Faculty of Health Sciences
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Diagnostic tests for lung and heart diseases in primary care – from quality assurance to epidemiology

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“Nikolai Astrup: Spring Night and Willow (1917).”
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“How do we produce work that touches the heart? We don’t want to live a frivolous life, we don’t want to live a superficial life. We want to be serious with each other, with our friends, with our work. That doesn’t necessarily mean gloomy or grim, but seriousness has a kind of voluptuous aspect to it. It is something that we are deeply hungry for; to take ourselves seriously and to be able to enjoy the nourishment of seriousness, that gravity, that weight”. *Leonard Cohen*
Kort norsk sammendrag - Short Norwegian summary

Spirometri og pulsoksymetri er i økende bruk i allmennpraksis. Spirometri brukes både i diagnostikk og oppfølging av lungesykdommer og enkelte legemedier krever utført spirometri før de berettiger refusjon på blå resept. Pulsoksymetri er en undersøkelsesmetode for analysering av oksygenmetning i arterielt blod (SpO₂). Testen er godt egnet for bruk i fastlegepraksis fordi den er enkel og rask å utføre. Lave verdier kan tyde på hjerte- og/eller lungesykdom.

Avhandlingen er basert på tre studier av voksne pasienter/individer, den første er et kvalitetssikringsprosjekt av egen praksis (Lillestrømstudien), den andre fra 7 fastlegepraksiser lokalisert i nord og sør Norge (DIOLUP studien) og den tredje fra en befolkningsundersøkelse (Tromsø 6). I alle tre studiene ble det utført lungefunksjonstesting med spirometri og i de to siste studiene ble oksygenmetning målt med pulsoksymetri. Lav oksygenmetning ble definert som SpO₂ ≤95 % i begge studier.

I Lillestrømstudien undersøkte vi allmennlegenes diagnosekoding før og etter endring av refusjonsreglene for inhalasjonssteroider i 2007. Forhåndsgodkjent refusjon til inhalasjonssteroider forutsatte diagnosen astma. Legene endret diagnose koder slik at de passet bedre med behandlingen som var gitt, flere fikk diagnosen astma. Spirometri var nyttig til å identifisere overforbruk av inhalasjonssteroider og bør sammen med sykehistorie og klinisk undersøkelse brukes til å kvalitetssikre pasientens behandling av obstruktive lungesykdommer i allmennpraksis.

I DIOLUP studien, basert på pasienter i en stabil fase av sin astma og/eller kronisk obstruktiv lungesykdom (KOLS), var lav SpO₂ forbundet med redusert lungefunksjon (FEV₁ % av forventet), diagnostisert koronar hjertesykdom og alder > 65 år. Dette tyder på at pulsoksymetri kan være nyttige hos denne pasientgruppen i allmennpraksis. Lave verdier bør medføre at fastlegen gjør en ekstra vurdering av om pasienten er for dårlig behandlet av sin lungesykdom og/eller har udiagnostisert hjertesykdom.

I befolkningsundersøkelsen Tromsø 6 ble sammenhengen mellom lave pulsoksymetriverdier og ekkokardiografiske målinger av venstre ventrikkels fylning undersøkt. Lav oksygenmetning var en signifikant prediktor for redusert diastolisk fylning (et mål for diastolisk dysfunksjon). Hypertensjon og overvekt var også signifikante prediktorer for redusert diastolisk fylning. Diastolisk dysfunksjon bør inkluderes blant mulig forklaringer når redusert oksygenmetning blir påvist.
English summary

Spirometry and pulse oximetry tests are in increasing use in general practice. Spirometry is used in both the diagnosis and monitoring of respiratory diseases and in Norway some drugs require spirometry to have been performed before a prescription is reimbursed. Pulse oximetry is a non-invasive method for measuring oxygen saturation (SpO₂). The pulse oximeter is a particularly helpful tool in primary care because it is tolerable for the patient, easy to use, acceptable within the time constraints of a busy practice and inexpensive. Decreased pulse oximetry values may indicate heart and/or respiratory disease.

The thesis is based on three studies of adult patients/participants. The first is a quality project at our own practice (Lillestrøm study), the second a cross-sectional study in seven GP practices located in north and south Norway (DIOLUP study) and the third a cross-sectional study based on the sixth (2007/2008) survey of the Tromsø Study. In all studies, pulmonary function testing with spirometry was performed; in Studies II and III, oxygen saturation was measured by pulse oximetry. Low oxygen saturation was defined as SpO₂ ≤ 95%.

In the Lillestrøm study, we described how GPs’ diagnoses changed after new conditions for reimbursement of costs for inhaled corticosteroids (ICS) were introduced in Norway in 2006. The principle was that costs for ICS should only be reimbursed with a diagnosis of asthma. GPs’ diagnostic practice changed to make the diagnoses fit better with the treatment given. A clinical audit including spirometry was found to be useful for identifying overuse of ICS.

Spirometry is useful in general practice for the follow-up of patients with obstructive lung diseases to assure their quality of treatment.

In the DIOLUP study, based on patients in a stable phase of asthma and/or chronic obstructive pulmonary disease (COPD), patients with moderately decreased oxygen saturation had an increased risk of severely reduced lung function (FEV₁% predicted) and co-morbid coronary heart disease. This suggested that pulse oximetry may be useful in these patients in general practice and that patients with SpO₂ values ≤ 95% should be given special attention and followed up more closely than patients with normal oxygen saturation.

In the sixth Tromsø study, the relationship between low pulse oximetry values and echocardiographic indicators of left ventricular filling was examined. Low oxygen saturation was independently associated with abnormal mitral Doppler flow as a measure of diastolic dysfunction. Hypertension and obesity were also significant predictors of impaired left ventricular filling. Diastolic dysfunction should be considered as a possible explanation of low SpO₂ values.
List of papers


Abbreviations

ATS – American Thoracic Society
A-wave – peak velocity flow in late diastole
BMI – body mass index
BSA – body surface area
CI – confidence interval
COPD – chronic obstructive pulmonary disease
CRP – C-reactive protein
CHD – coronary heart disease
CV – coefficient of variation
CVD – cardio-vascular disease
EDT – E-wave deceleration time
EPR – electronic patient record
ERS – European Respiratory Society
EUTRO – the Tromsø Study database
E-wave – peak velocity flow in early diastole
FEV$_1$ – forced expiratory volume in 1 second
FVC – forced vital capacity
GOLD – Global Initiative for Chronic Obstructive Lung Disease
GP – general practitioner
HF – heart failure
HFpEF – heart failure with preserved ejection fraction
Hunt Study – Nord-Trøndelag Health Study
ICS – inhaled corticosteroids
LA – left atrium
LV – left ventricular
LVEF – left ventricular ejection fraction
LLN – lower limit of normal
OECD – Organisation for Economic Co-operation and Development
OR – odds ratio
PaO$_2$ – partial pressure of oxygen in arterial blood
PaCO$_2$ – partial pressure of carbon dioxide in arterial blood
pH – value for expressing the concentration of H$^+$ ions
QRS complex – a combination of the Q wave, R wave and S wave represents ventricular depolarization on an electrocardiogram

SaO₂ – arterial oxygen saturation measured by blood gas test

SD – standard deviation

SpO₂ – arterial oxygen saturation measured by pulse oximetry

SPSS – Statistical Package for the Social Sciences

TDI – tissue Doppler imaging

WHO – World Health Organization
Definitions

BMI: body mass index, weight divided by height squared (kg/m$^2$).
Dyspnoea: uncomfortable awareness of one’s efforts to breathe.
Hypoxia: insufficient oxygen supply.
Hypoxaemia: low arterial oxygen supply; abnormally low level of oxygen in the blood.
Obesity: BMI $\geq 30$ kg/m$^2$.
Pulse oximeter: non-invasive device for estimating oxygen saturation.
Pulse oximetry: procedure of using a pulse oximeter.
SpO$_2$: normal value 96–100%; low value: $\leq 95%$. 
1. Introduction

This PhD thesis deals with methods of diagnosis and assessment of common pulmonary and heart diseases, which are frequently seen in general practice.

1.1 Chronic obstructive pulmonary disease (COPD)

Tobacco smoking is the most important cause of COPD in high-income countries and is also a risk factor for heart failure (HF)(1, 2). Other irritants, including workplace exposure to fumes, chemical substances, and dust, can also cause COPD (3), although the evidence that air pollution can cause the development of COPD is not conclusive (4). Genetic factors and childhood infections also play a role in the development of COPD (5). The disease develops when inflammatory mechanisms in the lung are activated and lead to tissue damage (6). Insufficient repair of alveolar structures leads to emphysema and repair with scarring causes airflow limitation and chronic bronchitis (6). Typical symptoms of COPD are chronic productive cough, wheezing, symptoms provoked by exercise and dyspnoea (7). Both crackles and wheezes are common findings on auscultation of patients with stable COPD and increase in frequency during exacerbations (8). However, disagreement about the use of terms describing lung sounds in patients with lung diseases weakens the diagnostic value of auscultation (9). Increased wheezing, as experienced by the patient, is associated with a drop in lung function during asthma and COPD exacerbations (8). An absence of wheezing or chest tightness does not exclude a diagnosis of COPD (9, 10).

1.2 Asthma

Asthma is a chronic inflammatory airway disease characterized by bronchial hyper-responsiveness and reversible airway obstruction (11). It is characterized by episodic and reversible attacks of wheezing, chest tightness, shortness of breath and coughing. COPD and asthma have clear differences, but some patients have a mixture of both diseases (12). A typical patient is an asthmatic smoker who develops an airway obstruction that is not fully reversible airway obstruction (12).

1.3 Heart failure (HF)

HF results from injury to the myocardium from a variety of causes (13). Ischaemic heart disease and hypertension are the main causes of HF. The typical patient in general practice is
an older woman with long-standing hypertension, often suffering from diastolic HF, while cardiologists see predominantly men in their 60s who have had a myocardial infarction and are suffering from systolic HF (14). The pathophysiology underlying diastolic HF is heterogeneous and the patients are often older and have concomitant cardio-vascular disease (CVD) and non-CVDs such as COPD, diabetes, obesity, chronic kidney disease and anaemia (15, 16). In Western industrialized countries, the mean systolic blood pressure and the mortality from ischaemic heart disease have decreased (17), but other conditions are increasingly associated with HF, such as diabetes, COPD, valvular diseases and the use of cardiotoxic drugs. HF does not have a simple objective definition: its diagnosis requires the presence of several clinical features and objective evidence of cardiac dysfunction (18).

Typical symptoms are breathlessness, orthopnoea, nocturnal dyspnoea, reduced exercise tolerance, fatigue and ankle swelling (15). Symptoms of HF are often non-specific and may be difficult to identify and interpret in patients with COPD (15). In a primary health care study from Finland, auscultation of the lung was usually performed in patients with HF (19). The prevalence of HF in this Finnish study was higher than in many clinical studies suggesting the occurrence of false-positive HF diagnosis in primary health care (19). Lung auscultation is commonly used in clinical practice but has limited diagnostic value in HF (20, 21).

With increasing life expectancy, HF has become an increasing health problem in industrialized countries. In high-income countries, it is the most common diagnosis in patients aged 65 years or older who are admitted to hospital (22). Hospital admissions for congestive HF can be avoided if high-quality primary care is provided (23). In Norway, in 2010 the rate of hospital admissions for congestive HF was 1.6 per 1000 population, which is much lower than the Organisation of Economic Co-operation and Development (OECD) average of 2.4 per 1000 (23). Access to primary care is generally good in Norway (23).

Despite some progress, the prognosis of HF is worse than that of most cancers (22). Coronary heart disease (CHD) carries the highest relative risk among the risk factors for HF (24). Registry studies have revealed that HF with preserved ejection fraction (HFpEF) represents approximately half the acute presentations of HF and has similarly high mortality and re-hospitalization rates as those for patients with HF and reduced EF (25).

