant seafood industry (salmon industry/trawl fishing)

2) in the Norwegian part of the study the general questionnaire allowed us to distinguish which *factory* (particular id number for each factory), and *department* (slaughtery/fillet departments) salmon workers work at. Question on *use of water hose* with two answer categories: never/seldom or often was also embraced in the questionnaire and considered as potential exposure determinant
3) in the Russian part of the study trawler workers were distinguished with four main *work tasks*: slaughtering, filleting, bagging, and freezing. Since trawler fishermen might be involved in the processing of different types of fish, we also included a list of relevant *fish species* (cod, haddock, flounder, herring, redfish, pollock, halibuts) in the questionnaire for this group of workers
4) *self-evaluated causes for work-related respiratory symptoms* were embraced in the second part of the questionnaire and had similar variants of answers in both, Russian and Norwegian questionnaires: 1) contact with fish; 2) contact with fish waste; 3) cold work environment; 4) contaminated indoor air; 5) use of disinfectants.

Acute respiratory symptom questionnaire

Acute symptoms were recorded by a short questionnaire (Appendix H), which was completed directly after shift each of the four days and asked for following respiratory symptoms: cough, wheezing, chest tightness, frequent sneezing, irritated nose, and irritated throat (Paper II). Similar questionnaire was previously used in other studies on organic dust exposed workers [93, 94].

Lung function measurements

Lung function testing was performed by means of a Vitalograph- MDI compact 1 (Vitalograph Ltd, Buckingham, England), and according to the American Thoracic Society (ATS) guidance [95]. Tests were conducted with the subjects seated, without nose clips. The highest values of FVC (L), FEV_1 (L/sec) and FEV_1/FVC (%) were retained for the analysis. Age/height/weight were recorded in order to calculate the percentage of the predicted values.

Calculations of predicted values in the Russian part of the study were based on equations proposed by Castellsague et al [96]. In the Norwegian part of the study we applied calculations of predicted values which were proposed by Langhammer specially for Norwegian adult population [97].

Reduced lung function was characterized as FEV_1 and FVC less than 80 % of predicted values. The practice of using 0.70 as the lower limit of the FEV_1/FVC ratio has been questioned in recent years, as it has been shown that the use of this fixed ratio underestimates airflow obstruction in 20-49 year-old individuals and overestimate it in the elderly [98, 99]. The analysis was therefore performed using FEV_1/FVC below the 5th percentile of the predicted value as the lower limit for FEV_1/FVC (LLN FEV_1/FVC) [100, 101].

In the Norwegian part of the study lung function tests were performed four times in salmon workers: before and after shift on Mondays and Thursdays. The percentage difference (cross-shift FEV_1) on Monday and Thursday work shifts was retained for analysis in Paper II (regression analysis) and was calculated as pre-shift minus post-shift, divided by pre-shift FEV_1, multiplied by 100.
To compare lung function values with reference population (Paper I) and with trawler workers (Paper IV) who underwent lung function test once, Thursday after shift lung function test results were chosen in salmon workers.
In order to compare lung function values between salmon workers and trawler fishermen in Paper IV, equations for predicted values proposed by Castellsague et al for European origin populations were applied in the analysis in order to make lung function parameters comparable between two worker populations.

Fractional exhaled nitric oxide (FE_{NO}) measurements

FE_{NO} was measured by chemoluminescence using an nitric oxide monitor (NIOX; Aerocrine AB, Solna, Sweden), according to the ATS guidelines [102] and expressed in parts per billion (ppb). Any exhalation not meeting ATS requirements was rejected by the NIOX system. The test was taken once in all study subjects.

Blood tests in participants of the Norwegian part of the study

Blood samples for determination of total and specific IgE to ten common inhalant allergens and to salmon (ImmunoCAP Systems, Phadia AB, Uppsala, Sweden) as well as for the measurements of C-reactive protein (Roche Diagnostics, Indianapolis) were collected by venipuncture into Vacutainer serum separation tubes. Analyses were performed at the University Hospital North Norway, Tromsø.

Personal exposure measurements

Levels of airborne TP, endotoxin and salmon parvalbumin were measured during four workshifts from Monday to Thursday (n=276) by means of personal portable air samplings pumps, which were placed into a backpack. Pumps were connected to filters in the breathing zones of the workers (Figure 7). Airflow through the filters for measurements of TP and parvalbumin was 2 L/min and for endotoxin was 2.5 L/min. Sampling time was equal to the duration of a workshift (8 hours), therefore exposure levels were presented as 8-hours time-weighted averages (TWA). The sampling period included lunch/breaks, through which the participants kept their backpack with the sampling pumps on, in the wardrobe room.

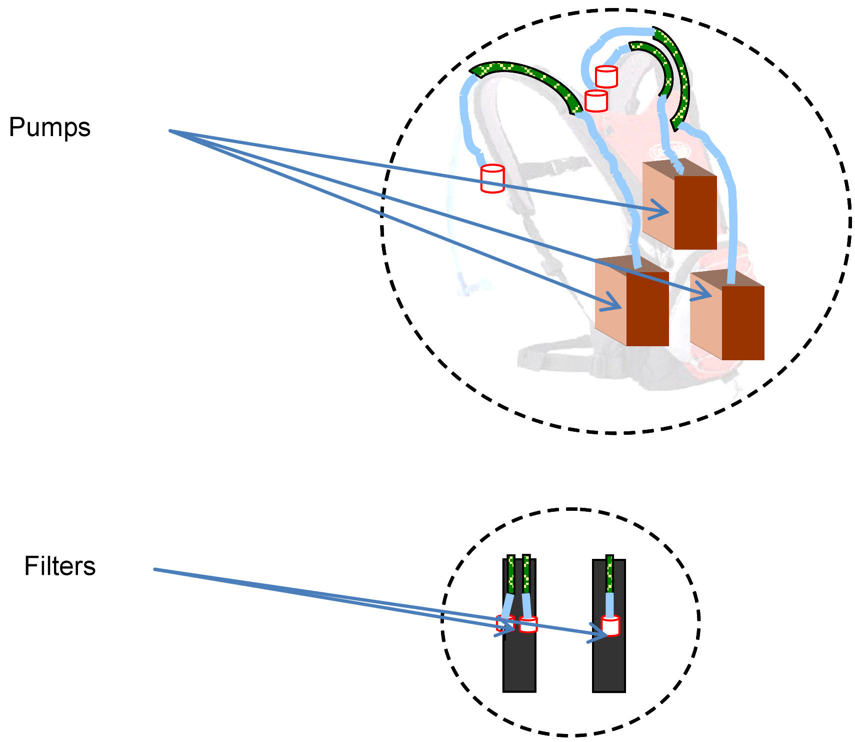

Figure 7. Method for sampling of airborne TP, endotoxin and parvalbumin. Backpack with pumps connected to filters. Filters were attached to braces of backpack.

Analysis of bioaerosol constituents

a) Total protein (TP)

Polytetrafluoroethylene (PTFE /teflon) filters on polypropylene support (37 mm, 1.0 µm SKC Ltd. UK) and cellulose support pad were used for collections of airborne TP. After sampling the filters were kept at 4 ° C for up to four days and then frozen at – 20° C until extraction. The proteins were extracted and then sonicated. The eluates were transferred to clean tubes and frozen at – 20°C until analyses. Bradford method for protein quantification was applied [103]. Analysis was performed at the University of Tromsø, Norway.

b) Endotoxin

Samples for determination of endotoxin were collected on glass fiber filters (Whatman GF/A, Maidstone, USA) with PAS6 cassettes (Personal Air Sampler with 6 mm inlet). The samples were stored at 4°C and analyzed by a quantitative kinetic chromogenic Limulus Amoebocyte Lysate assay (LAL) [104] at the Norwegian National Institute of Occupational Health (NIOH).

c) Salmon parvalbumin

After sampling the filters (PTFE filters on polypropylene support with cellulose support pads) were stored at -20° C until extraction. Allergens were extracted from the filters and the eluates were aliquoted and kept at –20° C until analysis [23, 105]. ELISA was developed by preparation of allergen, immunisation of rabbits and purification of antibodies [106]. Analysis was carried out at the Karolinska Institute, Stockholm, Sweden by our cooperators.

4.5 Data processing and statistical analysis

Separate datasets were constructed in SPSS software package (version 20.0 for Windows, Chicago, IL, USA) to analyse exposure and health data from participants in the Norwegian part of the study (Papers I) and in the Russian part (Paper III). Finally, datasets were merged into one dataset, which contains variables of interest on 266 seafood processing workers (139 salmon and 127 trawler workers) in order to perform comparative analysis (Paper IV).

The criterion for normal distribution was bell-shaped distribution of the data obtained through an informal graphical approach to testing normality - histogram of the sample data and also by application of Kolmogorov-Smirnov and Shapiro-Wilk tests [107]. Normally distributed variables were presented as means (standard deviation); non-normally as geometric means (range), categorical variables as numbers (percent). Single variable analyses were performed with independent-samples t-test for normal distributed data, Mann-Whitney U-test for non-normal distributed data (FE_{NO}, IgE total, and C- reactive protein levels), Pearson Chi-square test, and Fisher exact test for categorical data.

Data analysis in Papers I and III

Respiratory symptoms reported by study subjects in the present articles might be influenced by several factors (age, gender, smoking, etc.) which were different between exposed and non-exposed study populations, consequently, a multiple logistic regression analyses adjusted for potential confounders were chosen in order to estimate odds ratio of respiratory symptoms.

A multiple linear regression was used for analysis of spirometric parameters (continuous scale).

Multiple logistic regression analysis was employed to test the difference between exposed and control populations in terms of reduced lung function (FEV_1 and FVC less than 80% of predicted, and FEV_1/FVC below the 5^{th} percentile of the predicted values) treated as dichotomous variables.

A multiple logistic regression analysis was also applied to test interaction between exposure (characterized by being a salmon-processing worker) and smoking on work-related respiratory symptoms, smoking was categorized as ever-smokers (current and former smokers) and never-smokers (Paper I).

Simple regression analysis was applied for analysis of FE_{NO} levels associated with age/smoking/gender/atopy/asthma.

Data analysis in Paper II

Paper II presents analysis of exposure and respiratory variables measured repeatedly during a workweek.

Exposure data (levels of parvalbumin, endotoxin, and total protein) were not normally distributed, therefore they were log-transformed to normalize the distributions, and presented as geometric mean (range). Pearson's correlation coefficient was applied in order to analyse correlations between continuous log-transformed exposure variables. Univariate analysis by application of one-way ANOVA/t-test was performed to test the difference in exposure levels (log-transformed) between workdays and categorical exposure variables (*factory/department/use of water hose)*.
Cross-shift change in FEV_1 on Monday and Thursday was presented as percentage change from pre-shift measurements. Paired t-test was applied to test cross-shift and cross-week differences in FEV_1. Cochran's Q test was used to test differences in day-frequency of acute respiratory symptoms during a week.

To explore exposure-response relationships two statistical procedures were performed:

1) GEE (Generalized estimated equations) modelling of cross-week exposure and respiratory outcomes data. GEE allow the simultaneous examination of an association between a repeatedly measured responses within the subject while taking the intra-subject correlation into account [108-111]. In case of acute symptoms during a workweek as dependent variable, adjustment for age/gender/asthma/smoking (pack-years) was performed; in case of Δ FEV_1 (L) during a workweek as dependent variable, additional adjustment for height and baseline FEV_1 was done. Interaction terms of the exposure variables and time (days) were included in the GEE models in order to examine whether the effect of exposure on a respiratory outcome changed over studied period of one workweek. Categorical exposure variables (*factory/department/use of water hose)* were included in the exposure-response models on the basis of a significance level of $P<0.1$ in univariate analysis (t-tests and one-way ANOVA). Following parameters of the models were applied: exchangeable working correlation matrix, log link function with binominal distribution (dependent variables- symptoms) and identity link function with normal distribution (dependent variable-Δ FEV_1(L))

2) Multiple linear (cross-shift change of FEV_1(%)) and logistic regression (acute symptoms) analyses using individual day-to-day exposure and respiratory variables data was applied. Adjustment for age/gender/asthma/smoking (pack-years) (acute symptoms during a workshift - dependent variable), as well as height (cross-shift change of FEV_1 (%) – dependent variable) was made.

Data analysis in Paper IV

Internal statistical comparisons of demographic characteristics between men and women among salmon-processing workers (age, smoking habits, BMI, education, etc.) did not show significant differences. Therefore, to increase statistical power of the study, women and men from the Norwegian study population were included in the comparative analyses of respiratory variables with Russian trawler workers (presented only by males).

Parameters of lung functions between Russian and Norwegian seafood workers were analyzed by means of multiple linear regression analysis. In order to estimate Odds ratio (95% confidence interval) of respiratory symptoms between the two studied groups, multiple logistic regression was applied. Adjustment for age and smoking was made in both analyses. Multiple logistic regression was also applied to analyse respiratory symptoms in relation to length of employment with adjustment for smoking (analysis among trawler fishermen), as well as gender (analysis among salmon workers).

To analyze associations between FE_{NO} levels, age and height, Spearman correlation analysis was performed. All statistical analyses of FE_{NO} levels were performed only on males.

5. SUMMARY OF RESULTS

5.1 Respiratory impairment in Norwegian salmon industry workers: a cross-sectional study (Paper I)

Results of Paper I showed that Norwegian salmon workers experienced respiratory symptoms more often compared to the control population. Prevalence of the general (not associated with work situation) and work-related respiratory symptoms ranged up to 36.7% for daily morning cough and up to 20.1% for work-related running nose among salmon workers, and up to 14% and 7.0% for the same symptoms among the controls, respectively. Adjusted for potential confounders, odds ratios (ORs) of work-related running nose, sore throat, wheezing, and shortness of breath were elevated in salmon workers, as were ORs of all general respiratory symptoms except for prolonged cough. Prevalence of asthma in salmon workers (7.2%) was not significantly different compared to controls (9.3%).

Positive interaction was found between smoking and being a salmon worker for work-related upper respiratory symptoms and shortness of breath.

Salmon workers had reduced spirometric test results relative to the control group. The fractional exhaled nitric oxide (FE_{NO}) levels were higher among controls compared to salmon workers, significant results were found for never-smoking and non-atopic males (geometric mean (GM)=16.5 in controls vs. GM=11.8 ppb in salmon workers), and among never-smoking and non-atopic females (GM=12.5 ppb in controls vs. GM=8.2 ppb in salmon workers).

Sensitization to salmon (IgE against salmon $\geq$ 0.35 kU/L) was found only in salmon-processing workers (2.2%) and in none from the control population. Neither total IgE nor CRP levels differed significantly between salmon workers and controls. By comparing the prevalence of atopy among asthmatic salmon workers and controls, we found controls with asthma to be more often atopic compared to asthmatic salmon workers.

5.2 Respiratory effects of bioaerosols: exposure-response study among salmon-processing workers (Paper II)

Frequency of acute respiratory symptoms experienced by salmon processing workers and registered directly after work shifts, ranged from 1.4% for wheezing to 28.6% for irritated nose. Univariate analysis showed that the frequency of acute respiratory symptoms and cross-shift decline of FEV_1 were more pronounced in the beginning of a workweek compared to the end of a workweek, while exposure levels were relatively stable. Personal exposure to airborne TP varied up to 12.6 $\mu g \cdot m^{-3}$, parvalbumin up to 358.2 $ng \cdot m^{-3}$, and endotoxin up to 29.0 $EU \cdot m^{-3}$. Univariate analysis of exposure levels showed that parvalbumin levels were significantly different between factories (n=5) and were higher in fillet departments (GM=11.70 $ng \cdot m^{-3}$) compared to slaughtery departments (GM=1.91 $ng \cdot m^{-3}$). Workers who reported *use of water hose* during salmon processing had significantly higher levels of all three bioaerosol components measured in the study.

Multiple linear and logistic regression analyses of day-to day exposure and health data revealed significant results only for Monday shifts, showing cough, chest tightness and cross-shift FEV_1 (%) associated with TP levels. GEE analysis of exposure and respiratory outcomes data measured over a week period explored a time trend of exposure-response combinations and showed decrease of respiratory response in the course of a week, borderline significance was found for TP levels and change of FEV_1 (L) over a week period. Stratification of the respiratory outcomes as well as exposure-response analysis by atopic status did not show significant difference.

5.3 An analysis of the respiratory health status among seafarers in the Russian trawler and merchant fleets (Paper III)

Paper III indicated that doctor-diagnosed asthma was reported by trawler workers (3.9%) but not by merchant seafarers. Subjects with asthma had high FE_{NO} levels (up to 108,0 ppb) and reported filleting of fish as the main work tasks and cod as the main fish species processed. Prevalence of general and work-related respiratory symptoms ranged up to 31.9% for daily morning cough and 30.3% for work-related running nose among trawler workers, and up to 12.7% and 28.8% for the same symptoms among the controls, respectively. Odds ratios of respiratory symptoms were often elevated in trawler workers compared to merchant seafarers, significant results were found for daily morning cough, daily morning phlegm, and prolonged cough as general respiratory symptoms. When comparing spirometric test results, trawler workers had overall lower values compared to merchant workers, significant results were found for absolute values of FVC and FEV_1 and for FVC and FEV_1 % of predicted, as well as for fixed spirometric declines (FVC and FEV_1 <80%).

Comparative analysis of work-related respiratory symptoms between trawler workers engaged in different work tasks showed that workers reporting filleting of fish as main work task, had increased odds ratio of work-related respiratory symptoms compared to workers with other tasks, significant results were found for running nose (OR=3.0), cough with phlegm (OR=6.6), and frequent sneezing (OR=3.4).

5.4 Respiratory symptoms, lung function and exhaled nitric oxide (FE_{NO}) in two types of fish processing workers: Russian trawler fishermen and Norwegian salmon industry workers (Paper IV)

Results of Paper IV showed differences in pattern of respiratory symptoms reported by workers engaged in onshore salmon processing and trawler workers involved in offshore processing of different species of fish on board of trawl vessels. Adjusted ORs of shortness of breath with wheezing and prolonged cough as general respiratory symptoms were elevated in salmon workers, while ORs of work-related running nose and dry cough were elevated in trawler workers. A general tendency was found in relation of work-related respiratory symptoms to length of employment in both worker populations, showing significant results for work-related frequent sneezing and running nose. Analysis of spirometric parameters did not show significant differences between the workers, while FE_{NO} levels were found to be significantly higher among never-smoking and asthmatic trawler workers (GM=17.2 and GM=28.1 ppb, respectively) compared to never-smoking and asthmatic salmon workers (GM=11.5 and GM=12.6 ppb, respectively). Both worker groups ranked "*cold work environment*", "*use of disinfectants*" and "*contaminated indoor air*" as first, second and third most frequent causes for work-related respiratory symptoms, respectively.

6. GENERAL DISCUSSION

6.1 Main findings

6.1.1 Respiratory impairment in two seafood worker populations

6.1.1.1 General and work-related respiratory symptoms

The finding of increased prevalence of respiratory symptoms in both groups of exposed workers as compared to their respective control groups (Paper I and III), was in agreement with the findings of previous studies on seafood processing workers [5-23], and strengthen the statement that workers occupied in this industry are at risk to develop respiratory symptoms.

Prevalence of morning cough, morning phlegm, prolonged cough in both exposed groups in our present study (up to 36.7% in salmon workers and up to 31.9% in trawler workers) was higher compared to prevalence of wheezing, shortness of breath with wheezing (up to 19.4 in salmon workers and up to 9.8% in trawler workers). The prevalence and the pattern of the symptoms seen in our present study is comparable with that found among white fish workers (up to 13.3% in non-smokers and up to 33.9% in smokers) and workers in salmon slaughteries (up to 15.2% in non-smokers and up to 43.4% in smokers) in our previous study [21].

Work-related symptoms from upper airways were shown to be dominantly reported by seafood workers compared to symptoms from lower airways [21, 23], which is in agreement with the findings in our study, showing prevalence of work-related respiratory symptoms from upper airways ranging from 10.7 to 20.1% in salmon workers and from 6.6 to 30.3% in trawler workers, and symptoms from lower airways from 4.3 to 8.6% in salmon workers and from 2.4 to 13.1% in trawler workers, respectively.

In the present study we examined 12-months prevalence of the symptoms, therefore we were not able to identify the time of symptom onset, whether the workers started to experience the respiratory symptoms after commencement of the employment, and whether the symptoms have been worsening in the course of their employment. Interestingly, the pattern of reported respiratory symptoms was similar in exposed seafood workers and non-exposed control populations from both parts of the study (Paper I and III). The most frequent symptom was daily morning cough as general respiratory symptom, and running nose as work-related respiratory symptom among seafood workers and controls. However, the fact that adjusted ORs of studied respiratory symptoms were elevated among the exposed study groups compared to the control groups, indicate that workplace-related factors appear to affect the development of respiratory symptoms among the studied seafood workers to a greater extend than among the controls.

Despite the fact that pattern of the symptoms was similar in both exposed study groups when comparing with the controls, comparative analysis performed in Paper IV showed that distribution of the symptoms was different in salmon workers and trawler fishermen. The results of the study showed that ORs of shortness of breath with wheezing and prolonged cough as general respiratory symptoms were elevated in salmon workers, while ORs of work-related running nose and dry cough were elevated in trawler workers. The pattern of symptoms in salmon workers may indicate obstructive characteristics of respiratory symptoms, suggesting that the salmon workers could have asthma- or COPD – like conditions, which was previously shown in other groups of seafood workers [20]. The pattern of symptoms seen in trawler workers is often associated with short-term exposure to cold [53, 54], but may also be associated with other exposures and diseases. Rhinorrea is known to be associated with and often precede asthma [51, 112, 113]. Cough is a very unspecific symptom and may be present in most airway diseases and reactions. The fact that trawler workers associate their cough with the work situation – indicating a short-lasting, exposure-dependent cough, and the fact that the cough is described as "dry cough", fits an asthma-like condition rather than COPD-like, since the latter is characterized by a long-lasting cough with phlegm. The pattern of symptoms seen in trawler workers is, thus, often associated with asthma, as well as a short –term exposure to cold.

The results of the present study showed that trawler workers involved in filleting of fish at onboard factories experienced work-related respiratory symptoms more often compared to workers with other work tasks (Paper III). The difference in reported respiratory symptom may reflect variability in exposure to bioaerosols depending on which seafood tissue is exposed to the air and many other factors attributed to specific processing procedures [33, 35, 39]. The finding allows us to suggest that workers' exposure during specific work tasks was not uniform. This is further discussed in 6.1.2.

6.1.1.2 Asthma prevalence

We found 7.2% of salmon workers (Paper I) and 3.9% of trawler fish-processing workers (Paper III) with reported doctor-diagnosed asthma. Asthma prevalence seen in the present study is in agreement with previously reported prevalence of asthma among workers involved in processing of bony fish (2-8%) [50]. A" healthy worker effect", however, could cause underestimation of the actual asthma prevalence in the study since subjects with existing asthma may avoid working in seafood industry, and workers with developed asthma are more likely to quit work earlier than those without [114, 115].

In the Russian part of the study only trawler fish-processing workers reported doctor-diagnosed asthma (Paper III). Asthma has been documented previously in very few reports on fishermen [116-120].

Interestingly, most asthmatic subjects among trawler workers in our study reported filleting of fish as the main work task during onboard fish processing. It has not been previously reported that asthma in processing workers is associated with filleting of fish, but asthma has been associated with work near machines which generated respirable aerosol containing fish proteins [9]. The finding of higher asthma prevalence as well as higher prevalence of work-related respiratory symptoms among workers engaged in filleting of fish may imply that filleting of fish is associated with impaired respiratory health in trawler workers in our study.

Among the listed species of fish in the general questionnaire, all asthmatic subjects reported cod. Cod has been shown as the most frequent reported cause of fish allergy, and main cod allergen Gad c1 was shown to induce immune-mediated allergy via digestive route [121]. Reports on respiratory allergy or asthma due to inhalation of cod allergens in occupational settings are lacking. It is reasonable to suggest that trawler workers in our study are not only exposed via the inhalation route, but also have a diet with high consumption of cod and is thus exposed also via the digestive route. The relative importance of either route of exposure in allergy and asthma among the trawler workers is not possible to deduce from the present results. We cannot also exclude the possibility that cod in the diet may modulate the response to cod allergens via inhalation, such it has been suggested previously [63].

Asthma in workers engaged in salmon processing has been reported previously [9, 23, 122]. Mechanisms of asthma development in seafood worker populations have been shown to function predominantly through allergic pathways and associated with atopy. The mechanisms involved in asthma development could not be directly defined in our study. However, stratification of asthma cases by atopic status indicated that asthmatic salmon workers were more often non-atopic (Paper I), which allowed us to suggest that asthma causes in the investigated group of salmon workers do not seem to be attributable to atopy. Similar results were found in the study of Douglas et al. where authors showed that atopy was not a predisposing factor for asthma in a salmon workers [9].

Relation of atopy to asthma is still debatable; about two thirds of all asthma cases are shown to be attributable to atopy [87, 88]. In our study ”the healthy worker effect” might, however, have excluded atopic asthmatic salmon workers from the industry and therefore from the study.

6.1.1.3 FE_{NO} levels

Measurements of FE_{NO} levels are rarely performed in occupational studies. Medline search did not reveal any publications showing FE_{NO} levels among seafood worker populations, therefore it was of interest for us to shed more light on this term among this occupational category and find possible occupational as well as individual factors associated with FE_{NO} levels in the studied group of seafood workers. As an "inflammometer", FE_{NO} has been shown to provide information regarding the nature of underlying airway inflammation [123], and has been also presented as a good surrogate marker for eosinophilic airway inflammation [124] and as a biomarker of "allergic asthma" phenotype rather than asthma itself [123, 125].

In the Norwegian part of the study FE_{NO} levels were higher among controls compared to salmon workers (Paper I). This could possibly be explained by the effect of age on FE_{NO} levels, since controls were older than salmon workers and we found a significant correlation between age and FE_{NO} levels. However, epidemiologic studies measuring FE_{NO} levels in healthy populations found controversial results concerning the effect of age on FE_{NO} levels [126-129]. Moreover, anthropometric characteristics such as height, have been shown to influence FE_{NO} levels [129], which might also, in addition to age, affect results of comparative analysis between salmon workers and controls in our study.
Levels were increased among atopic asthmatic subjects compared to non-atopic, which is in accordance with increased prevalence of atopy among asthmatic controls. However, the effect of gender might be confounding in this analysis (simple regression analysis), since it has been found that FE_{NO} levels are higher in males compared to females [130, 131], which was also seen in our study.

In the Russian part of the study significant differences in FE_{NO} levels (stratified by smoking and self-reported doctor-diagnosed allergy) between trawler fish processing workers and merchant seafarers were not found when asthmatic trawler workers were excluded from the analysis (Paper III). However, crude analysis of FE_{NO} levels without allergy stratification among non-smoking subjects showed higher FE_{NO} levels among trawler workers compared to merchant seafarers (unpublished observation).

Comparative analysis of FE_{NO} levels between asthmatic salmon workers and trawler workers showed higher levels among trawler workers (Paper IV), which could not be due to smoking or gender effects, since percentage of never/former/current smokers was similar in both seafood worker groups with asthma and analysis was run only among men.