1.4 Coexistence of obstructive pulmonary diseases and heart failure

HF, COPD, and asthma frequently coexist (26). COPD and HF share one common symptom, namely shortness of breath. In clinical practice, the diagnosis of COPD and HF is often based
on history, without spirometry and echocardiography, which are needed for reliable diagnosis (26). Pulmonary congestion may cause airway obstruction because of external obstruction of alveoli and bronchioles in patients with heart failure leading to a false diagnosis of COPD based on the spirometry criterion of a ratio of forced expiratory volume in 1 second (FEV₁) to the total volume of air that the patient can forcibly exhale in one breath, forced vital capacity (FVC) (i.e., FEV₁/FVC) < 0.7 (27, 28). Both intra- and extra-broncheolar (fluid) obstruction can cause a reduction in FEV₁/FVC, but pulmonologists often consider only the first (28). Accordingly, the diagnosis of co-morbid COPD in HF should not be based on a single spirometry test in unrecompensated HF patients (27). This may be why the reported prevalence rates of COPD among HF patients range from 9 to 52% (18). COPD may be overdiagnosed in patients with HF; it is important to keep this in mind to avoid potentially harmful overtreatment with bronchodilators (27). Spirometry should be performed when patients are in a stable phase of their HF (28).

The coexistence of COPD and HF increases the risk of death (26). In the general population, COPD is more prevalent than HF and unrecognized HF is common in older patients with stable COPD diagnosed by a general practitioner (GP) (29, 30). CVD and COPD are the first and the fourth leading causes of death from disease worldwide (31). In general practice in the United Kingdom, the consultation rates for COPD exceed those for ischaemic heart disease (32). Many people suffer from COPD for years, and die prematurely from it or its complications (33). In a single primary care practice, the main causes of death in COPD patients were CVD, COPD exacerbation and lung cancer (34). Most deaths in people with mild to moderate COPD are the result of CVD or lung cancer, but in patients with severe COPD, death because of this respiratory disease is common (35). In 2014, 30% of deaths in Norway were caused by CVD and 5% were caused by COPD, chronic bronchitis or emphysema (36). Lack of awareness and late detection of these conditions are issues, and it is essential to support and develop the primary health care services required for their early detection and management (37). Treatment of COPD is now aimed at reducing the impact of symptoms and the risk of future adverse health events, which requires individualized assessment of the disease (38).

The relationship between COPD and CVD is clinically relevant because CVD is the most common co-morbidity and the leading cause of hospitalization in patients with mild to moderate COPD (39). Evidence suggests that patients with COPD should be screened for concomitant atherosclerosis and patients with CVD for concomitant airflow limitation (40). In the Lung Health Trial, in which 6,000 patients were followed over 14 years, impaired lung
function (assessed by FEV$_1$) was an independent predictor of dying from a myocardial infarction (41). COPD, independent of cigarette smoking and aging, doubles the risk of CVD hospitalization and death (39). Even in patients with mild COPD, evaluation for occult CVD is warranted and aggressive treatment to reduce the burden of both lung disease and atherosclerosis is needed to mitigate the future risk of acute cardio-vascular events in patients with COPD (42). Exertional breathlessness, paroxysmal nocturnal dyspnoea and nocturnal cough are common in both HF and COPD (18). No qualitative features of dyspnoea are unique to HF (43). Clinical symptoms require careful interpretation, together with objective evidence of each disease (18).

1.5 Pathophysiology of low oxygen saturation

Ventilation/perfusion mismatch in COPD is caused by airflow limitation and emphysema: hypoxia leads to pulmonary vaso-constriction and right cardiac chamber enlargement (*cor pulmonale*) (44). Pulmonary arterial hypertension is secondary to COPD and the prevalence of right ventricular hypertrophy and right cardiac chamber enlargement is higher in patients with severe COPD than in those with mild to moderate COPD (45). COPD patients also have a high prevalence of left ventricular diastolic dysfunction (DD), which is associated with disease severity (44). One explanation for this association may be that *cor pulmonale* alters left ventricular geometry because of interventricular septum deviation towards the left ventricle and then delayed filling of the left ventricle (46). Another explanation for the relationship between airflow limitation and DD is inflammation (44). In COPD, inflammation is one of the systemic manifestations that can lead to the development of atherosclerotic plaque, which can cause myocardial ischaemia and lead to left ventricular DD (44). A patient’s history and a physical examination should guide the selection of the initial diagnostic tests such as electrocardiogram, chest radiograph, pulse oximetry, spirometry, complete blood count and a metabolic panel. If these are inconclusive, additional testing is indicated (47).

1.6 Spirometry

Spirometry is an indispensable tool in primary care for the diagnosis and monitoring of chronic airway disease (48). Spirometry measures the flow and volume of air entering and leaving the lungs during respiration.
In the forced expiratory manoeuvre, a patient is asked to take the deepest breath possible, and then exhale into the spirometer (Figure 1) as hard and for as long as possible – for at least 6 seconds. The flow–volume loop is obtained by plotting flow against volume during the forced expiratory manoeuvre. During the test, soft nose clips may be used to prevent air escaping through the nose and filter mouthpieces to prevent the spread of microorganisms. Spirometry is used to assess ventilatory function and differentiates between normality and disease causing obstructive, restrictive and mixed defects (Figure 2). The spirometry procedure is standardized and reference values (called predicted values) based on sex, age and height are available for populations of healthy never smokers. The most commonly used values are FEV\textsubscript{1}, FVC and the FEV\textsubscript{1}/FVC ratio. FEV\textsubscript{1} is the maximum volume exhaled in the first second of a forced exhalation that follows a full inspiration. Both the configuration of the loops and the spirometry volumes are used to classify the pattern as normal (dotted line in Figure 2), obstructive (low ratio of FEV\textsubscript{1}/vital capacity in Figure 2 a and normal ratio of FEV\textsubscript{1}/vital capacity in Figure 2 b), restrictive (described in 1.6.2) (Figure 2 c) or mixed (Figure 2 d) (airflow limitation) (49).
According to the guidelines of the Global Initiative for Chronic Obstructive Lung Disease (GOLD), spirometry indicates the presence of an abnormality if $\text{FEV}_1 < 80\%$ of the predicted value, $\text{FVC} < 80\%$ of the predicted value and the $\text{FEV}_1/\text{FVC}$ ratio is $< 0.7$.

1.6.1 Obstructive pattern

In the obstructive pattern, there is a disproportionate reduction in $\text{FEV}_1$ compared with $\text{FVC}$ ($\text{FEV}_1/\text{FVC} < 0.7$). $\text{FVC}$ can be normal or reduced, usually to a lesser degree than $\text{FEV}_1$. Spirometry is required to make the diagnosis of COPD; the presence of a post-bronchodilator $\text{FEV}_1/\text{FVC} < 0.7$ confirms the presence of persistent airflow limitation (9). The fifth percentile lower limit of normal (LLN) for $\text{FEV}_1/\text{FVC}$ can be used instead of the fixed ratio of 0.7 because the fixed ratio overestimates airflow limitation in older people and underestimates it in young people (50, 51). Interestingly, the results from a population-based Canadian study in 2015 indicated that a low $\text{FEV}_1/\text{FVC}$ ratio by either the fixed ratio and/or LLN criterion coupled with a low $\text{FEV}_1$ (< 80% of predicted) is the most clinically relevant diagnostic criterion for COPD (52). LLN criterion used alone may lead to misdiagnosis of COPD (52).

1.6.2 Restrictive pattern

The gold standard for detection of a restrictive lung pattern is body plethysmography, which can measure total lung capacity (TLC) (53). Low $\text{FVC}$ is a screening criterion for a restrictive lung pattern because TLC cannot be measured with a spirometer. The restrictive pattern by
lungenvolumen ist charakterisiert durch eine Verminderung des FVC mit einer normalen oder erhöhten FEV₁/FVC-Ratio (FVC < 80% und FEV₁/FVC ≥ 0.7).

1.7 Spirometry in primary care


1.8 Arterial blood gas analysis

Der Goldstandard zur Schätzung der Sauerstoffaufnahme ist die arterielle Blutgasanalyse. Der Sauerstoffgehalt (SaO₂) misst die prozentuale Anzahl der Hämoglobin-bindenden Plätze im Blutstrom, die von Sauerstoff belegt sind (63). Die arterielle Blutgasanalyse misst die arterielle Sauerstoffspannung (PaO₂) und schätzt SaO₂, was der arterielle Sauerstoffgehalt im Blut ist. In addition, der arterielle Kohlendioxidpartialdruck (PaCO₂), Säurebase (pH) und Serum-bikarbonat (HCO₃⁻) Konzentration kann geschätzt werden. Änderungen in der Körpertemperatur, PaCO₂, 2,3-Diphosphoglycerat oder pH alter Sauerstoffbindung zum Hämoglobin und seinen Release to the tissue. Dies kann zu SaO₂ Messungen zu einer nicht korrekten Berechnung des Zusammenhang zwischen PaO₂ und SaO₂ (die Sauerstoffdissociation curve). In Fällen von Hypoventilation, es ist wichtig, um die arterielle Blutgasanalyse (pH, PaO₂ und PaCO₂), und nicht nur um die Pulse Oxymetry (SpO₂) weil die letztgültigen keine Information über arterielle PaCO₂ oder Säure–Basenstatus (64). Eine vollständige respiratorische Beurteilung umfasst sowohl Sauerstoffaufnahme (PaO₂, SaO₂ und SpO₂) und Ventilation (PaCO₂, i.e., how well a patient can exhale CO₂
produced by metabolic activities). Hypoventilation may cause hypoxaemia as shown by pulse oximetry, but this does not always indicate that it is appropriate to start treatment with oxygen supplementation. The treatment of hypoventilation is primarily directed at correcting the underlying disorder. For example, if respiratory depression occurs because of opioid overdose, the treatment is an opioid antagonist (naloxone). Treatment of hypoventilation is also aimed at assisting ventilation (mechanical-invasive or non-invasive). Arterial blood gas analysis should also be performed when dyshaemoglobin or carbon monoxide (CO) poisoning are suspected. Pulse oximetry (SpO\textsubscript{2}) is unreliable in these conditions.

Hypoxaemia (insufficient oxygen in the blood) is a sign of a problem related to breathing or circulation. There must be enough oxygen in the air being breathed, the lungs must be able to inhale the oxygen-containing air and exhale \( \text{CO}_2 \), and the bloodstream must be able to circulate blood to the lungs, take up the oxygen and carry it out to the body. Problems with some of these conditions, for example, high altitude, asthma/COPD or heart disease, might result in hypoxaemia. Other causes of hypoxaemia are chemical or gas poisoning, medications that reduce the effort of breathing, anaemia and/or conditions that destroy red blood cells.

The symptoms of hypoxia usually consist of shortness of breath, rapid breathing, fast heart rate, wheezing, sweating and coughing. A blood-gas reference study performed at sea level found a mean SaO\textsubscript{2} of 95.5\%–96.9\% (SD 0.4–1.4), depending on age (18 years or over) (65). Reference values for SaO\textsubscript{2} in older people (\( \geq 70 \) years) are sex-specific but age-independent: the mean SaO\textsubscript{2} was found to be 95.3\% (SD 1.4) for men and 94.8\% (SD 1.7) for women (66). SpO\textsubscript{2} values < 97\% are rare in asymptomatic, awake adults (median age 38 years, interquartile range, 28–48) (67).

An arterial blood gas analysis involves puncturing an artery, which may be painful; there is a small risk of bleeding, pseudo-aneurysm, infection or nerve injury. Arterial blood gas analysis is invasive, time-consuming and is seldom used in GP offices (68).