Interestingly, we found significantly higher levels of FE_{NO} among asthmatic compared to non-asthmatics among trawler workers but did not find the same among salmon workers. Significantly higher FE_{NO} levels were also found among never-smoking trawler workers compared to salmon workers with the same smoking status. These findings could accordingly point to a greater influence of allergic mechanisms on respiratory outcomes among trawler workers and non-allergic mechanisms and less "allergic type" of asthma in salmon workers. However, age might be an influential factor in the analysis, since trawler workers were older than salmon workers and FE_{NO} levels are shown to be age-dependent in asthma [132].

Interpretation of measurement of FE_{NO} levels is rather difficult due to many interfering and modifying factors that may influence it, and little is known about interactions between factors. To our knowledge, measurements of FE_{NO} levels have not been performed in occupational group of seafood workers in any of the earlier studies. Therefore, many yet unknown factors and exposures might affect FE_{NO} levels measured in our study and further complicate the comparative analysis between exposed and non-exposed study populations, as well as between populations exposed to similar exposure-factor.

6.1.1.4 Spirometric test results

Comparative analyses of measured spirometric test results between exposed and non-exposed study subjects revealed decreased spirometric parameters among salmon and trawler workers compared to the reference populations, which is in accordance with increased prevalence of respiratory symptoms (Papers I and III) and, therefore, confirm compatibility between objective and subjective methods applied in the study.

FEV_1 and FVC % of predicted found in the seafood workers in our study (95,4% and 96.5% in salmon workers, and 96.1% and 95.3% in trawler workers, respectively (Paper IV)) were comparable with the findings from our previous study among seafood workers (91.9% and 96.6%, respectively) [21].

Comparing spirometric test results between salmon workers and trawler workers we found no statistically significant results (Paper IV). Also no difference was found between the two seafood worker populations when comparing fixed lung function declines (FEV_1 and FVC<80% of predicted). A pattern of FEV_1/FVC less than 5^{th} percentile of predicted is indicative of a COPD [100, 133], did not differ significantly between salmon workers (5.1%) and trawler workers (5.7%). This pattern is in line with high prevalence of symptoms from lower airways in both exposed populations in our study, however, did not reflect elevated ORs of shortness of breath with wheezing and prolonged cough, symptoms attributable to obstructive airway disease, among salmon workers, which indicate that lung function is impaired in both worker groups. Age and smoking status was taken into account in the respective statistical analysis, however, we could not exclude that duration of employment might affect the result of the analysis. Similar results were shown in earlier mentioned study on workers processing pilchard and anchovy, where authors found 5% of workers with evidence of airway obstruction, however, unlike to the criteria used in our study, authors applied FEV_1/FVC<70% [20].

6.1.1.5 Blood test results in salmon workers

Total IgE

The rationale for total IgE measurements in the study was to investigate the levels among exposed and non-exposed study population and compare these with levels for Norwegian adult normal population presented by Omenaas et al [134]. We found levels of total IgE (geometric mean) of 25.3 kU/L among salmon workers and of 21.5 kU/L among controls, which were revealed to be higher compared to levels proposed by Omenaas et al (13.8 -17.8 kU/L). In our previous work we also found seafood workers with high total IgE levels (median 27.9 kU/L), which we explained by combined effect of allergen aerosol and non-allergenic dust and gas exposure [21].

High levels of total IgE seen in the controls in our present study could be explained by higher prevalence of atopy in asthmatic subjects (Paper I). It has been also suggested that total IgE levels might be influenced by many factors, such as gender, smoking, and age [135], and interactions between these factors [134], which could also affect levels of total IgE seen in our present study.

IgE to salmon

The results revealed IgE to salmon only among salmon workers (2.2%), which allow us to suggest that salmon workers are more likely to be sensitized to salmon compared to controls.
The prevalence of specific sensitization was lower compared to Douglas et al study where authors found 8.6% of salmon workers with specific IgE to salmon [9]. However, the plant investigated by Douglas et al. was selected on basis of increased frequency of airway symptoms, whereas our study subjects were selected only on basis of exposure to salmon in the working environment of processing plants.

Similar results to ours were found in a Swedish study, where authors did not observe IgE against salmon in processing workers with newly developed respiratory symptoms [23].

“Sensitizing” properties of salmon allergen has been shown after digestion of salmon, and elevation in sensitizing properties during the last decades has been shown, which was explained by increase in salmon production and, thus consumption [136].

“Sensitizing” properties of the salmon allergen through inhalation route has not yet been fully studied, although have been suggested to cause respiratory impairment in several studies [9, 23, 122].

Two workers found with IgE to salmon in our study were exposed to relatively high parvalbumin levels (89.4 ng/m^3 and 109.8 ng/m^3) and exhibited respiratory symptoms, however, too few cases prevent us from running statistical analysis. We also cannot exclude that these workers were sensitized through digestion route, or combination of digestion and inhalation routes.

Relatively low prevalence of specific sensitization in our study might, however, be due to the “selection out” of workers who developed specific sensitization to salmon, manifested symptoms and left the industry, which is consistent with “healthy worker effect”. Such an effect was clearly presented in a longitudinal study where new workers were found to have higher prevalence of specific sensitization compared to more experienced seafood workers [137].

C-reactive protein (CRP)

The rationale for CRP measurements was to be able to exclude subjects with ongoing infections from statistical analysis, and to see if variations in CRP were associated with airway symptoms, spirometric and FE_{NO} levels. We did not find significant differences in CRP levels between exposed (GM=1.3 μg/L) and non-exposed (GM=1.3 μg/L) study subjects (Paper I), and none of participants have CRP levels reflecting active inflammation and infection (40–200 μg/L) [138]. The associations between CRP and other parameters measured in the study did not reach statistical significance.

6.1.1.6 Acute respiratory symptoms and FEV_1 measured repeatedly over a week period in salmon workers

Analysis of repeatedly measured data showed more pronounced FEV_1 decline on Monday shifts compared to Thursday (Paper II). This pattern might be caused by compensatory tolerance mechanisms, which results in the most pronounced airways response on the first workday after being away from work for a weekend and gradual adjustment to exposure in the progress of a workweek. Similar pattern was also revealed for symptoms frequency, which was shown to be high on Mondays and followed by a reduction during the progress of the workweek. However, a "questionnaire fatigue", the phenomenon that workers are less likely to report symptoms they still experience, although, could not be excluded in our study. The presence of suggested toleance mechanism in the study is, however, supported by objective lung function measurements.

The most frequent reported symptoms were irritated nose (range during a workweek 22.4-28.6%), irritated throat (14.5-18.6%), and cough (10.4-21.4%) compared to less frequent chest tightness (2.8-10.0%) and wheezing (1.4-5.7%). The same pattern was also seen in other studies on workers exposed to organic dust, where authors showed higher prevalence of systemic symptoms and symptoms of irritation compared to other respiratory symptoms [93, 94].

In out study we observed significant decreasing of frequency of wheezing and chest tightness among studied group of salmon workers. The respiratory pattern seen in the present study is compatible with byssinosis, which is an occupational respiratory disease associated with

exposure to cotton dust [139]. "Monday effect" has been shown as attributable pattern of byssinosis and described as acute bronchoconstrictor response to the exposure on the first working day after a weekend which was not present at the end of the same week [140].
Similar results were not previously observed in seafood workers due to the lack of repeated measures design studies, however, our findings are in accordance with studies among other groups of workers exposed to organic dust [141-144], where tolerance effects as well as "Monday effect" have been suggested.
The mechanism of "Monday effect" has been extensively examined among workers exposed to cotton dust. It has been shown that immune reactions (principally IgE-mediated) in the individuals play a role in eliciting of respiratory response on exposure during first working day [143], moreover relationships between cross-shift declines in FEV_1 and atopy were observed in this occupational group [145]. In our study such relationships is unlikely as a contributor to the suggested tolerance effect. It has been suggested that "Monday effect" is a typical asthma-like disorder [146] and referred often as non-allergic respiratory disorder [147, 148], therefore one cannot exclude a non-allergic basis of the respiratory effect seen in the study subjects in the present study.

6.1.2 Work-associated exposures of relevance to respiratory symptoms

Bioaerosol exposure

In our study we measured a total protein (TP) fraction, which is a mixture of structural proteins, enzymes, binding proteins, etc (Paper II). The levels of TP were generally higher (up to 12 $\mu g \cdot m^{-3}$) compared to other existing reports, showing the highest levels up to 6 $\mu g \cdot m^{-3}$ (pilchard workers) in a study from South Africa [35]. The salmon factories we visited in our study were modern and generally characterized by highly developed industrial technologies and had a very high level of automation. The processing plants often had many machines in close vicinity to each other. Shielding between operators and aerosol-generating processes and equipment were often lacking or inadequate. Water nozzles above transport bands, which rinse the fish on its way through the production line as well as the frequent use of water hoses for cleaning floors and equipment may additionally contribute to high exposure levels of TP.

Measured parvalbumin levels (up to 358 $ng \cdot m^{-3}$) were higher compared to levels presented in a recently published study from Sweden performed at a salmon processing plant (up to 186 ng/m^3) [23], but lower compared to sea trout processing plant shown in one Danish study (up to 1,332 ng/m^3) [149], and seafood allergens in other processing plants showing levels ranged up to 1,919 ng·m^{-3} in pilchard and up to 75,748 ng·m^{-3} in anchovy processing plant ([35]. Higher levels were also observed during crab processing operations (up to 21,093 ng·m^{-3}) [22].

Endotoxin levels measured in the present study (up to 29 EU·m^{-3}) were comparable with levels seen in our previous study in salmon factories (up to 36 EU·m^{-3}) [21] and the earlier mentioned Swedish study where levels of endotoxins ranged from 1.6 EU·m^{-3} to 7.1 EU·m^{-3} [23], but considerably lower compared to endotoxin levels measured in herring processing plant (up to 1,350 EU/m^3) [21], and levels found in other occupational settings where workers are exposed to organic dust (up to 374,000 EU in farms) [150].

Exposure levels in our study were relatively stable during a week, but a slight insignificant trend of increasing in exposure concentrations was noted in the progress of a workweek, which might be explained by continuous productivity during workweeks. Closing down of machinery during weekends might cause lower exposure levels on Mondays and gradual elevation during the rest of the week.

Determinants of bioaerosols exposure levels

Higher airborne parvalbumin levels were found among workers in filleting departments compared to workers in slaughtery departments, which is consistent with findings of the two earlier referred Scandinavian studies [23, 149]. This finding could be explained by the fact that salmon muscles are the site of parvalbumin, the main salmon allergen [151], therefore filleting workers are exposed to higher airborne parvalbumin levels compared to other workers. The lower exposure levels of parvalbumin among workers from slaughtery departments in our study can be explained by the fact that workers in these departments are engaged in butchering and degutting of raw salmon and had no direct contact with fish muscles as opposed to workers in fillet departments.

Univariate analysis revealed also that parvalbumin levels were significantly different between factories (n=5). The differences between factories are numerous. Factors like amount of salmon processed, ventilation, building characteristics, organisation of process lines, distances between aerosol-generation machines and manual filleting processes, shieldings, water nozzles, cleaning frequency, cleaning methods and many more, may all influence the bioaerosol levels. Especially, factors related to the filleting processes and filleting departments at factories are likely to affect the parvalbumin levels, and reflect significant differences found between five studied salmon factories.

Comparable results to ours were found in a study from South Africa where authors observed the highest contrast in exposure levels of fish allergens between factories and departments [35].

Significantly higher exposure levels of all three measured bioaerosol components were found among workers reporting use of water hose during salmon processing. Water is extensively used during seafood processing. It has been shown that water molecules may influence the size, lifetime and other dynamics of small particles [2, 4]. Water may contribute to liberation of bioaerosols to the air when water beams hits surfaces containing organic matter. The finding of our study suggested that processes involving use of water hose posses increased risk with regard to the liberation of bioaerosols.

In spite of the fact that fish processing is a daily work activity in both investigated populations of seafood workers, there may be dissimilarities in the exposure characteristics at onshore and offshore workplaces explaining differences in respiratory symptoms experiences by processing workers.

Different types of fish processed, levels of automatization and different processes in salmon-processing plants and fish trawler factories, as well as conditions related to ventilation are expected to contribute to differences in exposure patterns in onshore and offshore seafood industry. Factory facilities on board of factory trawlers are often located in lower decks of the ships in confined premises with very often only natural ventilation, which further may lead to different exposure profile in offshore and onshore processing facilities. It has been shown that exposure levels on seafood-processing vessels might be considerably higher compared to land-based processing facilities [37]. Due to the spatial limitations and other vessel-specific factors, the exposure levels in vessel with fish processing equipment onboard, are generally be expected to be higher than at comparable onshore factories.

International publications on workers engaged in seafood processing aboard vessels are sparse. Beaudet' et al study on workers aboard crab-processing vessels revealed higher aerosolized crab allergen concentrations at butchering/degilling work stations compared to other work stations aboard vessels [22]. The authors also observed that size of vessel, i.e. size of onboard processing facility may play a role in higher allergen levels, since the highest allergen levels were found in the smallest vessel, which suggest that restricted spaces may be an important risk factor for exposure. Despite the fact that exposure in the referred study was measured during other activities/processes and crab-processing vessels are different from fish-processing vessels, the results of Beaudet study are of interest for our present study, since it is in agreement with our hypothesized differences in exposure levels between work tasks performed by trawler workers. In contrast to the finding in our study, Beaudet et al found no difference in respiratory symptoms reporting among crab workers from different work stations despite the different crab allergen levels. The authors explained this by a possible irritant airway response in the studied workers rather than allergic.

In our study significant results were found for an association of work tasks with running nose, cough with phlegm, and frequent sneezing, symptoms, which are rather unspecific. Therefore, results of the present study may imply that the environment in filleting sections onboard processing facilities contribute to triggering of unspecific symptoms in studied group of trawler workers.

Exposure to low ambient temperature

Exposure to low ambient temperature may be involved in the development of respiratory symptoms in the studied workers. The finding that Norwegian salmon workers as well as Russian trawler fishermen ranked cold work environment as the most important factor for work-related respiratory symptoms (Paper IV) are in agreement with results from our previous study [48] and underline the importance of exposure to low ambient temperature in the seafood processing facilities.

Breathing in cold air was shown to induce respiratory response [53, 54, 77]. It has been suggested that cold air is unlikely to be a causal factor initiating respiratory diseases but is a symptom trigger [54]. Nasal breathing of cold air induces an engorgement of the venous sinuses in the submucosa, which leads to rhinorrhea, congestion, and sneezing [152, 153]. Cooling of the lower airways was shown to induce vasoconstriction in the bronchial mucosa, followed by narrowing of the airways [54]. The effect of cold air on the airways is not only cooling but also drying, since hyperpnea of cold air may cause the airway surface fluid to evaporate more rapidly than it is replaced [154, 155], and therefore consequently provoke coughing [53].

For trawler workers the thermal conditions are expected to offer greater challenges compared to salmon workers as they perform regular outdoor work tasks in harsh climate conditions. The presence of only partly shielded block freezers in the production area, and open hatchways during loading activities, may in addition contribute to low temperatures also in indoor processing areas.

Higher prevalence of running nose and dry cough among the trawler workers compared to the salmon workers may point to a greater influence of cold work environment in offshore seafood industry.

Exposure to disinfectants

Both groups of exposed workers in our study ranked "use of disinfectants" as the second most frequent cause for work-related respiratory symptoms (Paper IV). Both groups of workers could be exposed to disinfectants either directly or to remains of the chemical agents in workplace air. It has been shown that exposure to disinfectants may lead to allergic type of asthma [81, 156], and to chronic respiratory health effects [80]. It has been also shown that disinfectants in free form may be captured in the upper part of the respiratory tract, and cause respiratory symptoms through irritative airway effects [79], which could explain high prevalence of frequent sneezing among salmon workers who reported "use of disinfectants" as a causative factor for work-related respiratory symptoms in our study. Duration of disinfection procedure may also play a role, and association with respiratory symptoms and declined lung function has been demonstrated previously [80]. Possible interactions or effect modifications due to simultaneous exposure to bioaerosols and disinfection agents has, to our knowledge, not been previously studied in seafood industry, but might however take place, therefore would be an interesting topic for future studies.

The finding of higher percentage of salmon workers (14.4%) reporting "use of disinfectants" as the cause for work-related respiratory symptoms compared to trawler workers (7.9%) would suggest that salmon workers to a greater extent associate their symptoms with use of disinfectants.

Other influential factors on respiratory symptoms

Length of employment

Upon relating respiratory symptoms to length of employment positive association with work-related frequent sneezing and running nose in both exposed study groups was revealed (Paper IV). The finding could possibly be explained by specific work tasks during long period of time among workers experiencing these symptoms. But whether long-term exposure to specific factors or agents in working environment during performing particular work tasks elicited these symptoms could not be drawn from our study.

Tobacco smoking

Tobacco smoking is a well-known confounder in epidemiological studies in occupational settings, especially when the respiratory outcomes are the main focus. Although, in our study we adjust all multiple models for smoking related variables, we cannot exclude that impact of smoking could be underestimated in the study.

The finding of positive interaction between smoking and exposure (being a salmon worker) on work-related upper respiratory symptoms and shortness of breath (Paper I) may suggest a synergistic effect of smoking and exposure on these respiratory symptoms and confirm the importance of smoking.

Due to significant interaction found between smoking and dichotomous exposure variable, models in analysis of associations between actual exposure levels to bioaerosols and respiratory outcomes measured repeatedly, were adjusted for number of pack-years for current and former smokers. This was done in order to exclude smoking as possible explanation for the finding.

Genetic factors

Genetic factors may affect respiratory symptoms seen in our study. We found that doctor-diagnosed asthma/allergy/eczema were associated with family history of these conditions in the Norwegian part of the study (Paper I). We also observed that asthma in childhood was more often reported by salmon workers with adult-onset asthma, but not by trawler workers (Paper IV), Genetic predisposition to respiratory disorders may influence the individual reaction to environmental factors, therefore subjects in our study with family or personal histories of respiratory diseases might have higher risk, or were more susceptible to develop respiratory impairment under conditions and exposures, which do not normally induce reactions in subjects without such a predisposition.

Level of physical activity

Physical strain may increase uptake of aerosolized agents as well as contribute to more pronounced exposure to cold due to increased pulmonary ventilation. Level of physical activity under work performance was not evaluated in the present study, however could additionally be involved in respiratory outcomes development in the workers.

6.1.3 Exposure-response analysis

Two statistical approaches were applied in order to explore exposure-response relationships between respiratory outcomes and actual exposure levels measured repeatedly during a week in salmon workers (Paper II). Results of GEE revealed a trend of decreasing effects of exposure during a workweek based on coefficients of interaction term – exposure and time on respiratory variables (acute symptoms and change in FEV_1 over a week period). Exposure-response analysis of individual day-to-day exposure and health data analyzed by multiple linear and logistic regression analyses showed significant associations only for Monday shifts, which is in agreement with the results of GEE. In both statistical procedures TP showed statistical significance (borderline in GEE).

Therefore, the suggested tolerance mechanism from univariate analysis of respiratory variables (section 6.1.1.5) is confirmed by the results of GEE and multiple regression analysis, showing significant results with exposure levels.

Comparable results were not published among seafood processing workers, however, have been found in studies on farmers, where authors showed that workers might develop tolerance to repeated exposure to organic dust [144]. It has also been shown that unexposed subjects may have a stronger airway reaction to organic dust exposure than longer exposed farmers [157, 158]. The authors suggested possible adaptation mechanisms in farmers, which was confirmed by *ex vivo* stimulation of alveolar macrophages from subjects exposed to organic dust and yielded a weaker IL-6-, IL-8- and TNFα-response after exposure than it did before the exposure [159]. Adaptation and tolerance to the occupational environment among farmers has been suggested as an explanation for the weaker inflammatory response. It was observed that previously unexposed subjects have reacted similarly to exposure of organic dust [142, 160], therefore the airways response in the unexposed subjects seems to be the normal inflammatory reaction to a stimulus, whereas the weaker response in the longer exposed subjects could be a sign of tolerance mechanisms.

Results of these studies were confirmed by *in vivo* studies where three groups of rats were exposed to pig barn air for a period of 8 hours/day for one day, 5 days or 20 days, respectively in order to mimic the work schedule at a pig barn, and showed that rats exposed to the swine barn air for one day showed increase in airway hyperresponsiveness compared to other groups, which may suggest adaptation to exposure [161].

Endotoxin has been suggested to play an important role in such mechanisms, since it is known that repeated exposure to endotoxin results in attenuation of the inflammatory response, referred to as endotoxin tolerance [162].

In our study, endotoxin exposure levels were generally low, and analysis revealed no significant results with respiratory outcomes in the workers. However, inhalation even of low levels of endotoxin may induce respiratory effects [163-165]. Moreover, a synergistic effects between endotoxin and other components of bioaerosols such as beta(1,3)-D-glucan was also documented [166]. We cannot, therefore, exclude that that endotoxin, even though observed at the low levels in the present study, may contribute to the respiratory response.

The effect of duration of employment may, however, be influential on exposure-response associations. Accordingly, Vogelzang et al found that pig farmers who had worked less than 5 years had more pronounced respiratory impairment than those who had been working for a longer period; authors suggest possible adaptation mechanisms [167]. The analysis in our present study was not stratified by duration of employment and was not adjusted for it, since simultaneous adjustment with age might lead to overadjustment. Therefore, one cannot exclude that more senior salmon workers might have weaker airway response compared to those who worked shorter.

It has been suggested previously that atopy is a modifying factor in exposure-response analysis of respiratory outcomes and number of studies have shown that the slope of the exposure-response relationship is steeper in atopics compared to non-atopic subjects [168-170]. The phenomenon was explained by higher risk of developing symptoms and more likely to respond at lower exposure levels to any irritant or allergenic stimuli by atopic subjects compared to non-atopic [171]. The finding that stratification of the respiratory outcomes (acute symptoms and change in FEV_1) as well as exposure-response analysis by atopic status did not show statistically significant results in our study, may suggest less influential effect of atopy on studied respiratory variables repeatedly measured during a workweek.

Recent *in vitro* study of our research group demonstrated that purified salmon trypsin can activate human pulmonary epithelial cells and induce secretion of the pro-inflammatory cytokine IL-8 [172], which was presented as a component of innate immune reaction not related to allergic mechanisms. Total protein fraction (TP) measured in our present study is a mixture of structural proteins, enzymes, binding proteins etc, as well as salmon trypsin. In both statistical analyses (GEE and multiple regression analysis) performed in the study, levels of TP showed statistical significance. Therefore, our findings from epidemiological and *in vitro* studies are in line and may accordingly suggest non-allergic mechanisms of respiratory impairment seen in the salmon workers. However, the suggestion needs confirmation from further *in vitro* as well as prospective epidemiological studies.

Multiple regression analysis of repeated data in the present study showed significant results for cough, chest tightness and cross-shift FEV_1 on Monday shifts. These symptoms as well as cross-shift FEV_1 decline have been described as features of the “Monday effect” documented in organic dust exposed worker populations. It has been shown that the clinical picture of “Monday effect” is different from typical occupational asthma picture, in which symptoms worsen as the week progresses. The acute respiratory symptoms of chest tightness and cough were shown to abate or disappear with no demonstrable cross-shift changes in lung function as the week progresses, even though the exposure was the same. As exposure continues, this pattern may worsen, and lead to chronic respiratory symptoms, and in advanced stages to obstructive lung disease. [173]. Due to the fact that duration of employment was not taken into consideration in the analysis in our study, we could not exclude that more senior workers might have faded “Monday effect”.

The funding that salmon workers had higher 1-year prevalence of respiratory symptoms and exhibited decreased spirometric test parameters compared to the controls (Paper I) indicate that work-related factors are involved in impaired respiratory health of studied salmon workers. Whether a primary tolerance mechanisms is later transformed into more persistent respiratory symptoms, and if so at which stage the shift happens, should be further studied in prospective studies.

6.2 Methodological considerations

6.2.1 Study design and subjects' selection

Study design

The presented study is designed as cross-sectional study on two seafood worker populations with repeated measurements over a week period in the Norwegian part of the study.

The main limiting factors taken into consideration for study design were: time, project funding and geographical criteria. Financial support of the project was limited for a time period of three years and in terms of geographical locations we aimed on studying populations of salmon factories geographically spread along the Norwegian coast in one part of the study.

Due to the mentioned limitations, the choice of a prospective study design was ruled out. Instead, we found it reasonable to conduct a cross-sectional study with extended repeated measures over a week period, which is suitable for investigating nonfatal diseases, symptoms, and physiological variability [111, 114, 174, 175]. In our project we were interested in prevalence as risk estimate to describe the present situation, as well as frequency of acute respiratory symptoms and variability of spirometric test parameters to describe respiratory outcomes measured repeatedly over a workweek period.

In our study the measurements of exposure were performed concurrently with the health outcomes measurements, and it is often difficult to determine whether exposure preceded health outcomes. The misclassification of historical exposures is often of concern in cross-sectional studies, since the measurement of outcome is prevalence rather than incidence [176].

Selection of exposed study subjects

Our participants in both parts of the study were selected on a basis of current exposure to fish during daily work activity. However, the ideal approach would be to study all active and workers who retired or changed jobs. In the present study we could not recruit retired workers or those who had changed jobs because enrollment of study subjects were performed through contact persons at the Norwegian part of the study, and only active workers undergoing clinical examination at CSP in the Russian part of the study were enrolled.

Selection of the non-exposed study subjects

1) Norwegian part of the study

The main criterion for selection of the control group was the absence of exposure to fish at work. Municipal workers formed the reference category for exposed study group in the Norwegian part of our study. It has been, however, suggested that in an occupational epidemiological study the ideal goal can best be achieved by using an internal control group of non-exposed employees, since in this way exposed and reference groups would be similar with respect to the known sources of variation other than the exposure of interest [114, 176]. In a previous study we have used employees from the management and administration of the factories as a control group [21]. But we revealed that such workers could be exposed at some degree during occasional visits to the production areas of the plants. In addition some workers in the administration had been moved from production departments due to health issues. Therefore a decision on recruitment of controls from other branches was made. However, there was little industrial activity, besides seafood industries in the regions where salmon factories were located, therefore choice on municipal workers from the same geographical areas as salmon factories, was made.

2) Russian part of the study

The approach in the Russian part of the study allowed us to choose a control population presented by merchant seafarers, which differed from trawler seafarers by absence of occupational exposure to fish, while were expected to have comparable variation in characteristics other than exposure of interest.

Measures to reduce dissimilarities between exposed and non-exposed study subjects

By means of the general questionnaire we gathered the relevant information on personal factors, lifestyle, personal and family history of respiratory diseases. Some of these variables were found to be different in exposed and non-exposed populations, and might, in fact, modify the effect measure. Therefore, depending on part of the study, statistical models were adjusted for relevant confounders: age, smoking, gender, height, family history of asthma/allergy/eczema, and education. This is a reliable method to produce “adjusted” or “corrected” estimates of the effect of exposure [177].

Applying “normative” values, providing either normal ranges or, in some instance, predicted values for individuals based on gender, ethnicity, anthropometric variables, or smoking habits are documented as valuable methods for comparative analysis in cross-sectional studies [175, 178]. In our study we used predicted values of FEV_1 and FVC in order to compare these lung function parameters between exposed and non-exposed study subjects. This method allowed us to control for age, gender, and height.

Selection bias

Self-selection into the Norwegian part of the study could be a source of bias if workers have special motivations for agreeing or refusing to participate. Workers who are concerned about their health because of disease symptoms or intense exposure may be more willing to participate than other workers. Generally, it is very difficult to avoid this type of bias in the occupational epidemiological studies.

Oppositely, we can rule out this type of bias in the Russian part of the study, as almost all workers (99%) scheduled to undergo medical check-up during period 12.09-01.10 agreed to participate in the study.