### 1.9 Pulse oximetry

Pulse oximetry is used to measure the peripheral oxygen saturation (SpO\textsubscript{2}), which can be used as an estimate of arterial oxygen saturation (SaO\textsubscript{2}). The pulse oximeter (Figure 3) is easy to use, acceptable within the time constraints of a busy practice and tolerable for the patients. Clinicians may consider pulse oximetry to be a vital sign. A decreased pulse oximetry value alerts the clinician that a disease-causing hypoxaemia may be the cause of a patient’s symptoms.
The technology makes it possible to distinguish between oxyhaemoglobin and deoxyhaemoglobin. It uses two different light-emitting diodes (LEDs), one emitting red light at approximately 660 nm and the other infrared light at approximately 940 nm (Figure 4). Because of its red colour, oxyhaemoglobin absorbs less red light than deoxyhaemoglobin. The light passing from the LED through the finger is measured by the photodetector positioned opposite to the LED. Each LED is illuminated at a programmed frequency. The software of the oximeter assumes that all the light reaching the photodetector has the wavelength of the illuminated LED. To differentiate between venous blood and arterial blood, calculation of the saturation is based on the difference between absorption through systole and diastole. During cardiac systole (denoted by the onset of the QRS complex), there is an increase in light absorption that is assumed to be created by the influx of arterial blood (Figure 5). The software determines the difference between absorption during diastole and systole at both wavelengths. Increased red-light absorbance is associated with increased deoxyhaemoglobin, i.e., lower SpO₂ (Figure 5). The microprocessors are calibrated using reference tables for healthy people exposed to SaO₂ values of 75–100%. The standard manufacturing claim for accuracy for pulse oximeters is ±2–3% over the range of 70–100% SpO₂ (69). In a study of pulse oximeters in use in hospitals in the U.K., 22% of those tested had inaccuracies in saturation estimation of <4% in the range of 70–100% saturation (69).
In a study in children, pulse oximetry was found to be reliable for exclusion of hypoxaemia (70). Using $\text{SaO}_2 < 90\%$ as the gold standard for hypoxaemia, its negative predictive value for $\text{SpO}_2 < 92\%$ was 98\% (70).

**Figure 4**

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**Figure 5**

A schematic diagram of light absorbance by a pulse oximeter (71).

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**1.10 Pulse oximetry in primary care**

Data on the role of pulse oximeters in general practice are limited (68). The advantage of pulse oximetry lies in the fact that it is non-invasive and is not affected by inter-observer or intra-observer variability in clinicians. In primary care, pulse oximetry may be a helpful diagnostic test in assessing the severity of disease and in clinical decision management.
An oxygen saturation (SpO$_2$) $\leq$ 92% indicates hypoxaemia, but values between 93% and 95% are lower than normal (10, 48, 68, 72). Examples of use in general practice are

- the management of acute exacerbations and when long-term oxygen therapy may be required in COPD patients,
- in grading the severity of an asthma attack,
- assessing the severity of cases of community-acquired pneumonia and in acute paediatric assessment for measurement of respiratory status (68).

It is not clear whether pulse oximetry has a role in acute assessment of children in general practice (68), but according to the U.K.’s National Institute for Health and Care Excellence guideline (73), SpO$_2$ $\leq$ 95% is an amber flag feature when assessing children with acute febrile illness. Under these conditions, the GP should consider pneumonia (73).

Pulse oximetry is not a valid method for diagnosis of COPD (74).

Recommendations from GOLD in 2015 (38) include:

“Pulse oximetry can be used to evaluate a patient’s oxygen saturation and need for supplemental oxygen therapy. Pulse oximetry should be used to assess all stable patients with FEV$_1$ less than 35% predicted or with clinical signs suggestive of respiratory failure or right heart failure. If peripheral saturation is less than 92%, arterial blood gases should be assessed (38)”.


Norwegian national guidelines for COPD recommend pulse oximetry examination in general practice (76). The patient should be informed of their SpO$_2$ value when they are in the stable phase of COPD, and should be referred to the pulmonary department at the hospital for arterial blood gas measurement if their SpO$_2$ is $< 92\%$ (76). Pulse oximetry measurements should be performed for the monitoring of patients with severe COPD and in patients with dyspnoea (Modified Medical Research Council Dyspnoea Scale $\geq$ 2) (76, 77). A change in SpO$_2$ value to SpO$_2$ $< 90\%$ during an exacerbation of COPD indicates a need for hospital admission (76). Oxygen supply should be used on flights over 1 hour by COPD patients with SpO$_2$ $< 92\%$ at sea level (76).
### Table 1: Decreased pulse oximetry value as a criterion for considering hospital referral

<table>
<thead>
<tr>
<th>Disease</th>
<th>Situation</th>
<th>Criterion for considering hospital referral</th>
</tr>
</thead>
<tbody>
<tr>
<td>COPD</td>
<td>Exacerbation</td>
<td>(\text{SpO}_2 &lt; 90%) (76, 78)</td>
</tr>
<tr>
<td>COPD</td>
<td>Screening for long-term oxygen requirement</td>
<td>(\text{SpO}_2 &lt; 92%) (76, 79)</td>
</tr>
<tr>
<td>Asthma</td>
<td>Acute asthma attacks in children and adults</td>
<td>(\text{SpO}_2 &lt; 92%) (75)</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>Assessing severity</td>
<td>(\text{SpO}_2 &lt; 94%) (80)(^a)</td>
</tr>
<tr>
<td>Febrile illness in children (pneumonia)</td>
<td>Assessing severity</td>
<td>(\text{SpO}_2 \leq 95%) (73)</td>
</tr>
</tbody>
</table>

\(^a\)In healthy individuals

### 1.11 Echocardiography

Transthoracic echocardiography is currently the most widely used diagnostic tool for evaluation of myocardial function and can assess pump function, anatomical changes, blood flow, valve function and wall movements of the heart. One disadvantage of echocardiography is that ultrasound waves cannot image through bone, tissue and air. Accordingly, it is difficult to examine the hearts of obese patients, patients with large breasts and those with emphysema. The ejection fraction (EF) expresses the volume of the left or right ventricular (LV or RV) chamber that is emptied during each contraction divided by the end diastolic volume. The normal value for LVEF is usually considered to be \(\geq 50\%\) (15). Doppler echocardiography is a useful tool for assessment of LV diastolic function (81). The methods for classification of diastolic function, which have been validated against mortality as an endpoint, include pulsed-wave Doppler examination of mitral inflow, Doppler recordings of pulmonary venous flow and tissue Doppler imaging (TDI) of mitral annular movement (82). According to the recent Recommendations for the Evaluation of Left Ventricular Diastolic Function by Echocardiography of the American Society of Echocardiography and the European Association of Cardiovascular Imaging, 2016 (83), the four recommended variables for identifying DD are mitral annular tissue Doppler velocity (e') (septal e' and lateral e'), average ratio of mitral passive inflow (E) and tissue Doppler velocity (E/e'), left atrial volume index, and peak tricuspid regurgitation velocity. LV diastolic function is considered to be normal if more than half of the available variables do not exceed the cut-off values for identifying abnormal function (83). This 2016 classification has not yet been validated against mortality or hospitalization for heart failure as end-points.
1.12 Pulse oximetry and cardio-vascular disease (CVD) in adults

CVD contributes to heart failure, which affects pulmonary function and gas exchange (84), and thus leads to decreased SpO₂. Decreased oxygen saturation measured by pulse oximetry has been found in association with acute heart failure (85). In patients admitted to hospital with acute myocardial infarction, pulse oximetry is useful in establishing the diagnosis and severity of heart failure (85); heart failure may be suspected when SpO₂ is < 93% (85). In an adult cohort study from Norway, low SpO₂ was significantly associated with death caused by heart failure (10). In the treatment algorithm for acute heart failure (86), pulse oximetry is one of the recommended tests, with a cut-off value for SpO₂ of < 90% (86).

1.13 Pulse oximetry in general practice: two patient stories

In February 2014, one of my patients came to a consultation for follow-up of her diabetes; she also had severe COPD and CHD. During the dialogue, she spoke less than usual, only answering yes or no to my questions. I asked her about breathlessness, which she denied. I measured her SpO₂, which was 90%. I told her that her oxygen saturation was lower than usual. She coughed several times before she answered that she had had increased purulent sputum in recent days and that she indeed had increased dyspnoea. She told me that she wondered if she would be able to leave the house on that day, but she did not want to worry me about this because I was so late and the consultation was ordered for diabetes control. The consultation ended with my treating her for a COPD exacerbation.

In January 2018, I received an electronic communication from one of my patients, a woman aged 46 years with a diagnosis of asthma. “I need help from you because of severe trouble in breathing, especially at night, and a cough with sputum. My oxygen saturation was 90% last evening before I went to bed.” I gave her an instant response and asked her about pulse oximetry measurements at home. She explained that her two children, aged 8 and 12 years, had severe asthma, and had been referred to hospital several times because of asthma attacks. In the general emergency departments, the GPs always measure SpO₂ and she had observed that the result was important in determining whether hospital treatment was required. She had bought a pulse oximeter and measured her children’s oxygen saturation when they had symptoms indicating an asthma attack. She was only able to speak in short phrases because of shortness of breath. The consultation ended with my referring her to hospital for treatment of her asthma attack.
2. Aim of the thesis

2.1 Background

This work was not initially planned as a PhD project. The first step was a quality assurance project in my own practice, including spirometry testing of patients with stable obstructive lung disease. During the writing process for this project, I encountered Hasse Melbye and the General Practice Research Unit in Tromsø. I was asked to participate in data collection in the DIOLUP (Better Diagnosis and Treatment in Exacerbations of Obstructive Lung Diseases in Primary Care) project. The first article from DIOLUP, not included in this PhD thesis, described the main baseline findings from the study (87). The aim was to describe lung function, symptoms during stable phases of illness, and diagnostic labels used in men and woman aged ≥ 40 years. A spirometry-based diagnosis of COPD could be made in 68% of the patients with a previous COPD diagnosis and in 17% of those diagnosed with asthma alone. A diagnosis of COPD that cannot be confirmed by spirometry represents a challenge in clinical practice. The ability of GPs to differentiate between asthma and COPD has improved, probably because of the dissemination of spirometry and guidelines for COPD diagnosis. It is important in primary care to focus on diagnosing COPD, for which spirometry is useful because diagnosing COPD may lead to the patient quitting smoking (88).

Pulse oximetry was one of the tests included in the data collection for the DIOLUP project and because of my interest in laboratory tests originating from my working in a clinical chemical laboratory (89), I seized the opportunity to work with those results. In this analysis process, an association between pulse oximetry and CHD was noted. This led me to the data from the Tromsø study (population-based survey), which has an emphasis on the epidemiology of cardio-vascular diseases. Then, the research question arose: “Is there a correlation between echocardiographic evidence of heart failure and low pulse oximetry values in the general population?” This was my research journey from quality assurance to epidemiology.
2.2 Aim

The main aim of this thesis was to describe the utility of the diagnostic tests, spirometry and pulse oximetry, in primary care patients with stable obstructive lung disease. The detailed aims were as follows.

1. To perform clinical audit including spirometry testing in my own general practice with the aim of quality assurance to ensure the correct prescription of ICS to patients with obstructive lung disease.

2. To explore the associations between decreased pulse oximetry values (SpO₂) and clinical, laboratory and demographic variables in general practice in patients diagnosed with obstructive lung disease.

3. To investigate the association between decreased pulse oximetry values (SpO₂) and echocardiographic measurements of diastolic ventricular dysfunction in a general population of adults.
3. Subjects

Study I: The Lillestrøm study

The Lillestrøm study (Figure 6) was undertaken in one group practice in the Skedsmo community (52,600 inhabitants) in south-east Norway. From the electronic patient record (EPR) database of 8,100 patients listed with six GPs, all patients ≥ 50 years old who had been prescribed ICS during the one-year period (1 October 2005 to 30 September 2006) before new terms for reimbursement of drug costs were introduced in Norway were identified (164 patients). A letter about the new reimbursement regulations and an invitation to a tailored consultation with their GP were sent to 162 patients and 114 (69.5%) patients attended a consultation. Two were excluded from the study because of invalid spirometry.