It has also been suggested that workers who suspect that they are experiencing job-related morbidity may be afraid of participating if detection of disease or physical impairment will force them to retire or to transfer to less desirable jobs. To avoid this type of bias it was stated in the consent paper that results of the project will not be giving to employer or any other company personnel and will not influence current employment.

However, among the workforce at salmon factories there was a substantial percent of foreign workers, most of which did not participate (n= 7 out of in total 139 participants; own unpublished results). We cannot rule out that language problems as well as general mistrust to authorities based on previous bad experiences might be reflected in the vey low participation among this group of employees. This bias could dilute at some degree any true association between the exposure and outcomes [178].

Healthy worker effect

The healthy worker survivor effect might influence the results of the present study, implying the selection of healthy workers into the workforce and staying of the healthiest workers in the most exposed jobs [179].

Possible healthy worker effect might affect the results of the study, as it is likely that compared with subjects without respiratory problems subjects with airway symptoms or disease will seek employment in less exposed jobs [180, 181]. The healthy worker effect might create underestimation of true exposure-response associations in our study if outmigration from the "exposed population" is related to exposure level: a processing worker with developed respiratory symptoms might be expected to be transferred to less exposed work.

The healthy worker effect is thought to be strong in prevalence studies because they include only actively employed workers [114, 181].

6.2.2 Data collection

6.2.2.1 Questionnaire data

General questionnaire

In spite of the fact that the general questionnaire was based on validated questionnaires and was previously used in other studies, we could not control for the information bias [182], which might appear in our study during filling in the questionnaire by the study subjects:

- response fatigue and/or skipping of questions. We noticed a tendency that some questions were skipped by subjects. For example, question regarding "running or blocked nose which was not a cold" were disregarded by many subjects. A possible reason for this could be difficulties in differentiation of running nose as a result of cold, and running nose as a result of other factors. Therefore, such questions were not included in the analysis
- faking bad (respondents try to appear sick)
- faking good (respondents try to appear healthier).

Translation of the questionnaire from Norwegian to Russian language

For the Russian part of the project the general questionnaire was translated from Norwegian into Russian by a Russian licensed translator, who has a long working experience in different projects between Russia and Norway. Wording and sentencing aspects were taken into considered during translation, in order to make questions clear and easy to understand and at the same time saving the same meaning of the question in original questionnaire.

Short questionnaire on acute respiratory symptoms

The short questionnaire (Appendix H) applied in the repeated measurements in the Norwegian part of the study embraced few short questions that were straightforward and concrete. This type of questionnaire is, however, prone to information bias due to possible questionnaire fatigue, since the respondents were asked to fill in the questionnaire every day for four day.

6.2.2.2 Physiological and laboratory tests

Physiological (spirometry and measurements of FE_{NO} levels in exhaled air) and laboratory (blood analysis) tests performed in the study aimed to support our findings from the questionnaire and find whether results from objective and subjective methods were in line, as well as to relate tests results to categorical and actual exposure data in order to examine exposure-response associations.

6.2.2.3 Exposure assessment

Categorical determinants of exposure (qualitative exposure data)

Exposed/non-exposed categorization

In Paper I and III a dichotomy was used to identify exposed and non-exposed study populations. This criterion has been applied very often in occupational epidemiological studies. Category- exposed subjects (salmon workers/trawler workers) were used in the present study as the basic exposure surrogate in seafood industry (salmon industry/trawl fishing). The criterion is rather crude and gives no specific information on exposure, although thought to reflect general exposure situation in the studied industries.

Work tasks (Russian part of the study)

Categorical exposure classification was assessed based on employee's work tasks in the Russian part of the study. The underlying assumption was that subjects within each work task experience similar levels and variation of exposure characteristics (homogeneous exposure categorization). Trawler fish-processing workers were divided into main groups based on self-reported information from a questionnaire. Several studies have examined the validity and reliability of self-reported occupational exposure information and revealed that self-reports were sensitive and specific tools [183-185]. Therefore, possible misclassification is thought to be non-differential. We could not, however, exclude the possibility that exposure may differ in workers having same work tasks because of differences in individual work practices. Such differences may influence exposure-response relationships [186].

Determinants of bioaerosol exposure levels (Norwegian part of the study)

Potential determinants of exposure levels (factory/department/use of water hose) in the Norwegian part of the study were withdrawn from the general questionnaire and studied in univariate analysis in order to find whether exposure levels were affected by these factors. We did not run statistical analysis separately for worker groups defined by these determinants when examining relationships between actual exposure levels and respiratory variables measured repeatedly during a workweek, and instead the potential determinants were taken into account in relevant statistical analysis. Some studies, however, perform analysis separately for exposure groups and find different exposure-response associations between groups, which often results in more solid conclusions. In our study exposure measurements were implemented on relatively small number of participants and grouping by some factors might lead to very small groups, which might further lead to distortion in statistical analysis.

Quantitative exposure data

We presented the quantitative data for airborne endotoxin, parvalbumin and total protein using geometric mean and range due to skewed distribution of the measured exposure components (Paper II). Such skewed distributions are common in exposure measurement data sets. The geometric mean is considered to be more representative than arithmetic mean since it puts less weight on extreme values in a data set. Due to skewed distribution, we log-transformed the monitoring data of airborne agents to get a distribution of the data closer to normal before performing statistical analysis.

Exposure data was presented as 8-hour time-weighted averages of bioaerosols in air samples. This metric is the most frequent metric used in the occupational studies, although it has several limitations. Little information exists about the variations of exposure in the work environment. Workers may be exposed to a high number of peaks over a work shift, which are usually associated with a range of different tasks. Between the peaks, exposure may be low. A study among bakery workers showed that more than 75% of the work shift time-weighted average exposure could be explained by peak exposures [187]. It has been suggested that peak exposure and averages without peaks may be more appropriate metric for examining of health outcome compared to daily average exposure [188].

6.2.3 Statistical analysis

In the present study we applied logistic regression adjusted for potential confounders in order to calculate odds ratio of binominal outcomes of interest (Paper I, III and IV). This is an accepted method to reduce the effect of the differences between exposed and control populations [175], however the use of this method has been questioned in cross-sectional studies [189]. An effect measures in cross-sectional studies can be expressed as either ratios or differences of prevalence. The prevalence odd is a basic outcome measure in cross-sectional study because it is directly proportional to the disorder incidence that is of intrinsic interest. Hence, the prevalence odds ratio, which is the ratio of the prevalence odds in the exposed to the prevalence odds in the non-exposed, is a convenient estimate of the relative risk. This means that the methods for estimating odds ratios in case-control study (logistic regression) can also be applied in cross-sectional studies [107, 114].

We used the same analysis in situations when there were only few subjects with outcomes of interest, which resulted in low prevalence. It has been suggested that regression analysis is not advisable in such cases since logistic regression can produce seriously biased effect estimators and misleading information on confounding and bias because of very sparse strata [190]. It has been proposed that exclusion of covariates and alternative coding of variables may detect this problem [114]. In our study we did not perform such sensitivity analysis, therefore, the results of logistic regression analysis where prevalence of outcome of interest was very low, should be interpreted with caution.

In the Norwegian part of the study some of the data were collected repeatedly (Paper II). The analysis of data of this kind is more complex than other types of data because the repeated observations on the same individuals are likely to be correlated. The assumption about independence of observations is violated in such data, thus the correlation structure should be taken into account. In the present study we applied GEE models, which is a refined approach that explicitly models the correlation structure of the data [108-111]. GEE fit linear models for sets of repeated measures from each subject and use the data to calculate the correlations among each individual's repeated variables, and then employ this correlation to estimate model variances. An advantage of GEE is that it gives a possibility to choose correlation structure, select a link function and distributional option.

Since we were also interested in exposure-response relationships between health and exposure data measured each specific day we applied multiple logistic and linear regression analysis in addition to GEE.

6.2.4 Validity of results

In the Norwegian part of the study data sampling was undertaken during several visits. Consequently, the validity of the study results to a great extent depends on the quality of the physiological and laboratory tests performance and the precision of the exposure measurements, and the comparability between the examinations performed at different time points [191]. Following precautions were taken to strength the validity of the study:

- all the tests as well as exposure measurements were performed by our own research group. By doing this we tried to insure good compatibility and comparability between tests and measurements performed at five salmon factories at six time points by the same researchers
- spirometry and measurements of FE_{NO} were performed in accordance with American Thoracic Society (ATS) guidance [95, 102], equipment used for these tests met the specification of the ATS
- researchers used written protocols (spirometry, FE_{NO} measurements, blood tests, exposure measurements)
- members of our research group involved in instrumental examinations underwent training before and during the study.

Performing multiple measurements of respiratory and exposure data also aimed to reduce possible measurement errors in the study since it has been suggested that multiple measurements are an effective method of decreeing the measurements error, in comparison with the use of a single measurement [114, 191].

Data gathering in the Russian part of the study was carried out by one researcher, who underwent training before the study. Validation of the dataset was done in cooperation with the EPINOR research school in order to evaluate the completeness ant correctness of the collected data [192].

In Paper IV we performed comparative analysis on populations in two different types of seafood industries from two different nations: Russian and Norwegian, therefore the aspect related to cultural differences between the two nations might affect results of the study. In general, cultural differences are difficult to adjust for, therefore, we cannot exclude their influence on questionnaire data.

Different approaches in the recruitment of the two worker populations, as well as the fact that two exposed groups were examined in two different time periods might have had impact on the results. Recruitment of the salmon worker population was performed with the help of the factory managements, therefore selection bias is more likely in this part of the study compared to the Russian part of the study where the trawler workers were recruited during annual health examinations. None of the workplaces had to our knowledge undergone drastic changes during the total period of two years, which allow us to suggest that exposure has been relatively constant. Other differences between the two studied populations related to demographic characteristics were adjusted for in statistical analysis.

6.2.5 Generalization and representativeness of the study results

The five salmon factories that participated in the study are representative for modern salmon factory technology, were among the largest (> 50 employees) in Norway and had both slaughter and filleting departments. We have no reason to believe that the present work environment differs much from the other salmon factories in this category, which rejected participating, therefore we assume that the results of our study is representative for other salmon-processing plants.

Relatively low participation rate (29.6%) reached in the Norwegian part of the study could be explained by the fact that we were unable to control the number of workers approached/asked for participation by the contact persons in the salmon factories. The inclusion/exclusion criteria for the study participation given to the contact persons were relatively strict (Section 4.1). The main criterion was - work in the production area of the factory more than 50% of work shifts. We set this limit because workers having most work tasks outside the production areas of the plants were expected to be less exposed to fish. More flexible inclusion criteria would probably have increased the participation rate, but at the cost of increased variability with respect to exposure.

In spite of the low participation rate, we feel that the examined population is representative for workers being exposed to salmon in their daily work, as no other health parameter or exposure parameter were used as inclusion criteria.

In the Russian part of the study most study subjects were working on medium sized vessels with bottom trawls as their main fishing gear (for catching cod, halibuts, redfish, flounders, etc). Onboard processing equipment is implied to have comparable technical characteristics between trawl vessels of this type. Therefore, we believe that the findings of the Russian part of the study is representative for other trawler work environments with fish processing on board having similar factory technology, size and working patterns.

We are not aware of obvious reasons for such a high response rate (99%) in the Russian part of the study, but some explanations could be speculated upon. No additional visits or extensive amount of time spent were demanded from the participants and questionnaire completion together with examination without any invasive procedures was organized in the most efficient way - these are factors, which could possibly encourage workers to participate. In spite of our effort to inform all participants of the voluntariness, we cannot exclude the possibility that cultural differences in the apprehension of health personnel as authorities, combined to the close linkage of the project to regular obligatory health examinations, may have influenced on the participation rate. However we expect such effects to affect exposed and non-exposed study groups similarly.

7. MAIN CONCLUSIONS AND FUTURE ASPECTS

Following main conclusions can be drawn from the study:

- Norwegian salmon-processing workers and Russian trawler fishermen exhibit impaired respiratory health status compared to control populations without occupational exposure to fish. No difference was found in the prevalence of doctor-diagnosed asthma between Norwegian salmon-processing workers and their controls (municipal workers), whereas Russian trawler fishermen reported doctor-diagnosed asthma more often than their control group (merchant seafarers).

- Symptom-reporting and asthma diagnosis do not seem to be associated with atopy in Norwegian salmon workers, although working in this industry seems to be associated with increased risk of sensitization to salmon allergens. A probable "healthy worker effect", implying that the most affected persons tend to leave the industry, prevents strong conclusions on this data.

- Salmon industry workers are exposed to bioaerosols containing bioactive agents including the main salmon allergen, parvalbumin, other proteins and endotoxins in their work environment. The total protein levels are higher than previously measured in other fish industry workplaces. Exposure levels of parvalbumin levels vary between fillet and slaughtery departments, as well between the factories. The work tasks associated with the highest levels of bioaerosols are work tasks involving the use of water hose.

- Filleting of fish is a specific work task associated with respiratory symptoms in Russian trawler workers.

- Exposure–response analyses show associations between exposure to proteins (the total fraction) and respiratory health outcomes, measured as symptom reporting and cross-shift decline in FEV_1 values. Significant results were found only for Monday shifts. A tolerance development in the course of a workweek is suggested.

- The two seafood worker populations investigated in this study both report respiratory symptoms, but the pattern of symptoms is different. Russian trawler workers report more work-related dry cough and running nose whereas Norwegian salmon workers report more shortness of breath with wheezing and prolonged cough. Differences in the degree of exposure to low ambient temperature and bioaerosols between the two worker populations are suggested, but more comprehensive studies of thermal factors in both workplaces as well as bioaerosol exposure measurements in the trawlers are needed to confirm this.

Combining all the findings together we suggest that bioaerosols plays an important role in the respiratory symptoms and impaired lung function among the studied groups of onshore and offshore seafood processing workers. We cannot exclude a possible contribution of other specific or combined physical and chemical exposures as well as individual factors.

Although the results of our study are in agreement with the findings of others, showing that seafood processing workers have impaired respiratory status, the actual mechanism for the causality remain unknown. Future research may shed more light on this area.
Our recommendations for further research:

- prospective cohort studies of the incidence of respiratory health outcomes and exposure
- investigations of bioaerosols: physical, biological and chemical characteristics of bioaerosols constituents, compositions in the different occupational settings in seafood industry, influence of different kind of processing on bioaerosols components, investigations of single and mixed exposures. Deterministic modelling of bioaerosol exposure, describing the relationship between agents on the basis of the physical, chemical, and biological mechanisms governing these relationships
- longitudinal studies of exposure-response relationships on onshore and offshore seafood-processing workers (actual and retired workers and those who changed work due to health issues)
- causal mechanisms of the respiratory outcomes in the seafood workers; investigation of the interaction of exposures with host factors in respiratory response
- mechanisms of a possible tolerance effect should be explored further
- evaluation of intervention measures (exposure controls) in onshore and offshore seafood processing environments.

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Paper I

Paper II

Paper III

Paper IV

Appendix A

Forespørsel om deltakelse i et forskningsprosjekt i regi av Arbeids- og miljømedisinsk avdeling, Universitetssykehuset Nord-Norge

"Luftveisplager hos ansatte i lakseindustrien"

Universitetssykehuset Nord-Norge har tidligere gjennomført en undersøkelse om arbeidsmiljø og helse i fiskeindustrien i Nord-Norge. Et av de viktigste funnene i den forrige undersøkelsen var en økt forekomst av luftveisplager i tilknytning til arbeid og kontakt med råstoffet.

Hovedformålet med denne undersøkelsen er å skaffe ny kunnskap om sammenhenger mellom eksponeringer og luftveisplager i lakseindustrien for å kunne forebygge helseplager. Vi ser det som viktig å tilbakeføre denne kunnskapen til næringen. Dette mener vi skal gi næringen et utgangspunkt for å peke ut satsingsområder og gjøre prioriteringer innen arbeidsmiljøarbeid.

Vi spør deg derfor om du vil svare på spørsmål om arbeidsmiljøet og helsen din. Det er frivillig om du vil være med i undersøkelsen, og du må ikke begrunne hvorfor du eventuelt ikke vil delta. Det vil heller ikke få noen konsekvenser for forholdet til arbeidsplassen eller på annen måte om du ikke vil delta eller trekker deg på et senere tidspunkt. Selv om du bestemmer deg for å delta nå, kan du senere trekke deg når du ønsker, og opplysningene som er samlet inn om deg vil bli slettet hvis du ønsker det.

Prosjektet er finansiert av Helse-Nords forskningsmidler. Undersøkelsen er tilrådd av Personvernombudet for forskning, Norsk samfunnsvitenskapelige datatjeneste AS. Regional komité for medisinsk forskningsetikk, Nord-Norge, har vurdert prosjektet og har ingen innvendinger mot at prosjektet gjennomføres.

Det kan bli aktuelt å gjennomføre en oppfølgingsstudie ved et senere tidspunkt, og vi ønsker derfor å oppbevare de innsamlede opplysningene med personidentifikasjon i inntil 10 år i påvente av en slik undersøkelse. Opplysningene vil bli oppbevart ved en arkivinstitusjon som er godkjent av datatilsynet for oppbevaring av persondata. Ingen data vil være tilgjengelig for andre. Vi spør derfor om ditt samtykke til at opplysningene om deg blir arkivert etter prosjektets avslutning.

Bedriften har mottatt spørreskjemaet og delt det ut til alle ansatte. Hvis du velger å delta skal det utfylte spørreskjemaet og samtykke-erklæringen sendes direkte til oss i lukket konvolutt. Ingen fra bedriften har adgang til besvarelsene. Prosjektlederne lager en liste der navn og referansenummer kobles. Svarene blir behandlet strengt fortrolig. Det er kun prosjektlederne som kjenner din identitet, ingen andre som handterer spørreskjemaet kjenner din identitet.

Samtykke-erklæringen, der du skriver navnet ditt, vil bli oppbevart adskilt fra spørreskjemaet. Ved senere publisering vil ingen opplysninger kunne føres tilbake til enkeltpersoner eller bedrifter.

Vi ønsker etter hvert også å gjøre enkle medisinske undersøkelser, som lungefunksjonsundersøkelser og allergitester (blodprøver), på noen av dere. Disse undersøkelsene vil ikke føre til ubehag utover et stikk i armen. Vi spør også om din tillatelse til å kontakte deg med forespørsel om en slik undersøkelse på et senere tidspunkt. Selv om du samtykker til å bli spurt har du likevel mulighet til å la være å samtykke til deltakelse i de medisinske undersøkelsene hvis du får henvendelse om dette.

Du får to kopier av dette brevet. Hvis du velger å delta sender du inn ett underskrevet eksemplar en ferdigfrankert konvolutt. Det andre eksemplaret beholder du selv. Besvart spørreskjema sendes i den andre ferdigfrankerte konvolutten.

Du kan når som helst ta kontakt med prosjektlederne på tlf 77628498 eller 77627463.

Med vennlig hilsen

Lisbeth Aasmoe og Berit Bang (prosjektledere)
Universitetssykehuset Nord-Norge

Referansenummer:

Samtykke-erklæring

	Ja
Jeg samtykker i å delta i spørreundersøkelsen	☐
Jeg samtykker i å bli spurt om å delta i en begrenset helseundersøkelse ved et senere tidspunkt	☐
Jeg samtykker i at opplysningene om meg arkiveres etter prosjektets avslutning	☐

____

Dato/Navn (blokkbokstaver) signatur

Appendix B

Forespørsel om deltagelse i begrenset helseundersøkelse i forbindelse med forskningsprosjekt i regi av Arbeids- og miljømedisinsk avdeling, Universitetssykehuset Nord-Norge

Lakseindustriarbeidere

Navn_______________________________

Universitetssykehuset Nord-Norge (UNN) i Tromsø gjennomfører nå en undersøkelse om luftveisplager hos ansatte i lakseindustrien i Nord-Norge. Hovedformålet med dette forskningsprosjektet er å skaffe ny kunnskap om hvilke faktorer i arbeidsmiljøet som kan gi økt risiko for luftveisplager. Denne kunnskapen er viktig for å kunne forebygge plagene.

I dette prosjektet trenger vi deltakelse fra arbeidstakere som ikke jobber i fiskeindustrien, som skal fungere som en kontrollgruppe som vi kan sammenligne funn fra lakseindustriarbeidere med. Vi spør deg derfor om du vil delta i en begrenset helseundersøkelse med fokus på lunger og luftveier. Det er frivillig om du vil være med i undersøkelsen, og du må ikke begrunne hvorfor du eventuelt ikke vil delta. Det vil heller ikke få noen konsekvenser for forholdet til arbeidsplassen eller på annen måte for deg om du ikke vil delta eller trekker deg på et senere tidspunkt. Selv om du bestemmer deg for å delta nå, kan du senere trekke senere, og opplysningene som er samlet inn om deg vil bli slettet hvis du ønsker det.

Prosjektet er finansiert av Helse-Nords forskningsmidler. Deltakerne i helseundersøkelsen er forsikret gjennom Norsk Pasientskadeerstatning. Undersøkelsen er tilrådd av Personvernombudet for forskning, Norsk samfunnsvitenskapelige datatjeneste AS. Regional komité for medisinsk forskningsetikk, Nord-Norge, har vurdert prosjektet og har ingen innvendinger mot at prosjektet gjennomføres.

Du har tidligere gitt tillatelse til at vi kan kontakte deg med forespørsel om å delta i en helseundersøkelse i sammenheng med dette prosjektet.

Undersøkelsene består av følgende tester:

- Allergitest – Vi tar en blodprøve fra en blodåre i armen, som i ettertid skal analyseres på Universitetssykehuset Nord-Norge.
- Lungefunksjonstest – Vi måler mengden av- og hastighetene på luften som pustes inn og ut ved at det pustes gjennom et rør som er koblet til et måleapparat.
- Test av neseslimhinne – Vi måler tykkelsen av slimhinnen i nesen før arbeidet starter mandag morgen, og etter arbeidet er avsluttet torsdag ettermiddag. Det foregår ved å plassere en tynn slange fra et måleapparat ytterst i hvert av neseborene. Du puster enkelt gjennom munnen under undersøkelsen.
- NO-test. Vi måler mengden NO-gass i pustelufta. Den kan være forhøyet hvis luftveiene er irriterte eller betente.

Dette er enkle standardundersøkelser som normalt ikke fører til ubehag utover et stikk i armen ved blodprøvetakingen.

Enkeltpersoner med avvikende funn vil bli kontaktet direkte med oppfordring om å kontakte bedriftslege og/eller fastlege avhengig av problemstilling. Du kan når som helst ta kontakt med prosjektlederne på tlf 77628498 eller 77627463.

I tillegg til helseundersøkelsen vil vi be deg om å bære en liten sekk med 3 bærbare pumper i 4 arbeidsdager. Hensikten med dette er å ta prøver av pusteluften der du arbeider, for å undersøke om du er eksponert for stoffer vi vet kan gi luftveisplager. Sekken er enkel å bære, og vil ikke være til hinder i arbeidet. Den tas av i pauser.

Resultatene av disse eksponeringsmålingene vil bli sendt bedriften, uten navn knyttet til måleresultatene. Ingen opplysninger om helse eller eksponeringer kunne føres tilbake på enkeltpersoner eller bedrifter i andre rapporter fra prosjektet.

Blodprøven vil bli oppbevart etter at analysene er gjennomført. Selv om du bestemmer deg for å delta nå, kan du trekke deg senere, og blodprøven destrueres hvis du ønsker det.

Med vennlig hilsen

Lisbeth Aasmoe og Berit Bang (prosjektledere)
Universitetssykehuset Nord-Norge, Tromsø

Samtykke-erklæring

Jeg har lest /er blitt forklart informasjonen om prosjekt "Luftveisplager i lakseindustrien" og samtykker i å delta i den begrensede helseundersøkelsen.

…………………………………………………………………………………….
Dato/Navn

Appendix C

Forespørsel om deltakelse i et forskningsprosjekt i regi av Arbeids- og miljømedisinsk avdeling, Universitetssykehuset Nord-Norge

Kontrollgruppe

Universitetssykehuset Nord-Norge har tidligere gjennomført en undersøkelse om arbeidsmiljø og helse i fiskeindustrien i Nord-Norge. Et av de viktigste funnene i den forrige undersøkelsen var en økt forekomst av luftveisplager i tilknytning til arbeid og kontakt med råstoffet. Vi er nå i gang med et nytt forskningsprosjekt der hovedformålet er å skaffe ny kunnskap om sammenhenger mellom eksponeringer og luftveisplager i kongekrabbeindustrien. Denne kunnskapen er viktig for å kunne forebygge plagene.

I dette prosjektet trenger vi også deltakelse fra arbeidstakere som ikke jobber i kongekrabbeindustrien, som skal fungere som en "kontrollgruppe" som vi kan sammenligne funn fra krabbeindustriarbeidere med. Vi spør deg derfor om du vil svare på spørsmål om arbeidsmiljøet og helsen din. Det er frivillig om du vil være med i undersøkelsen, og du må ikke begrunne hvorfor du eventuelt ikke vil delta. Det vil heller ikke få noen konsekvenser for forholdet til arbeidsplassen eller på annen måte om du ikke vil delta eller trekker deg på et senere tidspunkt. Selv om du bestemmer deg for å delta nå, kan du senere trekke deg når du ønsker, og opplysningene som er samlet inn om deg vil bli slettet hvis du ønsker det.

Prosjektet er finansiert av Helse-Nords forskningsmidler. Undersøkelsen er tilrådd av Personvernombudet for forskning, Norsk samfunnsvitenskapelige datatjeneste AS. Regional komité for medisinsk forskningsetikk, Nord-Norge, har vurdert prosjektet og har ingen innvendinger mot at prosjektet gjennomføres.

Det kan bli aktuelt å gjennomføre en oppfølgingsstudie ved et senere tidspunkt, og vi ønsker derfor å oppbevare de innsamlede opplysningene med personidentifikasjon i inntil 10 år i påvente av en slik undersøkelse. Opplysningene vil bli oppbevart ved en arkivinstitusjon som er godkjent av datatilsynet for oppbevaring av persondata. Ingen data vil være tilgjengelig for andre. Vi spør derfor om ditt samtykke til at opplysningene om deg blir arkivert etter prosjektets avslutning.

Vi har henvendt oss til bedriftshelsetjenesten for å få hjelp til å finne egnede arbeidstakere som kan inngå i en kontrollgruppe. Bedriftshelsetjenesten har mottatt spørreskjemaet og delt det ut til ansatte i din og andres bedrifter. Hvis du velger å delta skal det utfylte spørreskjemaet og samtykke-erklæringen sendes direkte til oss. Ingen fra bedriftshelsetjenesten har adgang til besvarelsene. Prosjektlederne lager en liste der navn og referansenummer kobles, og det er kun de som kjenner din identitet.

Samtykke-erklæringen, der du skriver navnet ditt, vil bli oppbevart adskilt fra spørreskjemaet. Ved senere publisering vil ingen opplysninger kunne føres tilbake til enkeltpersoner eller bedrifter.

Noen av de som besvarer spørreskjemaet vil senere få spørsmål om å delta i enkle medisinske undersøkelser, som lungefunksjonsundersøkelser og allergitester (blodprøver). Disse undersøkelsene vil ikke føre til ubehag utover et stikk i armen. Vi spør derfor om din tillatelse til å kontakte deg med forespørsel om en slik undersøkelse på et senere tidspunkt. Selv om du samtykker til å bli spurt har du likevel mulighet til å la være å samtykke til deltakelse i de medisinske undersøkelsene hvis du får henvendelse om dette.