Study II: The Better Diagnosis and Treatment in Exacerbations of Obstructive Lung Diseases in Primary Care (DIOLUP) study

The DIOLUP study (Figure 6) was carried out in seven Norwegian GP group practices from south-east and northern Norway. The practices were not randomly selected, but were chosen based on the availability of spirometry and the type of medical record system used. Of the 43,241 patients listed at the seven practices, 18,931 were ≥ 40 years old; among these, 1,784 had been diagnosed by the GP with asthma and/or COPD within the previous five years. Each group practice decided the proportion of registered patients that they would invite to participate in the study. A total of 1,111 patients were invited to participate and in all the practices these were randomly selected in alphabetical order from the eligible patients. Invitations were sent by surface mail without additional reminders. Of the 1,111 patients invited, 380 (34.2%) accepted and attended the baseline examination including spirometry and pulse oximetry. Eight patients were excluded from analysis, two because they were undergoing an acute exacerbation, two because they did not complete post-bronchodilator spirometry and four because they did not undergo pulse oximetry. A total of 372 patients were included in the study.

Study III: The Tromsø 6 study

The Tromsø study (Figure 6) was initiated in 1974 (90). It is a repeated cross-sectional population-based study; the seventh survey was carried out in 2015–16. Tromsø is the largest city in northern Norway (70,000 inhabitants). In the sixth survey, Tromsø 6, carried out in
2007–2008, participants were recruited from four different invited groups. Of all those who took part in the second visit for Tromsø 4, a random 10% sample of inhabitants aged 30–39 years, a random 40% sample of inhabitants aged 43–59 years and all inhabitants aged 40–42 and 60–97 years were invited to participate, making a total of 19,762. The attendance rate was 66% (12,984 individuals). Participants were invited to take part in a second visit for a more extended medical examination if they fulfilled one of the following criteria: they had attended the second visit in Tromsø 4, were aged 50–62 or 75–84 years, or were included in a random 20% sample of inhabitants aged 63–74 years. Thus, 7,958 individuals were invited to take part in the second visit, and 7,307 did so (92% attendance rate). SpO\textsubscript{2} was measured in 6,477 of the participants who took part in the second visit and spirometry was performed in 6,437; 11% did not complete the pulse oximetry and lung function testing because of technical problems or absence of staff. Participants in the second visit were randomly allocated to two lines of examinations, one of which included echocardiography by which 2,285 subjects were examined. Valid recordings for SpO\textsubscript{2} and mitral Doppler inflow were obtained in 1,979 participants. After excluding participants < 50 years (n = 188) and subjects with SpO\textsubscript{2} < 70% (n = 9), 1,782 individuals were included in the analysis.
Figure 6
Outline of the three studies.

**LILLESTRØM STUDY**
- Descriptive study
- Quality assurance
- 1 general practice
- 164 patients aged ≥ 50 years identified
- 2 deceased
- 162 invited
- 50 did not participate
- 114 attended the tailored consultation (70.4%)
- 2 excluded (incomplete spirometry)

**DIOLUP STUDY**
- Cross-sectional
- 7 general practices
- 1,784 patients aged ≥ 40 years identified
- 1,111 patients invited (randomly selected)
- 380 attended baseline examination (34.2%)
- 8 excluded (2 incomplete spirometry, 4 did not undergo pulse oximetry, 2 with acute exacerbation)

**TROMSØ STUDY**
- Cross-sectional population-based survey
- 19,762 subjects invited
- 12,984 attended first visit (65.7%)
- 7,958 invited to second visit
- 7,307 attended second visit randomly allocated to two lines of examinations
- 2,285 examined by echocardiography
- 188 excluded (age < 50 years) 9 excluded with SpO₂ < 70%
- 1,782 valid measurements of SpO₂ and mitral Doppler inflow

Study population
- Paper I
  - n = 112
- Paper II
  - n = 372
- Paper III
  - n = 1,782
4. Methods

Study I

The Lillestrøm study (Figure 7) was a quality assurance project, with the main aim of evaluating whether ICS was correctly prescribed. Tailored consultations included the patients’ history, physical examination and spirometry with reversibility testing. The patients’ previous pulmonary diagnoses were recorded. Patients were instructed not to use any inhaled medications on the day of investigation prior to spirometry. The spirometry was carried out by trained staff in accordance with criteria of the American Thoracic Society (ATS)/European respiratory Society (ERS) (91). The spirometer used was a Microloop II with Spirare® software (Diagnostica AS, Oslo, Norway) and the European Coal and Steel Community reference for spirometry was used (92). Reversibility tests were performed 20 minutes after patients inhaled 0.4 mg salbutamol. Reversibility was defined as increased FEV₁ of ≥ 12% and 200 ml (11). The spirometry criterion for COPD was based on the GOLD guidelines and was defined as a ratio of FEV₁/FVC < 0.7 after bronchodilation (88). Based on FEV₁% predicted, patients were categorized into COPD stages based on the GOLD guidelines (88). Data from the tailored consultation were recorded from each patient’s medical record. The decision about follow-up of findings was left to individual GPs in collaboration with their patients. In April 2008, 15 months after the audit was completed; a retrospective EPR data search was performed regarding GPs’ diagnoses and prescribing patterns for patients who had participated in the clinical audit.
Study II

Participation in this part of the study required patients to complete a questionnaire and undergo a consultation during a stable phase of their disease for clinical examinations including spirometry. The participants were instructed not to take their regular respiratory medication on the day of the examination. The GPs recorded co-morbidities including CVD on a computerized questionnaire linked to the patients’ medical record. On a separate questionnaire, patients recorded their smoking habits. The patients’ height and weight were recorded to calculate their body mass index (BMI). Oxygen saturation was measured with an Onyx II® digital hand-held pulse oximeter (model 9550; Nonin Medical, Inc., Plymouth, MN, USA). The highest value obtained from three measurements was recorded. The HemoCue Hemoglobin system (Quest Diagnostics, Madison, NJ, USA) was used for haemoglobin measurements. The thresholds for raised values were based on the reference values used at the University Hospital of North Norway. The upper normal limit was 16.0 g/dL for women and 17.0 g/dL for men. C-reactive protein (CRP) was analysed using an Afinion AS100 Analyser (Axis-Shield, Oslo, Norway), Orion Quickread CRP (Orion Diagnostica, Espoo, Finland) or ABX Micros CRP (Horiba ABX SAS, Montpellier, France), all of which could display values down to 8 mg/L. Spirometry was carried out after the pulse oximetry test, following ATS/ERS guidelines (91), using a Spirare SPS310 spirometer (Diagnostica AS, Oslo, Norway). During spirometry, the patients were seated, and a nose clip was not used. Post-
bronchodilator spirometry was carried out 20 minutes after inhalation of 0.4 mg salbutamol. The post-bronchodilator FEV₁ and FVC were used in the analyses. Norwegian reference values for spirometry were applied (93).

**Study III**

A questionnaire including questions about smoking habits, previous diseases and daily medication was enclosed with the letter of invitation to participate and was collected at the subsequent visit, during which height and weight were measured. Participants who reported having myocardial infarction or diabetes were classified as “self-reported” diabetes and “self-reported” myocardial infarction. During the first examination, participants were given a second questionnaire, which they were instructed to complete and return by mail or to the examination site. The second questionnaire covered dyspnoea. Height and weight were measured in standing subjects wearing light clothing without shoes. BMI (in kg/m²) was calculated.

SpO₂ values were measured with an Onyx II® digital hand-held pulse oximeter (Nonin Medical, Inc.). Participants rested for at least 15 minutes before examination. The best of three measurements was recorded. The manufacturer’s testing has shown that only values between 70% and 100% are accurate to within ±2 digits, and therefore values below 70% were regarded as invalid. None of the participants received supplemental oxygen.

After the pulse oximetry, spirometry was performed using a Vmax Encore 20® (VIASYS Healthcare Respiratory Technologies) and the ATS/ERS criteria were followed (91). Norwegian reference values were used (93). A reversibility test was not performed. The instrument was calibrated every morning and when demanded by the machine. Three trained technicians conducted the spirometry, which was performed with subjects in a sitting position and using a nose clip. The subjects were instructed to exhale for as hard and long as possible – for a minimum of 6 seconds. At least three exhalations were required. For a valid measurement, the difference between the highest and next highest FEV₁ and FVC should not be > 150 mL (FVC ≤ 1.0 L, not exceeding 100 mL) or vary by > 5%. Current drug therapy was not interrupted before the test. The spirometry results were excluded if the test was not performed properly. The inclusion criteria were FEV₁ > 0.3 L, forced expiratory volume in 3 seconds (FEV₃) ≥ 0.0 L and FVC > FEV₃.

Echocardiographic measurements of systolic and diastolic left ventricular function were measured using a Vingmed CFM 750 (Vingmed Sound A/S, Horten, Norway) (Figure 8) with a combined 3.25 MHz mechanical and 2.5 MHz Doppler probe. The examinations were
performed by two expert cardiologists, using the standard apical and parasternal long- and short-axis views. Standard 2D-guided M-mode registrations of antero-posterior left atrium (LA) size, internal dimensions of the left ventricle (LV) and wall thickness of the septum and posterior wall were made using the leading-edge to leading-edge convention (94). The measurements of peak mitral flow velocity in early diastole (E-wave) and during atrial contraction (A-wave), the calculated E/A ratio and the E-wave deceleration time (EDT) were assessed online on one heart cycle. The influence of heart rate was minimized by measuring EDT as the time between the peak E-wave and the upper deceleration slope extrapolated to the zero baselines (95). TDI of the septum at the mitral annulus was performed with measurement of early diastolic mitral annular velocity (e') and subsequent calculation of average septal and lateral E/e'. LVEF was measured in short axis (M-mode). LA size was indexed by body surface area (BSA) and systolic dysfunction defined as LVEF < 50%. A reproducibility study of the echocardiographic data was performed (96).

Figure 8
The Vingmed CFM 750 ultrasound system used in the Tromsø study.

4.1 Statistics

In Study I, frequency analyses were performed. Spirometry findings in the 112 patients treated with ICS were described as were the number of patients who continued or discontinued ICS.

In Study II, we defined low pulse oximetry values as SpO₂ ≤ 95%. SpO₂ did not show a normal distribution and was dichotomized using two different thresholds: ≤ 92% and ≤ 95%.

We compared the characteristics of two diagnostic groups of patients defined based on whether the GP’s diagnosis was coded as R96 (COPD) or R95 (asthma) according to the
International Classification for Primary Care (97). Patients who had been given both diagnoses within the previous 5 years were allocated to the COPD group. The significance of the differences in frequencies was analysed using the chi-squared test. The frequencies of decreased SpO2 were analysed according to age, sex, smoking habits, self-reported diseases, spirometry, BMI, CRP and haemoglobin. Continuous variables (age, BMI, FEV1% predicted, CRP and haemoglobin) were categorized. Categorization of the continuous variables was made before analysis and with clinical justification (98) to facilitate presentation and interpretation of findings. Age was dichotomized into < 65 years and ≥ 65 years. BMI was categorized as underweight (< 20 kg/m²), normal weight/overweight (20–30 kg/m²) and obese (≥ 30 kg/m²) (99). The FEV1% predicted was categorized as severely reduced (< 50%), moderately reduced (50–80%) and normal (≥ 80%), in line with the GOLD classification for COPD (38). CRP values were dichotomized into ≥ 8 mg/mL and < 8 mg/mL. Haemoglobin values were dichotomized into above normal (> 16.0 g/dL in women and >17.0 g/dL in men) and normal and low (≤ 16.0 g/dL in women and ≤ 17.0 g/dL in men). Age, sex, and variables significantly associated with a decreased SpO2 (P < 0.05) in the chi-squared test were entered into a multivariable binary logistic regression. The multivariable analysis was also performed without categorizing the continuous variables.