Du får to kopier av dette brevet. Hvis du velger å delta sender du inn ett underskrevet eksemplar sammen med spørreskjemaet til oss i en ferdigfrankert konvolutt. Det andre eksemplaret beholder du selv. Besvart spørreskjema sendes i egen konvolutt.

Du kan når som helst ta kontakt med prosjektlederne på tlf 77628498 eller 77627463.

Med vennlig hilsen

Lisbeth Aasmoe og Berit Bang (prosjektledere)
Universitetssykehuset Nord-Norge

Referansenummer:

Samtykke-erklæring

	Ja
Jeg samtykker i å delta i spørreundersøkelsen	☐
Jeg samtykker i å bli spurt om å delta i en begrenset helseundersøkelse ved et senere tidspunkt	☐
Jeg samtykker i at opplysningene om meg arkiveres etter prosjektets avslutning	☐

____

Dato/Navn

Appendix D

Forespørsel om deltagelse i begrenset helseundersøkelse i forbindelse med forskningsprosjekt i regi av Arbeids- og miljømedisinsk avdeling, Universitetssykehuset Nord-Norge

Kontrollgruppe

Navn________________________________

Universitetssykehuset Nord-Norge (UNN) i Tromsø gjennomfører nå en undersøkelse om luftveisplager hos ansatte i lakseindustrien i Nord-Norge. I dette forskningsprosjektet trenger vi kontroller som ikke jobber med fisk.

Du har tidligere gitt tillatelse til at vi kan kontakte deg med forespørsel om å delta i en helseundersøkelse i sammenheng med dette prosjektet.

Vi spør deg derfor om du vil delta i en begrenset helseundersøkelse med fokus på luftveier og lunger

______dag ________ kl. ______ ved ________________________________

Svarene blir behandlet strengt fortrolig. Det er kun prosjektlederne som kjenner din identitet hvis du velger å delta. Ved senere publisering vil ingen opplysninger kunne føres tilbake til enkeltpersoner eller bedrifter.

Undersøkelsene består av følgende tester:

- Allergitest – Vi tar en blodprøve fra en blodåre i armen, som i ettertid skal analyseres på Universitetssykehuset Nord-Norge.
- Lungefunksjonstest – Vi måler mengden av- og hastighetene på luften som pustes inn og ut ved at det pustes gjennom et rør som er koblet til et måleapparat.
- Test av neseslimhinne – Vi måler tykkelsen av slimhinnen i nesen før arbeidet starter mandag morgen, og etter arbeidet er avsluttet torsdag ettermiddag. Det foregår ved å plassere en tynn slange fra et måleapparat ytterst i hvert av neseborene. Du puster enkelt gjennom munnen under undersøkelsen.
- NO-test. Vi måler mengden NO-gass i pustelufta. Den kan være forhøyet hvis luftveiene er irriterte eller betente.

Dette er enkle standardundersøkelser som normalt ikke fører til ubehag utover et stikk i armen ved blodprøvetakingen.

Enkeltpersoner med avvikende funn vil bli kontaktet direkte med oppfordring om å kontakte bedriftslege og/eller fastlege avhengig av problemstilling.

Hvis du ikke kan kommer til det oppsatte tidspunktet så kan du ta kontakt med en av oss enten pr brev, eller pr telefon. Du kan når som helst ta kontakt med prosjektlederne på tlf 77628498 eller 77627463. Vi er ikke på jobb i romjula, og treffes fra 2. januar.

Med vennlig hilsen

Lisbeth Aasmoe og Berit Bang (prosjektledere)
Universitetssykehuset Nord-Norge, Tromsø

Appendix E

UNIVERSITETSSYKEHUSET NORD-NORGE
DAVVI-NORGGA UNIVERSITEHTABUOHCCEVIESSU

Карта информационного согласия на участие в анкетировании

Имя ______________________________ Идентиф. номер: [ ]

Исследовательский проект проводится под руководством отделения профессиональной медицины и медицины окружающей среды, Университетская больница г.Тромсё, (Норвегия) при сотрудничестве с медицинским центром им.Семашко, Архангельск. Отделение профессиональной медицины и медицины окружающей среды несколько лет проводит исследования в области здоровья работников рыбной промышленности. Основная цель данного проекта - увеличить знания о факторах рабочей среды, которые оказывают влияние на развитие симптомов со стороны дыхательной системы. В последующем выявленная информация может оказаться полезной в проведении профилактики.

Мы просим Вас об участии в анкетировании, где вы будете опрошены о состоянии здоровья и характеристике рабочей среды.
Анкетирование проводится однократно.

Участие добровольное.

Проект одобрен норвежской и российской региональными этическими комиссиями.

Конфиденциальность информации
Вся информация, полученная в ходе проекта, будет в дальнейшем заархивирована и недоступна для других. В исследовании будут использованы идентификационные номера вместо имён, в целях защиты предоставляемой информации.
В публикациях и презентациях не будет представлена личная информация участников.

Вы получили 2 копии данного документа. В случае вашего согласия на участие в анкетировании, вы подписываете оба, 1 экземпляр оставляете себе, а второй отдаёте представителю исследования.

Одобрительное утверждение

Я ознакомился с выше описанной информацией и согласен участвовать в анкетировании.

Дата: Подпись:

Appendix F

ARBEIDSMILJØ OG HELSE I LAKSEINDUSTRIEN

Referanse nr ☐

PERSONALIA

1. Kjønn: Mann ☐ Kvinne ☐

2. Fødselsår (eks.: 1963) ☐

3. Er du norsk eller nordisk statsborger med fast bosted i Norge? Ja ☐ Nei ☐

4. Har du bodd sammenhengende i Norge de siste fem årene? Ja ☐ Nei ☐

5. Hvor mange års utdanning har du totalt (inkludert barneskole, ungdomsskole, videregående skole, senere skolegang/studier)

☐ år

6. Spiser du fisk? Ja ☐ Nei ☐

7. Hvis ja, hvor ofte spiser du fisk? _________ ganger pr uke

_________ ganger pr måned

8. Jobber du i lakseindustrien? Ja ☐ Nei ☐

Hvis nei, gå til spørsmål 15

GENERELT OM ARBEIDSFORHOLD

9. I hvor mange år har du totalt jobbet i lakseindustrien? ☐ år

10. Hvor i bedriften jobber du - hvilken avdeling?

	Ja, mer enn halvparten av tida	Ja, mindre enn halvparten av tida
Slakteri	☐	☐
Videreforedling av laks (Filetering, porsjonspakking etc.)	☐	☐
Administrasjon/kontor	☐	☐
Annet	☐	☐

11. Hvor i bedriften jobber du – hvilke arbeidsoppgaver har du?

	Ja, mer enn halvparten av tida	Ja, mindre enn halvparten av tida
Bløgging	☐	☐
Sløyemaskin	☐	☐
Etterrensing	☐	☐
Skjæring/kutting av filet med maskiner	☐	☐
Filetkutting for hånd	☐	☐
Røyking av fisk	☐	☐
Vektsortering/kvalitetskontroll av fisk	☐	☐
Pakking av fisk	☐	☐
Kjølerom/kjølelager	☐	☐
Fryselager	☐	☐
Håndtering av fiskeavfall	☐	☐
Produksjon av fiskemat/videreforedling av produkter	☐	☐
Teknisk vedlikehold av produksjonsmaskiner	☐	☐
Laboratorium	☐	☐
Kontor/administrasjon	☐	☐
Annet	☐	☐

12. Arbeider du med spyling (f. eks gulv, maskiner) på din arbeidsplass?

Ja, ofte (hver dag) ☐   Ja, iblant ☐   Nei, sjelden ☐

Hvis ja, ofte, hvor ofte gjør du det? _________ *ganger pr dag*

	Alltid	Av og til	Sjelden/aldri
13. Bruker du maske/munnbind når du jobber?	☐	☐	☐

14. Hva slags aktivitet har du vanligvis hatt i <u>arbeidet</u> ditt siste 12 måneder? *(ett kryss)*

Lett fysisk aktivitet, for det meste stillesittende/stående arbeid ☐
(f.eks kontorarbeid, filetkutting)

Arbeid som krever at du beveger deg mye ☐

Arbeid som krever at du beveger deg og løfter mye ☐

Tungt fysisk arbeid ☐

GENERELT OM HELSETILSTANDEN

15. Har du eller har du hatt en eller flere av følgende plager/sykdommer etter du fylte 15 år? (*flere kryss er mulig)*

		Hvis ja, har en lege bekreftet det?	
	Ja	Ja	Nei
Astma	☐	☐	☐
Kronisk bronkitt/emfysem/KOLS	☐	☐	☐
Tuberkulose	☐	☐	☐
Angina pectoris (hjertekrampe)	☐	☐	☐
Hjerteflimmer (atrieflimmer)	☐	☐	☐
Hjerteinfarkt	☐	☐	☐
Høyt blodtrykk	☐	☐	☐
Andre hjertesykdommer	☐	☐	☐
Hudeksem	☐	☐	☐
Allergi	☐	☐	☐
Reumatisk sykdom	☐	☐	☐

16. Har du som barn hatt en eller begge av følgende plager/sykdommer? (*flere kryss er mulig)*

Astma (barneastma)? ☐

Eksem (atopisk eksem)? ☐

17. Hvis du er allergisk, hva er du allergisk mot? (*flere kryss er mulig)*

Laks	☐	Pollen, gress	☐
Sild	☐	Støv	☐
Torsk	☐	Mat	☐
Reker/skalldyr	☐	Dyr	☐
Annen fisk	☐	Annet (hva) _______________	

	Ja	Nei
18. Har du i løpet av de siste 12 måneder hatt piping i brystet?	☐	☐
19. Hvis ja på spørsmål 18, var du tungpustet også?	☐	☐
20. Hoster eller harker (kremter) du vanligvis om morgenen?	☐	☐
21. Hvis ja på spørsmål 20, har du vanligvis oppspytt?	☐	☐
22. Hoster du nærmest daglig til sammen 3 måneder eller lenger i løpet av et år?	☐	☐

23. Har du i løpet av de siste 12 månedene hatt rennende eller tett nese som ikke har vært forkjølelse eller influensa?

Ja ☐ Nei ☐

Hvis nei, gå til spørsmål 30

24. Hvis ja på spørsmål 23, har du samtidig hatt

	Ja	Nei
kløende, rennende øyne	☐	☐
søvnproblemer	☐	☐

25. Hvis ja på spørsmål 23, tror du at det kan være spesielle faktorer (lukt, irriterende stoffer, temperatur o.l.) som forårsaker neseplagene?

Ja ☐ Nei ☐

Hvis ja, hvilke faktorer du tror det er? ________________________________

26. Hvis ja på spørsmål 23, i hvilken av de siste 12 månedene har du hatt disse symptomene?

Januar	☐	Mai	☐	September	☐
Februar	☐	Juni	☐	Oktober	☐
Mars	☐	Juli	☐	November	☐
April	☐	August	☐	Desember	☐

27. Hvis ja på spørsmål 23, når oppstår neseplagene?

	Ja	Nei
Hvert år, og alltid på samme årstid	☐	☐
I forbindelse med arbeidet ditt	☐	☐
Hvis ja, forsvinner plagene i helger og ferier?	☐	☐
I forbindelse med bruk av dispril eller andre smertestillende medisiner	☐	☐

Hvis ja, hvilke medisiner ________________________________

28. Hvis du har hatt neseplager siste 12 måneder, hvor ofte har du hatt disse plagene?

Mindre enn 4 dager pr uke eller til sammen mindre enn 4 uker siste år ☐
Mer enn 4 dager pr uke og til sammen mer enn 4 uker siste år ☐

29. Hvis du har hatt neseplager siste 12 måneder, har de hemmet deg i dine daglige gjøremål som skole, arbeid, fritidsaktiviteter og/eller sport?

Nei, ikke i det hele tatt ☐
Litt ☐
Noe, endel ☐
Mye ☐

30. Har du noen gang hatt

	Ja	Nei
Høyfeber	☐	☐
Astma	☐	☐
Hudallergi	☐	☐

31. Har noen i din familie noen gang hatt

	Ja	Nei
Astma	☐	☐
Hudallergi	☐	☐
Neseallergi	☐	☐

32. Hvordan vurderer du din egen helse sånn i alminnelighet? *(ett kryss)*

Meget god ☐
God ☐
Verken god eller dårlig ☐
Dårlig ☐
Meget dårlig ☐

33. Hvordan synes du at helsen din er sammenlignet med andre på samme alder? *(ett kryss)*

Mye bedre ☐
Litt bedre ☐
Omtrent lik ☐
Litt dårligere ☐
Mye dårligere ☐

HELSEPLAGER I FORBINDELSE MED ARBEIDET

Spørsmålene under dette punktet omhandler helseplager som kommer mens du er på jobb eller like etter du har vært på jobb. Selv om du har svart på lignende spørsmål tidligere i dette spørreskjemaet, ber vi deg svare på disse i tillegg.