In Study III, the characteristics of the study population were compared by sex, and the differences were explored by independent-sample t test (for continuous variables) and chi-squared test (for categorical variables). The frequency of abnormal mitral Doppler inflow was analysed by sex, smoking status, self-reported diseases (myocardial infarction and diabetes), dyspnoea, hypertension, spirometry, BMI, LVEF < 50% and SpO2 ≤ 95%. The significance of differences was analysed by a chi-squared test. BMI, LVEF and SpO2 were dichotomized. Because of the small number of participants with dyspnoea categorized as moderate, severe and very severe, these three categories were merged into one category. The FEV1% predicted was categorized as indicated by the GOLD classification (9).

The analysis proceeded in two steps. First, univariable binary logistic regression models were fitted to the data to identify variables that were associated with abnormal mitral Doppler inflow. Second, variables with P ≤ 0.1 in the univariable analyses were entered into the multivariable binary logistic regression models. The explanatory variable dyspnoea was included in model 2, but not in model 1.

For Study I, the analyses were performed using IBM SPSS Statistics version 17, while version 18 was used for Study II and version 22 for Study III.
5. Summaries of the papers and main results

5.1 Paper I

Paper I included 112 patients from one GP group practice who were aged \( \geq 50 \) years and had been prescribed ICS (including in combination with long-acting beta-2 agonists) the year before the 2006 regulation for drug-cost reimbursement for ICS prescription according to which it became mandatory that the diagnosis was confirmed by spirometry. The principle became that costs for ICS should only be reimbursed with a diagnosis of asthma. Patients with COPD could also be reimbursed, but only after a special and individual application, and mainly for those with severe COPD (FEV\(_1\)% predicted < 50). The 112 patients were invited to a tailored consultation including post-bronchodilator spirometry. Fifteen months after the audit was completed; a retrospective EPR data search was performed for GPs’ diagnoses and prescribing patterns for the 112 patients who had participated in the clinical audit. The spirometry results showed post-bronchodilator airflow limitation indicating COPD (FEV\(_1\)/FVC < 0.7) in 55 patients. Reversibility \( \geq 12\% \) and 200 mL was found in 13 patients, of whom eight also met the spirometry criteria for COPD. The number of patients diagnosed with asthma increased (from 25 to 62) after the reassessment. Because of the non-standardized way in which different GPs diagnosed asthma, we found the statistical analysis to be of limited value, and it was not included in the final version of the paper. ICS was discontinued in 31 patients; 20 with spirometry results indicating mild to moderate COPD and 11 with normal spirometry. Seven of these 11 had no history, symptoms or signs indicating obstructive lung disease, and the remaining four had episodic asthma without the need for long-term ICS treatment. Only one patient who had ICS treatment discontinued restarted this medication within the following year. This audit found that spirometry was useful for identifying ICS overuse. GPs’ diagnoses were challenged by the formal regulations and there was a tendency to adjust the diagnosis to the treatment given, instead of vice versa.

5.2 Paper II

Paper II included 372 patients aged \( \geq 40 \) years from seven Norwegian GP group practices, who were diagnosed by their GP with asthma and/or COPD. The patients were examined during a stable phase of their disease. Patients diagnosed with COPD (including those with combined COPD/asthma) and those with asthma only were analysed separately. Two
thresholds of abnormal SpO\textsubscript{2} values were used as outcome measures: ≤ 95\% and ≤ 92\%. In both asthma and COPD patients, SpO\textsubscript{2} ≤ 95\% was significantly associated with reduced lung function (FEV\textsubscript{1}\% predicted ≤ 80\%), a self-reported diagnosis of CHD and older age (≥ 65 years). In the COPD group, haemoglobin above normal was associated with SpO\textsubscript{2} ≤ 95\%. The binary multivariable logistic regression confirmed these associations, including the association with CHD. The most important predictor of low SpO\textsubscript{2} ≤ 95\% was FEV\textsubscript{1}\% predicted < 50\%, which had an odds ratio (OR) of 6.8. Multivariable analysis with SpO\textsubscript{2} < 92\% as outcome was not performed because of the low number of patients with such values (n = 11).

The study concluded that patients in general practice asthma and/or COPD who had low oxygen saturation (SpO\textsubscript{2} ≤ 95\%) should be given special attention and followed up more closely than patients with normal oxygen saturation. The GP should consider revising the diagnosis and treatment and look for co-morbid CHD.

\textbf{5.3 Paper III}

Paper III included 1,782 participants from a population-based survey, Tromsø 6, aged ≥ 50 years who had been evaluated with pulse oximetry and echocardiography. The primary outcome was left ventricular DD. Mitral Doppler indices were used for evaluating DD. The associations between this outcome and possible predictors, including SpO\textsubscript{2} ≤ 95\%, were analysed using univariable and multivariable logistic regression. DD was found in 595 participants. Male sex, self-reported myocardial infarction, dyspnoea, former smoker, hypertension, BMI ≥ 30 and SpO\textsubscript{2} ≤ 95\% were all significant predictors of abnormal mitral Doppler flow in the multivariable analyses. SpO\textsubscript{2} ≤ 95\% was an independent predictor for DD with an OR of 1.6. Hypertension and BMI ≥ 30 significantly predicted impaired filling with ORs of 1.7 and 1.5, respectively.

The study concluded that DD should be included among possible explanations when decreased oxygen saturation is found.
6. General discussion

6.1 Methodological considerations

The three studies are based on data from one GP group practice, seven non-randomly selected GP group practices and a population-based survey. All three studies must be critically assessed for bias because of both the design and the conduct of the studies. Internal and external validity are required for generalization beyond the study populations (100).

6.1.1 Internal validity

Internal validity refers to scientific interference within the study population; it implies bias in the way the data is collected, analysed or interpreted. Three major types of error can influence internal validity: selection bias, information bias and confounding (100).

**Selection bias** concerns the representativeness of the study participants in relation to the source population. Selection bias can result from procedures used to select study participants or other factors influencing study participation (101). Selection bias is present when people have different probabilities of being included in the study sample according to relevant study characteristics (102). If the association between exposure and outcome is different in those who participate in the study compared with those who choose not to participate, the effect estimates from the study will differ from those existing in the source population (100).

**Information bias** results from a systematic tendency for participants selected for inclusion in the study to be erroneously placed in different exposure/outcome categories, thus leading to misclassification (102). When we study categorical variables, the misclassification can be either differential or non-differential (100). Differential misclassification occurs when incorrect classification of a variable depends on the value of other variables. Such misclassification can either exaggerate or under-estimate the effects in a study. Recall bias is an example of differential misclassification that results from inaccurate recall of past exposure (102). Non-differential misclassification arises when incorrect classification of a variable is unrelated to other variables and is identical for all study subjects. Such misclassification can dilute the strength of the associations between groups in a study, thereby biasing the association towards the null hypothesis (99, 100, 102).

In Studies II and III, questionnaires were used for some of the variables (smoking habits, self-reported diseases, dyspnoea and blood pressure treatment). Differential misclassification may occur when the patient is asked about an event a long time after it occurred (recall bias) (102), and this may influence the sensitivity and/or specificity of the questions. This could bias the
results of the study, but it is a particular concern in case–control studies, when cases and controls are asked about exposures in the past. Questions about smoking habits may have been a difficult topic for some participants who may feel stigmatized by their habit, which could lead to inaccurate answers. Therefore, there may have been bias in categorizing smokers, former smokers and never smokers. However, self-reports of smoking are usually accurate (103, 104).

Non-differential misclassification might have occurred when we chose to categorize some of the variables in Studies II and III (outcome variables SpO₂ and mitral Doppler inflow, age, CRP, dyspnoea, FEV₁% predicted, BMI, haemoglobin, LVEF, LA diameter/BSA and abnormal ratio of TDI and mitral passive inflow E/e'). Although such misclassification could have resulted in a dilution of associations (100), it is probably more likely that the results are an under-estimation than an overestimation (105).

*Measurement error* can be mismeasurement of a quantitative variable, or misclassification of a categorical variable. These errors are typically the result of instrument error and/or sampling error (101). Instrument error arises when we are unable to measure a specific quantity defined at a specific point because of limitations of the measuring device used. Errors are classified as differential (systematic) or non-differential (random). Accuracy of measurement can be achieved through minimizing systematic error and random error (high validity and reliability). Validity is the ability of a test to indicate which individuals have the disease and which do not. Reliability is the degree to which an assessment tool produces stable and consistent results.

**Spirometry**

Spirometry was performed in all three studies, but the instrument used varied. In Study I, spirometry was performed using a Microloop II spirometer with Spirare® software; in Study II, with a Spirare SPS310 spirometer; and in Study III with a Vmax Encore 20® spirometer. The Spirare SPS310 sensor uses bidirectional ultrasound transit time measurements.

Spirometric indices obtained by trained general practice staff using the Microloop II with Spirare® software are justifiably comparable with those measured in a pulmonary function laboratory (106). The digital technology makes recalibration obsolete, although a sensor quality control routine is included. The spirometers used in Studies I and II did not require daily calibration (and it was technically not possible to adjust the spirometers in the practices), but spirometric values should be checked either by a calibration pump or by using a biological control (a healthy person working in the laboratory). We have no information
about how regularly this was carried out in the GP offices participating in Studies I and II. In Norway, guidelines recommend an official agency for quality control of spirometers and spirometry examinations in the health services (76), but this is not yet established. In Study I, the spirometry was carried out by trained staff at the GP’s office. The staff in this six-GP practice had attended a course that included professional tuition on the practical application of spirometry. Accurate spirometry was also ensured by appropriate training during the years before this audit. Results were excluded if the spirometry was not performed adequately (two results in Study I and two in Study II, which accounted for 1.8% of the total Study I sample and 0.5% of the total Study II sample).

In Study III (Tromsø 6), calibration of the instrument was performed every morning and when prompted by the machine. Three trained technicians conducted the spirometry. If the spirometry was not performed adequately, the results were excluded (19 results in Study III, which accounted for 1.1% of the total sample in Study III).

A limitation is involved in the validity of the reference values when they are applied in the oldest age group, and this might have played a role in Study III in which a high number of participants were aged ≥ 75 years (24.0%). However, this factor was minimized by categorizing FEV₁% predicted in the analysis.

Day-to-day variability of FEV₁% predicted, expressed by the coefficient of variation (CV), is higher in COPD patients (2.8%) and clinically stable asthma patients (2.3%) than in healthy individuals (0.7%) (107). This could be a differential error because the probability of being misclassified differed across the groups of audit subjects. In Study I, 49% had a post-bronchodilator FEV₁/FVC < 0.7 indicating COPD, and most of the patients in Study II had either COPD or stable asthma. In addition, the FEV₁% predicted was categorized for analysis in all three studies, which should have minimized this potential error.

A nose clip was only used in Study III. Use of nose clips during spirometry does not systematically affect the results obtained or the within-subject repeatability (108). The use of a nose clip is uncommon in primary care.

**Pulse oximetry**

Pulse oximetry was performed in Studies II and III. SpO₂ was measured in resting patients in Study II and in resting participants in Study III. In Study II, the patients completed two questionnaires in the waiting room before SpO₂ measurement; in Study III, the participants had been waiting in a queue or had been to other non-demanding examinations. Accordingly, the participants/patients rested for at least 15 minutes before the examination, and the best of
three measurements was recorded. Correct probe placement was checked, and a green light indicated a valid measurement. Accuracy is reduced with SpO₂ values < 70% (69); nine participants in Study III and none in Study II were excluded because of this.
Pulse oximetry measurements have limitations that can cause false SpO₂ values, either lower or higher (71, 109, 110). Although pulse oximeters do not require user calibration, awareness of their inherent limitations is important (110). Possible causes and mechanisms of unreliable SpO₂ readings are as follows.

- Causes of intermittent drop-outs or inability to read SpO₂: poor peripheral perfusion (e.g., hypovolaemia, vaso-constriction), cold extremities or hypothermia.
- Causes of falsely normal or elevated SpO₂ readings: CO poisoning and sickle cell anaemia vaso-occlusive crises (71).
- Causes of falsely low SpO₂ readings: venous pulsations, excessive movement, intravenous pigmented dyes, inherited forms of abnormal haemoglobin, dark fingernail polish, severe anaemia (with concomitant hypoxaemia).
- Causes of falsely low or high SpO₂ readings: methaemoglobinaemia, sulphaemoglobinaemia, poor probe positioning, sepsis and septic shock.
- CO poisoning in chronic heavy smokers (can achieve up to 10% arterial carboxyhaemoglobin), which may overestimate SpO₂ (111, 112).
- Different nail polish colours may cause lower pulse oximeter readings (109, 113), although a systematic review concluded that the changes in SpO₂ readings were not clinically significant (114).
- Exposure to strong external light while taking measurements may result in inaccurate readings, so it is important to shield the sensors from bright light.

In Studies II and III, errors may have led to overestimated readings in heavy smokers and in people with type 2 diabetes and possibly high haemoglobin A₁C levels, and under-estimated readings in people wearing nail polish. Current smoking was associated with decreased SpO₂ in our studies, and high CO levels in smokers were probably not an important source of bias. The reliability of the measurement was improved by using the highest of three measurements.

Confounding and effect modification (interaction)
A confounder is commonly defined as a variable that could influence the outcome and at the same time could be associated with exposure (101). Three conditions must apply to a confounding factor: the association between the factor and the outcome must come from a causal pathway other than the main exposure; the factor must also be associated with the
exposure; and the factor must not be an intermediate step in the causal pathway between the exposure and the outcome. A confounding factor can cause both under-estimation and overestimation of the outcome variable (100). An example is the influence of carboxyhaemoglobin concentration on SpO₂, which can lead to overestimation of the actual SaO₂ (115). Once inhaled, CO can bind to haemoglobin to form carboxyhaemoglobin, reducing the oxygen-carrying capacity of the red blood cells by direct competition for the binding sites. Hypoxia occurs, and secondarily, the number of red blood cells increases. The result may be that the measured haemoglobin value increases.

Randomization, multivariate adjustment, stratification, subject restriction and matching are common methods used to control for potential confounding factors in studies. Double-blind randomized trials are the gold standard when it comes to avoiding confusion of effects because this method allows the comparison of groups with common background characteristics. In our studies, there was no randomization.

The significance of the differences was first analysed by chi-squared test, after categorizing continuous variables, and by the independent-sample t test for continuous variables. In Study III, the data were stratified to determine whether there were any differences between men and women. In the Tromsø 6 study, men had significantly lower SpO₂ values (116), and this was also shown in Study III with participants recruited from Tromsø 6. The explanation for higher oxygen saturation in morbidly obese, (BMI ≥ 40 kg/m²) women than in morbidly obese men is that women have less abdominal obesity, and abdominal obesity is associated with reduced gas exchange (117). In Study III, this effect of male sex may have been reduced if we had included waist-to-hip ratio in the analysis. Dyspnoea was more frequently reported in women, and although mild dyspnoea was not a significant predictor in the multivariable analyses, this might have been influenced by the sex effect.

The method that was applied in Studies II and III to avoid confounding was multivariable analyses. Logistic regression is a mathematical method that gives an adjusted OR, which means that its value has been adjusted for the other covariates, including confounders (118). We chose logistic regression analysis because it allowed us to predict categorical outcomes. In Study II, predictors of low SpO₂ with a significance of < 5% (except low BMI, which was only significant in the COPD group) were entered into the multivariable binary logistic regression. In Study III, variables associated with DD (P ≤ 0.01) in the univariable binary logistic regression analysis were entered in the final multivariable logistic regression models. It is also important that there was no multicollinearity among the predictor variables.
Interaction describes a situation in which two or more risk factors modify the effect of each other with regard to the occurrence or level of a given outcome, that is, effect modification. There can be positive or negative interactions (102). We did not check for interactions in the categorized multivariable regression used in this study. All the variables in the multivariable analyses were categorized, except age.

All statistical tests involve the possibility of making type I and type II errors. A type I error is the incorrect rejection of a true null hypothesis, and this can lead to the conclusion that an association exists when in fact it does not. This may be solved by shifting the significance level from 0.05 to 0.01, thereby reducing the chance of a type I error from 5% to 1%. A type II error is the failure to reject a false null hypothesis. The risk of committing a type II error is decreased by ensuring that the test has sufficient power, which can be increased with a larger sample size. In logistic regression models, the risk of a type II error increases with the number of variables included in the models because the degrees of freedom decrease, and thus the power decreases (100). Excluding relevant variables from the logistic regression model will lead to biased estimates, and including irrelevant variables may increase the standard error, increasing the risk of type II error.

Effect modification occurs when the effect measure varies across levels of another variable. This is not a bias, but an important finding that should be reported and not corrected for. There is a positive interaction if the presence of the effect modifier strengthens the effect of the exposure of interest, and a negative interaction is where the presence of the effect modifier diminishes or eliminates the effect of the exposure of interest (102). In Study II, we checked for interactions between age and the other predictors, and found no significant interactions.

Confounding can persist also after adjustment. There could be unknown confounders and confounders not measured during the process of data gathering (118). Statistical power depends on statistical significance; in Studies II and III, the statistical significance level was set to 0.05 (5%).

6.1.2 External validity

The external validity or generalizability of a study refers to the ability to apply the results from a study to people outside the study population (119). To achieve a high external validity, it is important that the study sample is representative of other groups in the population or of other populations.
6.2 Study I

6.2.1 Introduction
The main finding from the Lillestrøm study was that the GPs’ diagnostic practice changed after implementation of new reimbursement terms and the audit suggested that there was overtreatment with ICS in middle-aged and older patients.
The numbers of patients with an asthma diagnosis more than doubled after the tailored consultations. This could represent a tendency to adjust the diagnosis to the treatment given, but it was also an opportunity for the use of spirometry in the tailored consultations to improve the accuracy of diagnosis of the patients.
Use of the EPRs was helpful in this project to identify a group of patients, and may also be useful in other projects in general practice. The study shows that spirometry should be performed in all GP offices.

6.2.2 Methodological considerations
The Lillestrøm survey of one GP group practice included a limited number of patients and the validity of the extrapolation to Norwegian general practices depends on the representativeness of the patient sample and of the six GPs working in this general practice. The sample estimates may differ substantially from the true parameters because of random error, especially when the study sample is small (102).

The Lillestrøm study was a descriptive study used to describe the characteristics of patients in one group GP practice who were prescribed ICS. Descriptive research cannot identify causality of the observations. This was also a longitudinal non-randomized intervention study reporting the therapeutic responses as findings.

Audit or research?
The Lillestrøm study was classified as a quality assurance project. However, research and audit have many similarities. They both start with a question, both expect the answer to change or influence clinical practice, both require formal collection of patient data, and both depend on using an appropriate method and design to reach sound conclusions (120). The major distinction between audit and research is that research aims to generate new knowledge about health and disease (121), whereas audit investigates whether the aims of the practice have been achieved (122). Unlike research, clinical audit projects do not need to be submitted to a Research Ethics Committee (REC) for ethical approval because clinical audit does not involve anything being done to patients beyond their routine clinical management. We asked the question: “Are we following the best practice?” As for research, an ethical framework is
important in a clinical audit, which means ensuring patient confidentiality and that data are collected and stored appropriately.

The standards for audit in terms of design, data collection and analysis should be the same as those for research; audit leads to change more often than research does (120). In the Lillestrøm study, we investigated how changed terms for drug payment influenced GPs’ diagnoses and their prescribing practice for ICS. The results of the tailored consultations with their patients on GP diagnoses and prescribing patterns were assessed by a retrospective EPR data search after the clinical audit was finished. The decision about discontinuation of ICS and follow-up of findings was left to individual GPs in collaboration with their patients. A new retrospective EPR data search of the patients who discontinued ICS was performed 15 months after the audit. One patient had restarted ICS because of relapse of asthma. Decisions about whether a project is a clinical audit or research are not straightforward; we presented the audit for retrospective evaluation by the Regional Committee for Medical and Health Research Ethics, South-East Norway, who agreed that this was a clinical audit.

6.2.3 Internal validity

Selection bias
In this quality assurance project, 70% (114 of the 164) of the invited patients attended the study. Of the 50 non-participants, 14 no longer used ICS, which indicates that they were healthier than the participants. Three patients were too ill to participate, one was followed up at the hospital, two were deceased and one letter was returned because of an unknown address.

Information bias
No questionnaire results were used in this report; the diagnoses of asthma and COPD were recorded from the EPR database. The quality of the GPs’ diagnoses could be questioned.

Measurement errors
Spirometer measurement error is described in section 6.1.1.

Statistical power
In Study I, the sample size was small and from only one GP practice. Associations are harder to detect in smaller samples. Random errors occur because the associations we observe are based on samples, and samples may not accurately reflect the population at large. In large samples, random errors have less impact. The diagnostic criteria for asthma were not standardized, limiting the value of statistical assessment.
The participation rate was 69.5%. A high participation rate is important for internal validity.

6.2.4 External validity
The Lillestrøm study included a limited number of patients and the validity of its extrapolation to Norwegian general practices depends on the representativeness of the sample of patients, the GPs and the place and time it took place. The group practice had six GPs whose mean age was 50 years, three (50%) of the GPs were female, and each GP had a patient list of 1,500. This is relatively close to the average in Norway in 2006 where the mean age of GPs was 48 years, 31% of GPs were female and the average patient list was 1,196 (123). One of the GPs had a long-term interest in obstructive pulmonary diseases, and the performance of the practice in this field was not inferior to the average Norwegian general practice. Lillestrøm is a town of 12,500 inhabitants in the outer ring of Oslo; in 2006, it had a population of 5.9% non-Western immigrants and 3.6% Western immigrants (124). This study was undertaken 3–6 months after it became mandatory that for drug-cost reimbursement for asthma/COPD, the diagnosis must be confirmed with spirometry. Therefore, because of this change, the GPs could have had a consultation with their patients before our tailored consultation. Hence, we believe that our study sample from one group practice is applicable to other Norwegian urban GP practices.

6.2.4 Strengths of Study I
This practice-based clinical audit with an invitation to a tailored consultation including spirometry for all patients > 50 years who were using ICS was a way of improving the quality of treatment and diagnosis. Our aim was to improve the quality of health care; only one patient who ceased ICS had to restart the treatment. The audit including spirometry led to revised treatment in more than a quarter of the patients on ICS therapy.

6.2.5 Limitations of Study I
Study I had a number of limitations.
1. The main limitation was the low number of patients and GPs who were all from the same GP group practice. Thus, caution is required in drawing the conclusion that these findings are representative of Norwegian general practice.
2. With respect to internal validity, the participant rate was 69.5%: 27 (54%) of the 50 non-responders among those invited to participate no longer used ICS or had only a single ICS prescription. These patients probably considered that there was no advantage in participating in a quality assurance study to monitor use of a medication they no longer used.
3. Sixty-nine (61.6%) patients did not have a diagnosis of asthma and/or COPD when they were prescribed ICS during the year before the tailored consultation. Other diagnoses were bronchitis, chronic cough, breathing problems and pulmonary fibrosis. After the audit, only 21 (18.8%) of the patients had a diagnosis other than asthma and/or COPD. These figures are based only on the GP diagnosis recorded in the EPR and are not considered in the context of spirometry results and patient history in the EPR. This is a major weakness of the study and makes it difficult to interpret the results. However, we know that 25 of the 62 patients given a diagnosis of asthma after the audit had spirometry findings suggesting COPD (FEV₁/FVC < 0.7). Some of these 25 patients may have “asthma–COPD overlap syndrome” (ACOS), a condition in which a patient has clinical features of both asthma and COPD (125). The syndrome is estimated to be present in 15–45% of the population with obstructive airway disease (125). It is difficult to provide treatment guidance for patients with ACOS because of the lack of randomized intervention studies, but treatment with ICS is probably appropriate in patients with long-standing asthma even if a component of irreversible airway obstruction develops (125).

4. The results of the statistical analysis described in Paper I (“The distribution of the GPs’ diagnoses recorded in EPRs changed significantly after the implementation of the new reimbursement terms”) were not specified in Table 2 of that publication.