34. Har du i forbindelse med arbeidet du utfører hatt noen av følgende symptomer/plager siste 12 måneder?
(Hvis du ikke har hatt noen symptomer setter du ingen kryss. Flere kryss er mulig)

	Ja, ofte (hver uke)	Ja, iblant
Tørrhoste	☐	☐
Hoste med slim	☐	☐
Piping i brystet	☐	☐
Trykk over brystet	☐	☐
Brystsmerter	☐	☐
Åndenød, tett i brystet	☐	☐
Hyppig nysing	☐	☐
Irritert, tett eller rennende nese	☐	☐
Heshet, sår hals eller irritasjon i halsen	☐	☐
Tung i hodet/hodepine	☐	☐
Kløe, svie, irritasjon i øynene	☐	☐
Unormal tretthet	☐	☐

Frysninger/muskelsmerter/feber uten at du har hatt influensa aller annen infeksjon ☐ ☐

35. Dersom du har opplevd noen av plagene som er listet opp under spørsmål 34, under/etter hvilket arbeid eller hvilken arbeidsprosess oppstod plagene? *(Flere kryss er mulig)*

- Bløgging ☐
- Sløyemaskin ☐
- Etterrensing ☐
- Skjæring/kutting av filet med maskiner ☐
- Filetkutting for hånd ☐
- Røyking av fisk ☐
- Vektsortering/kvalitetskontroll av fisk ☐
- Pakking av fisk ☐
- Kjølerom/kjølelager ☐
- Fryselager ☐
- Håndtering av fiskeavfall ☐
- Produksjon av fiskemat/videreforedling av produkter ☐
- Teknisk vedlikehold av produksjonsmaskiner ☐
- Laboratorium ☐
- Kontor/administrasjon ☐
- Annet ☐ Hva? ____________________

36. Dersom du har opplevd noen av plagene som er listet opp under spørsmål 34, hva tror du selv kan være årsak til plagene? *(Flere kryss er mulig)*

- Sprut fra maskiner og/eller fra dyser ☐
- Sprut i forbindelse med bløgging ☐
- Kontakt med laks ☐
- Kontakt med innvoller/fiskeavfall ☐
- Kalde omgivelser/kulde ☐
- Vaskemidler / desinfeksjonsmidler ☐
- Spyling ☐
- Forurenset luft ☐
- Eksos ☐
- Annet (hva?)____________________

37. Har du noen gang skiftet arbeidsoppgaver i bedriften på grunn av luftveisplager?

Ja ☐ Nei ☐

Hvis ja, hvilke arbeidsoppgaver måtte du skifte fra? ____________________

	Nesten alltid	Av og til	Aldri
38. Bruker du hansker under arbeid?	☐	☐	☐

39. Har du i forbindelse med arbeidet du utfører hatt noen av følgende symptomer/plager siste 12 måneder? *(flere kryss er mulig)*

Kløe, svie, irritasjon i øynene	☐	Tørr hud	☐
Hudkløe	☐	Sprukken hud	☐
Utslett	☐	Sår som gror dårlig	☐

40. Hvis du har hudplager, angi hvor på kroppen du har disse plagene: *(flere kryss er mulig)*

Hender	☐	Underarm	☐
Ansikt	☐	Hele kroppen	☐
Andre steder	☐		

RØYKING

41. Røykevaner *(sett bare ett kryss)*

Røyker daglig ☐ Røyker av og til ☐ Har røkt tidligere ☐ Nei, har aldri røkt ☐

Hvis nei, har aldri røkt; gå til spørsmål 46.

42. Hvis du har røkt tidligere, hvor mange år er det siden du sluttet?

Antall år ☐

43. Hvor mange sigaretter røyker eller røkte du vanligvis daglig?

Antall sigaretter ☐

44. Hvor gammel var du da du begynte å røyke daglig?

Antall år ☐

45. I hvor mange år til sammen har du røkt?

Antall år ☐

TERMISK MILJØ

46. Fryser du når du er på arbeid?

Ja, ofte ☐ Ja, iblant ☐ Nei, sjelden/aldri ☐

47. Hvor oppholder du deg mesteparten av arbeidstiden din? *(ett kryss)*

Oppvarmet lokale ☐ Ikke oppvarmet lokale ☐ Kjølelager/utendørs ☐

48. Besvares hvis du jobber mesteparten av tiden på kjølelager eller utendørs:

Har du noen gang opplevd noen av disse symptomer mens du oppholder deg i kjølelager/utendørs?

	Ja	Nei
Pusteproblemer	☐	☐
Langvarig hoste	☐	☐
Pipende pust	☐	☐
Slim fra lungene	☐	☐
Brystsmerter	☐	☐
Forstyrrelse i hjerterytmen	☐	☐
Nedsatt blodsirkulasjon i hender/føtter	☐	☐

Appendix G

UNIVERSITETSSYKEHUSET NORD-NORGE
DAVVI-NORGGA UNIVERSITEHTABUOHCCEVIESSU

Идентиф.номер: ☐

АНКЕТА

Поставьте крест при положительном ответе, ответов может быть несколько.

Личные данные.

1. Пол

❑ Мужчина ❑ Женщина

2. Возраст ☐

3. Количество лет образования (включая школу, училище, институт и т.д.) ☐

4. Употребляете ли в пищу рыбу?

❑ Да ❑ Нет

5. Если да, то, как часто?

☐ раз в неделю ☐ раз в месяц

6. Сколько лет вы работаете на флоте?

☐ Лет

7. Вы работаете на *рыбном* траловом флоте?

❑ Да ❑ Нет

Если нет, укажите наименование флота. И следуйте далее к вопросу 12. ....

8. а) В ваши рабочие обязанности входит работа с рыбой? (имеется ввиду любая, даже несущественная работа с рыбой и которая может не относиться к вашим прямым обязанностям и рассматриваться как помощь вашим сотрудникам).

❑ Да ❑ Нет

б) Какой вид рыб добывается на судне, где вы непосредственно работаете?

Скумбрия	❑	Морской окунь	❑
Сельдь	❑	Краб	❑
Треска	❑	Пикша	❑
Морская камбала	❑		

Другая рыба (указать название) ....

....

9. Какая ваша конкретная задача (при условии, что вы включены в работу непосредственно с рыбой)?

	Это моя основная задача	Иногда	Ранее
Потрошение рыбы	❑	❑	❑
Чистка рыбы	❑	❑	❑
Нарезка рыбы с помощью механизированного оборудования	❑	❑	❑
Нарезка рыбы вручную	❑	❑	❑
Контроль качества рыбы (весовой контроль)	❑	❑	❑
Упаковка рыбы	❑	❑	❑
Заморозка рыбы	❑	❑	❑
Работа с рыбными отходами	❑	❑	❑
Консервирование рыбы	❑	❑	❑
Работа по производству рыбной муки	❑	❑	❑

Другая ....

.... (указать)

10. Вы используете перчатки при работе с рыбой?

❑ Да ❑ Нет ❑ Иногда

11. Вы используете маску при работе с рыбой?

❑ Да ❑ Нет ❑ Иногда

12. Степень физической активности, которую требует ваша работа

Лёгкая физическая активность	❑
Требует много движений	❑
Требует много движений и подъём груза	❑
Тяжёлая физическая работа	❑

Общее состояние здоровья

13. Имеется ли у вас, или когда-нибудь наблюдалось после исполнения вам 15 лет следующее:

	Да	Подтверждено врачом? Да	Подтверждено врачом? Нет
Астма	❑	❑	❑
Бронхит	❑	❑	❑
Туберкулёз	❑	❑	❑
Стенокардия	❑	❑	❑
Инфаркт сердца	❑	❑	❑
Высокое кровяное давление	❑	❑	❑
Заболевания сосудов	❑	❑	❑
Экзема кожи	❑	❑	❑
Аллергия	❑	❑	❑
Ревматизм	❑	❑	❑

14. Была ли у вас в детстве

Астма	❑
Аллергия	❑
Экзема	❑

15. Имеется ли у вас аллергия на:

Рыба	❑	Пыльца растений	❑
Пыль	❑	Пищевые продукты	❑
Животные	❑	Другие факторы	❑
Креветки	❑		

16. Наблюдали ли вы у себя за последние 12 месяцев хрипы/свист в груди?

❑ Да ❑ Нет

17. Наблюдалось ли сжатие в груди (скованность в дыхании) за последние 12 месяцев?

❑ Да ❑ Нет

18. Наблюдается ли кашель по утрам?

❑ Да ❑ Нет

19. Наблюдается ли мокрота при кашле?

❑ Да ❑ Нет

20. Пробуждаетесь ли вы ночью по причине кашля?

❑ Да ❑ Нет

21. Имеется ли у вас ежедневный кашель в течение 3-х месяцев или продолжительнее чем 1 год?

❑ Да ❑ Нет

22. Испытывали ли Вы ощущение нехватки воздуха за последние 12 месяцев?

❑ Да ❑ Нет

23. Сколько раз за последние 12 месяцев у вас было ОРЗ (простуда)?

0-2 раза	❑
Больше 2-х раз	❑

24. Имеются ли у вас за последние 12 месяцев насморк, заложенность или раздражение в носу не связанные с простудой?

❑ Да ❑ Нет

Если да на вопрос 24, наблюдалось ли одновременно с насморком:

Жжение и слёзоточивость глаз	❑
Проблемы со сном	❑

Если да на вопрос 24, как вы считаете, может ли это быть связано с особенными условиями (например, запахом, раздражающими веществами в рабочей зоне, температура в помещении)?

❑ Да ❑ Нет

Если да на вопрос 24, в какой(ие) месяц обычно наблюдается?

Январь	❑	Май	❑	Сентябрь	❑
Февраль	❑	Июнь	❑	Октябрь	❑
Март	❑	Июль	❑	Ноябрь	❑
Апрель	❑	Август	❑	Декабрь	❑

Если да на вопрос 24, когда преимущественно появляется насморк?

В одно и тоже время года ❑
Связано с работой ❑
Если связано, исчезает ли во время выходных или отпуска? ❑
Появляется при использовании обезболивающих ❑

Если да на вопрос 24, как часто наблюдается такого рода насморк?

Меньше чем 4 раза в неделю ❑
Больше чем 4 раза в неделю ❑
В общем меньше чем 4 недели за последний год ❑
В общем больше чем 4 недели за последний год ❑

25. Как бы вы оценили своё здоровье?

Очень хорошее	❑	Плохое	❑
Хорошее	❑	Очень плохое	❑
Нормальное	❑		

26. Как бы вы оценили ваше здоровье по сравнению с другими людьми того же возраста?

Лучше чем у других ❑
Такое же ❑
Хуже ❑

27. Непосредственно во время выполнения своей работы наблюдалось ли у вас следующее за последние 12 месяцев:

	Да, часто (кажд.неделю)	Иногда
Сухой кашель	❑	❑
Раздражение в горле	❑	❑
Кашель с мокротой	❑	❑
Головная боль	❑	❑
Хрип/свист в груди	❑	❑
Раздражение в глазах	❑	❑
Сжатие в груди	❑	❑
Необычная усталость	❑	❑
Боль в груди	❑	❑
Озноб, боли в мышцах	❑	❑
Стеснение в груди	❑	❑
Заложенность носа, насморк	❑	❑
Частое чихание	❑	❑

28. Если вы испытывали 1 или больше из выше перечисленных жалоб, при выполнении каких задач преимущественно это появлялось (при условии что вы включены в работу с рыбой)?

Потрошение рыбы ❑
Чистка рыбы ❑
Промыв рыбы ❑
Нарезка рыбы вручную ❑
Нарезка рыбы с помощью механизированного оборудования ❑
Сортировка ❑
Проверка качества рыбы ❑
Консервирование ❑
Заморозка ❑
Упаковка рыбы ❑
Продукция муки ❑
Утилизация рыбьих отходов ❑
Варка рыбы ❑
Сушка рыбы ❑
Техническое обслуживание оборудования на фабрике ❑

Другое..

....

29. Если вы испытывали выше изложенные жалобы (один или несколько) в вопросе 27, как вы думаете какая причина может быть тому?

Контакт с рыбой ❑
Контакт с рыбьими отходами ❑
Контакт с рыбной мукой ❑
Холодный воздух ❑
Горячий воздух ❑

Использование дополнительных средств (химических, дезинф.) при работе ❑
Загрязнённый воздух рабочего помещения ❑

Другое ....

....

30. Вы когда-нибудь меняли работу по причине жалоб со стороны дыхательной системы?

❑ Да ❑ Нет

31. При выполнении работы, наблюдалось ли у вас следующее:

Раздражение в глазах ❑
Зуд кожи ❑
Сыпь ❑
Сухость кожи ❑
Трещины на коже ❑
Плохо заживающие раны ❑

32. Есть ли у вас имеются повреждения кожи? где на теле они располагаются?

Руки ❑ Предплечья ❑
Лицо ❑ Всё тело ❑

Другие места ....

....

33. Курение

Курю ❑
Бросил ❑
Курю иногда ❑
Нет, не курю ❑

34. Сколько лет вы курите (курили ранее)?

[ ] Лет

35. Сколько сигарет вы курите (курили) в неделю?

[ ] кол-во сигарет

36. Испытываете ли вы холод на работе?

❑ Да ❑ Нет ❑ Иногда

37. Рабочее место, где вы находитесь большую часть времени имеет:

Централизованный обогрев ❑
Местный обогрев (переносной обогреватель) ❑
Не обогревается ❑

38. Испытываете ли вы ощущение холода на работе?

❑ Да ❑ Нет ❑ Иногда

39. Если вы работаете большую часть времени в холодном помещении или снаружи судна имеются ли у вас следующие жалобы:

Длительный кашель ❑
Хрипы при дыхании ❑
Кашель с мокротой ❑
Боль в груди ❑
Затруднённое дыхание ❑
Проблемы с сердцем ❑
Холодные конечности ❑

Большое спасибо за ваше участие в исследовании!

Appendix H

Spørsmål om symptomer/ plager under arbeidet

Navn med blokkbokstaver____

Dag____

Har du hatt noen av følgende plager under arbeid i dag?

	Sett kryss hvis du har hatt plager
hoste	
piping i brystet	
åndenød, tett i brystet	
hypping nysing	
irritert eller tett nese	
heshet eller irritasjon i halsen	
tung i hodet/hodepine	
unormal tretthet	
frysninger/muskelsmerter	
kløe, svie irritasjon av øynene	

Var arbeidet (Sett kryss)

Lettere enn normalt ?	
Som normalt ?	
Tyngre enn normalt ?	

Hvordan opplevde du temperaturen i arbeidslokalet (sett kryss)

Passe	
For varmt	
For kaldt	

Har du utfyllende kommentarer, så noter dette her:

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