6.3 Study II

6.3.1 Introduction
The main finding from general practice including patients with stable asthma and/or COPD was that decreased pulse oximetry values (SpO₂ ≤ 95%) were associated with both reduced lung function (spirometry test) and with a diagnosis of CHD. In Study II, the GPs recorded co-morbidities in the patients, including CHD. In both asthma and COPD patients, CHD was a significant predictor of decreased pulse oximetry values. Despite the increasing use of pulse oximetry in family practices, current clinical guidelines do not inform the GPs how to deal with SpO₂ values ≤ 95%. Such values in patients in general practice who have stable asthma and/or COPD may prompt the GPs to consider whether the patients are receiving adequate treatment and/or have undiagnosed co-morbidity. Cardiac co-morbidities are frequent in patients with COPD and influence its severity and prognosis.
6.3.2 Methodological considerations

The study was carried out at seven GP group practices. The number of patients in each practice that were invited to participate was decided based on the workload associated with each patient, as well as the capacity for such tasks at each office (87). The GP offices volunteered to take part in the DIOLUP study and might not be representative of Norwegian practices (87).

6.3.3 Internal validity

Selection bias

In this study carried out at seven dedicated GP offices, the participation rate was only 34% (380 of the 1,111 participants invited); therefore, it cannot be assumed that the study sample was representative of the background population. Patients who had been given a diagnosis of both asthma and COPD participated much more frequently than those with a single diagnosis of COPD (87). A double diagnosis may reflect frequent visits to the practice and accordingly more severe illness. The low participation rate among those with a single diagnosis of COPD may reflect that the most severely impaired COPD patients were less inclined to participate (87). This could be because they were followed up by a pulmonary specialist or in a pulmonary outpatient clinic in hospital. However, patients who had once had a diagnosis of asthma or COPD but now felt healthy might also have been less interested in taking part in the study (87). Thus, the study could have had selection biases away from both the most ill and the healthiest patients. However, such selection biases probably had little influence on the main findings of the study in terms of associations between explanatory variables and outcome. In Study II, there were very few patients with missing results (< 1% in multivariable analysis) and missing data are a negligible problem.

Measurement errors

Pulse oximeter error is described in 6.1.1.

BMI

Weight and height were measured by dedicated health secretaries in the seven different GP offices. BMI was calculated using a standardized method. Incorrect calibration of body weight may cause systematic error if the sensitivity and specificity vary between different ranges of the scale. Different types of scales were used for weight measurement in Study II and there could be a systematic error between the instruments.
**Haemoglobin**

Haemoglobin was analysed from venous blood samples drawn from the cubital vein. In Study II, the HemoCue Hemoglobin system was used. Blood samples were drawn by a medical technologist or other qualified person while the patients were in a sitting position. The samples were analysed within 24 hours. All blood samples for haematological analysis were stored at room temperature until analysed in the GP’s office. The reference method for the measurement of haemoglobin is based on the spectrophotometry characteristics of haemoglobin cyanide (126). Point-of-care testing with HemoCue was used; this method uses a modified azide methaemoglobin reaction to spectrophotometrically measure total haemoglobin. The most common source of error in haemoglobin measurement is the treatment of the reagents. Internal quality control of the HemoCue photometer was checked on a daily basis using the control cuvette and a standard of known concentration and external quality control was performed by the Norwegian Quality Improvement of Laboratory Examinations (Noklus) organization using control material sent to the GPs’ offices twice a year.

**CRP**

CRP was analysed from whole blood in Study II. Blood was drawn in the same way as described above for haemoglobin. There is no agreed reference method for CRP analysis. The range of CRP concentrations that can be encountered is wide, and one source of error is the high-dose hook effect at very high values. CRP was analysed using point-of-care testing (immunoturbidimetric) using an Afinion AS100 Analyser (analytical CV 6%), Orion Quickread CRP (analytical CV 5%) and ABX Micros CRP (analytical CV 3%). The analytical CVs for these three CRP test devices were obtained from Noklus. The advantages of these assays is that they are fully automated, rapid, and reproducible; however, they have a lower detection limit of around 5 mg/L, which precludes their use in risk assessment for CHD, where significant changes in the range of 0.5–3.5 mg/L have been reported (127).

**Statistical power**

Statistical power depends on statistical significance, and in Study II the statistical significance level was set at 0.05 (5%). The statistical power also depends on the prevalence of the outcome and the effect size. The prevalence of SpO$_2 \leq$ 95% was 22.0% in Study II. The sample size in Study II was 372 patients. Associations are more difficult to detect in smaller samples. Random error occurs because the associations we observe are based on
samples, and samples may not accurately reflect the population at large. In large samples, random errors have less impact.

In the multiple regression analysis, we included several covariates and the power for detecting an effect of a given size is related to the variance of the covariate. Because different covariates will have different variances, their powers will also differ.

The participation rate was only 34% in Study II. A high participation rate is important for internal validity, and in Study II, it cannot be assumed that the study sample was representative of the background population. This selection bias in Study II may have influenced the prevalence of low SpO₂ values but it probably did not influence the main findings of associations between decreased SpO₂, reduced lung function and co-morbid CHD.

6.3.4 External validity
The DIOLUP study was carried out at seven GP group practices that were not randomly selected but were chosen based on the availability of spirometry and the type of electronic medical record used. This may have influenced the generalizability (external validity) of the study results because the GP offices might not be representative of Norwegian practices. In three of the seven offices, the GPs had special interests in spirometry and obstructive lung diseases.

6.3.5 Strengths of Study II
GP patients were included from different areas of Norway, from both city and rural areas. In general practice, it may be difficult to differentiate asthma and COPD (87), and the inclusion of patients diagnosed with either or both of these conditions makes our results relevant for patients with obstructive lung diseases in primary care. This reflects daily clinical practice in which the GP examines patients with stable asthma and/or COPD. There is no information in current guidelines about how GPs should deal with moderately decreased oxygen saturation (SpO₂ ≤ 95%) in stable patients with asthma/COPD, and this study initiated the work required to help GPs to interpret values from pulse oximetry measurements in the follow-up for these patients.

6.3.6 Limitations of Study II
The main limitation was the low participation rate (34%), which implies that the study sample may not be representative of patients in general practice with asthma and COPD. However, the low participation rate is not likely to have substantially influenced the associations between decreased SpO₂ values and the predictors (128).
6.4 Study III

6.4.1 Introduction
To find out more about the association between low oxygen saturation and heart disease, we chose to examine this relationship in an epidemiological study, the Tromsø 6. We used DD as the outcome measure. DD is a common finding in the elderly and a known result of hypertension and CHD. The relationship between low pulse oximetry values and echocardiographic indicators of left ventricular filling was examined. Low oxygen saturation was independently associated with abnormal mitral Doppler flow as a measure of DD. DD should be considered as a possible cause of moderately decreased pulse oximetry values.

6.4.2 Methodological considerations
The Tromso study is population-based, a term that is traditionally used to describe a study that involves a defined “general population”. The common usage of the term implies sampling of individuals from the general population.

6.4.3 Internal validity
Selection bias
In Tromsø 6, 66% of those invited participated in the first visit and 92% of those invited to the second visit attended, which represents a moderate decrease in participation rates from earlier Tromsø studies. People were sent reminders and social media was used to improve the participation rate. One reason for non-participation may be a lack of time: more comprehensive data collection, for example, from the echocardiography examination, means that the second visit is more time-consuming.

Most non-participants were in the youngest and oldest age groups and in men. Severe co-morbidity among non-participants may be the reason for the low participation rate in the oldest age group, and the effect of age could have been under-estimated. The most ill and the oldest participants may have had difficulty with transport to the central location where Tromsø 6 took place. Some people are concerned about issues with data security and may not want to provide informed consent to have their data stored in a database. Because there are few short-term benefits from health surveys, healthy age groups are less willing to participate. Some people are afraid of personal discomfort and so do not want to participate. The education level of the participants was higher than that of the general Norwegian population and the Tromsø population (90). The subjects who attended the first visit were given a second questionnaire that they were asked to complete and return by mail and 88.2% did so. The
responders tended to be married, non-smokers and to report respiratory symptoms less often than non-responders (129). The Tromsø study is comparable with the Nord-Trøndelag Health (HUNT) study. In that study, non-participants had lower socio-economic status, higher mortality and a higher prevalence of several diseases including COPD and myocardial infarction than participants (130). Non-participants in HUNT 3 had poorer general health, and a less healthy lifestyle in terms of tobacco smoking and physical inactivity (130). Non-response bias is a major concern for studies based on data collected through questionnaires and the differences described above may lead to bias in prevalence estimates and bias in associations. However, in a study from the Netherlands, no differences were found between respondents and non-respondents for the associations between smoking or socio-economic status and subjective health (131), and non-response did not cause bias in the examined associations.

Participants with missing data are a common and unavoidable problem in clinical and epidemiological studies (101). This is problematic because methods for statistical analysis assume that the data are complete. There are many reasons for missing data; examples from our studies include a participant failing to complete some of the items on a questionnaire, the laboratory/test personnel forgetting to do a test (e.g., of a blood sample, BMI measurement) or the tests are technically unsatisfactory (e.g., pulse oximetry, spirometry, echocardiography). We have excluded participants with missing data from our univariable and multivariable analyses. This is called complete case analysis (101), and usually introduces bias unless the data are randomly missing. In our analysis, it is difficult to justify that the missing data are completely random. In addition, we lost information because we discarded the incomplete observations, which might have resulted in decreased precision in our results. However, if the proportion of missing data is very low, little harm is done by using the complete case analysis method instead of more complicated missing data methods (132). In Study III, there were missing data (3.8% in the multivariable analysis); an alternative approach to deleting cases would have been imputation, in which missing values are replaced by some plausible value predicted from that individual’s available data (132).

**Measurement errors**

**Echocardiography**

The various sources of measurement variability need to be considered when applying cardiovascular ultrasound to clinical research. Echocardiography is an operator-dependent technique
and variability of measurements may lead to collection of inaccurate data (133). Echocardiography is also dependent on image quality.

In Study III, echocardiography was performed by two expert cardiologists as described in Section 4. The accuracy of the measurement of 2D/M-mode LV diameters is described as fair, and that of the measurement of EDT and E/e' as good (133).

In Tromsø 6, the available echocardiographic measurements for the diagnosis of diastolic HF were the E/A ratio and EDT, LA diameter and TDI of the septal mitral annulus (and thereby calculation of the E/e' ratio).

M-mode-derived LVEF has inherent limitations and is known to both over- and underestimate the severity of dysfunction; M-mode measurements do not necessarily reflect the true minor-axis dimension (134). However, because the majority of the participants were healthy individuals, the shortcomings of the method are of less importance.

**BMI**

In Study III, weight and height were measured by laboratory staff. BMI was calculated using a standardized method. Incorrect calibration of body weight measurement may cause systematic errors if the sensitivity and specificity vary between different ranges of the scale.

**Statistical power**

In Study III, the statistical significance level was set at 0.05 (5%). The sample size was 1,782 participants. This large sample increased the statistical power and the chances of finding associations. However, the statistical power also depends on the prevalence of the outcome and the effect size. The prevalence of SpO₂ ≤ 95% was higher in Study II than in Study III (22.0% and 6.4%, respectively).

The participation rate in Tromsø 6 was 65.7%; a high participation rate is important for internal validity. In Study III, the participation rate was lower in the oldest age group, and this potential selection bias may have decreased the observed relationships between the findings.

**6.4.4 External validity**

In the Tromsø study, the invitation to participate came from the Norwegian Population Registry. Tromsø is the seventh largest Norwegian city, dominated by Caucasians of mainly Norwegian origin, and may be representative of a Northern European, white, urban population (135). The study is limited with regard to ethnic diversity (90).
6.4.5 Strengths of Study III

The participation rate was high, which is important for the validity of the results. Previous adult population studies have not investigated the association between low oxygen saturation and DD.

6.4.6 Limitations of Study III

Cross-sectional data cannot establish causal relationships between pulse oximetry values and echocardiographic variables.

In Study III, DD was classified by Doppler examinations of mitral inflow and of septal TDI at the mitral annulus, and LA size by M-mode diameter because only these variables were available. With some adjustments, we classified DD according to well-validated measures of DD that have been validated against mortality as an end-point (82). In their study, Redfield et al. (82) required participants to have two Doppler criteria consistent with DD to be so classified. Only one Doppler criterion was used in our definition of DD in Study III and this is a clear limitation.

According to the 2016 recommendations for the evaluation of LV diastolic function by echocardiography, there are four recommended variables for identifying DD; if more than two of these do not meet the cut-off values for abnormal function, LV diastolic function is considered to be normal (83).

In contrast with the previous guidelines, the 2016 classification has not yet been validated against mortality or hospitalization for heart failure as end-points. It is not possible to convert this study designed before 2016 to comply with the new guidelines because they incorporate variables rarely collected in population surveys.

The echocardiographic data for DD were not connected to symptoms and we were unable to distinguish between participants with preclinical DD (PDD) and HF with HFpEF. N-terminal pro b-type natriuretic peptide was not measured in the Tromsø 6 study.

PDD is prevalent and is defined as DD without a diagnosis of HF and with normal systolic function (136). Figure 10 shows the progression from preclinical DD to symptomatic HF including dyspnoea, oedema and fatigue. PDD is clinically significant, and it is essential to identify the risk factors for progression to HF and to delay progression to HFpEF using therapeutic intervention (136). In our study, the participants with DD included those with both PDD and HFpEF. Although this is a clear limitation, it is important to identify both conditions (Figure 10).
Figure 9
Cardio-vascular and non-cardiac risk factors in the development and progression of PDD and HFpEF.

The accuracy of SpO₂ measurements could have been checked using arterial blood gas analyses in a subsample of the survey but this was not done in Tromsø 6.
6.5 Ethics

Study I
The study was presented to the Regional Committee for Medical and Health Research Ethics, South-East Norway, who judged this to be a clinical audit project, and therefore, not requiring formal approval by the committee. All patients provided signed informed consent allowing the analysis and publication of the results at an aggregated level that did not compromise patient anonymity.

Study II
Participating patients signed a written consent form and the study was approved by the Regional Committee for Medical and Health Research Ethics, North Norway.

Study III
The Regional Committee for Medical Research Ethics, North Norway approved the Tromsø 6 survey. All the participants gave written informed consent and were able to withdraw their data from the study. Data were secured to maintain confidentiality, integrity and availability. An IT solution, the Tromsø Study database (EUTRO), was designed to protect and manage metadata, data and projects. Data security is in accordance with the requirements of the Data Inspectorate, and data storage and security are handled by the university’s central IT department.
7. Clinical implications

In recent years, technological advances have led to more point-of-care testing. This near-patient testing has potential benefits for primary care. The GP is the first contact with the health care system for most patients with asthma and COPD in Norway. Primary care spirometry is a valuable tool in the evaluation of patients with respiratory symptoms (137). More accurate diagnosis of asthma and COPD patients is important and may lead to improved management, fewer symptoms and better quality of life (138). Spirometry data from the DIOLUP study showed that 64% of the patients with obstructive spirometry (FEV₁/FVC < 0.7) had a diagnosis of COPD registered in their electronic medical record (87). This was an improvement in detection of COPD in routine care compared with previous studies (139, 140). In a study from Denmark, a diagnosis of COPD and subsequent treatment were supported by spirometric data in only 50% of cases (141). Under-use of spirometry is a major reason why COPD is underdiagnosed in primary care (142). Better implementation of spirometry testing in general practice is important. In a study from the U.K., women were more likely to have a GP diagnosis of COPD that was amended after spirometry (143). In recent years, the prevalence of COPD has been growing faster for women than for men in many countries (144), and this highlights the importance of spirometry in general practice.

In the Lillestrøm study, primary care spirometry was useful for identifying ICS overuse. The limited use and implementation of spirometry do not necessarily correlate with a limited use of pulmonary medications. Other studies also indicate that ICS are overprescribed for COPD in general practice (145-147). In Denmark, improved prescribing of ICS according to the guidelines was achieved through education of the GPs and their staff (147). Spirometry needs to be more widely used to improve the accuracy of respiratory diagnoses in general practice (138). Early diagnosis is an issue, but it optimizes the opportunities to prevent worsening of disease and prevention of co-morbidities (142). Oxygen saturation measured by pulse oximetry is considered to be the “fifth vital sign” in addition to heart rate, temperature, blood pressure and respiratory rate (148). Pulse oximetry is now in common use in general practice and it is easy and safe to perform. The diagnostic benefits of pulse oximetry for diagnosis and treatment in general practice remain to be established. In the DIOLUP study, pulse oximetry seemed to be a useful measure in the follow-up of asthma and COPD patients, where decreased values may reflect suboptimal treatment and/or co-morbidity. Data from DIOLUP, not part of this PhD project, also show
that a severe decrease in SpO$_2$ was a strong predictor of a drop in lung function during asthma and COPD exacerbations (8). It may be useful to take low pulse oximetry into account when considering treatment with oral corticosteroids (8). Low SpO$_2$ was associated with increased all-cause mortality in a general adult population, probably because of a strong association with death caused by pulmonary disease and HF (10). SpO$_2$ > 90% was an independent predictor of survival among lung cancer patients (149). This indicates that low pulse oximetry values may provide crucial clinical information in the follow-up of all patients with lung disease, including in general practice, but this should be confirmed in new studies. A diagnosis of CHD in the DIOLUP study and of DD in the Tromsø study was independently associated with decreased pulse oximetry values and these conditions should be included among possible explanations for low SpO$_2$ values. In a Swedish register-based study, primary care was the only care provider to 21% of patients with coexisting HF and COPD (150). To understand the clinical consequences of this co-morbidity (18), greater collaboration is required between cardiologists, pulmonologists and GPs caring for such patients (18).

Driver’s licence regulations prepared by the Norwegian Directorate of Health (151) advise the GP to refer to specialist assessment if patients have SpO$_2$ < 90% or FEV$_1$% predicted < 30%. This exemplifies that it is important for GPs to have experience in measuring and interpreting results from pulse oximetry and spirometry in everyday work.
8. Conclusion and future perspectives

Through our three studies, we have according to the detailed aims:

1. Gained knowledge about the use of spirometry and pulse oximetry in general practice for patients with lung and/or heart diseases. A clinical audit including spirometry was useful for identifying overuse of ICS.
2. Pulse oximetry was shown to be a valid measure in the follow-up for asthma and COPD patients in general practice; it is also important to look for co-morbidities, including a diagnosis of CHD.
3. DD should be included among possible explanations when decreased oxygen saturation is found.

8.1 What is a good diagnostic test for a GP?

There is no easy answer to this question; the answer lies not only in the sensitivity and specificity of the diagnostic tests, but it has also to do with the GP’s skills in using these tests in clinical practice. It is important that more research be conducted in general practice to confirm these associations and to determine the best cut-off points for SpO₂ and the implementation of spirometry. We are in the process of establishing a research network in general practice in Norway that may be viewed as a laboratory for primary care research (152). This will make it easier to include patients from representative medical centres and regions in Norway and hence achieve better external validity for future studies. Other fields of interest for testing pulse oximetry values in general practice are patients having acute consultations because of breathing problems and/or chest pain, children with signs of pneumonia, and for follow-up of patients with HF. With more knowledge available, we could ask: “How are low pulse oximetry values useful in decision-making about the treatment of patients in general practice, for example, for patients with COPD, asthma, HF or pneumonia? Which SpO₂ values does the GP act on in different settings?” A new diagnosis of obstructive lung disease was associated with increased rates of smoking cessation in COPD patients (153); the new diagnosis of COPD gave the participants motivation to stop smoking (153). This indicates that spirometry is a useful diagnostic test for all smokers. We also need more research about the association between pulse oximetry and HF (both systolic and diastolic) from patients followed up in primary care.
In the fast-moving context of telehealth care, spirometry and pulse oximetry are tests that fit well for implementation in telemonitoring in primary care. In 2008 in Greenland, a computer-based telemedicine system called “Pipaluk” was implemented to provide citizens living in rural areas with easier access to health care. The computer-based system was connected to various medical devices, including for oxygen saturation and spirometry, and to an examination camera (61). Greenlandic citizens regard telemedicine as a facilitator of improved access to health care in the Greenlandic Settlements (61).

There are no reliable data to support or refute patient use of pulse oximeters to monitor oxygen saturation levels when experiencing an asthma attack (154). Some patients have a reduced perception of the severity of their own breathlessness when exposed to hypoxia (154). Pulse oximetry might be beneficial for those who have such a lowered perception of their hypoxia, but this has not been studied in patients having an asthma attack (154). Pulse oximetry used incorrectly in this setting could delay the patient seeking appropriate medical help and worsen outcomes. Pulse oximetry needs to be interpreted in the context of the whole clinical scenario, not in isolation (155).

A low-cost phone oximeter is now available; this might be important in low- and middle-income countries because these areas of the world remain largely without access to advanced health technology, while phones are widely available (156). The quality of these measurements needs to be assessed. We also need more evidence from general practice about the usefulness of pulse oximetry to allow its further implementation in patient care.
References


55. Haugen T, Bakken IJ, Storro O, Oien T, Langhammer A. Utvikling i diagnostisering og helsetjenesteforbruk ved obstruktiv lungesykdom. (Utilization of diagnostic tools...


154. Welsh EJ, Carr R. Pulse oximeters to self monitor oxygen saturation levels as part of a personalised asthma action plan for people with asthma. Cochrane Database Syst Rev. 2015(9):CD011584.


Errata
Paper II
Paper III
Appendix 1

Letter of Invitation

Questionnaires from the Lillestrøm study
Lillestrøm legesenter
CJ Hansens v 3a
2007 Kjeller
64 84 69 60

Kjeller 5/10 2006

Nye regler for forskrivning og refusjon for legemidler til inhalasjon ved astma og KOLS.

Kjære

Astma og KOLS er to sykdommer som kan ha ganske sammenfallende symptomer, men som er ganske forskjellige biologisk sett. Behandlingen av de to sykdommene har langt på vei vært lik, og de har også blitt behandlet sammen i bløreeptordningen (§9 p2). Fra og med 1/6 2006 skal medisiner mot astma refunderes under §9 p 44 og medisiner mot KOLS under §9 p 45.

De nye refusjonsreglene vil kunne få betydelige konsekvenser for mange pasienter med kronisk lungesykdom ved at de ikke lenger får sin medisin på blå resept. Lillestrøm legesenter vil aktivt gå ut til alle aktuelle pasienter som vil kunne bli berørt av disse endringene. Vi vil sørge for at alle som har krav på refusjon etter §9 p 44 skal få det.

Hva går endringene ut på?
Rene kortikosteroidpreparater ("kortison-") til inhalasjon er ikke lenger godkjent til pasienter med KOLS. Dette gjelder for eksempel Flutide og Pulmicort.
Kombinasjonspreparater som inneholder kortikosteroider og langtidshvirkende bronkiodtvingende medisin kan forskrives til pasienter med KOLS, men dekkes ikkje av på vanlig "blå resept". Fastlega kan søke spesialt for hver enkelt pasient om refusjon etter folketrygdens § 10a. Dette medfører at pasienter som bruker disse medisinene må gjennom en undersøkelse for å godtgjøre at de fortsatt har krav på "blå resept" for sin lungemedisin.

Hva er astma og hva er KOLS?

Enkelt kan det sies at Astma starter i unge alder hos mennesker, og som ofte har arvelig disposisjon for astma og allergi. Sykdommen er i begynnelsen alltid variabel og tilstanden kan endre seg raskt. Mange "vokser av seg" sin astma i tidlig voksen alder.
KOLS er vanligvis sterkt assosiert med langvarig påvirkning av tobakk og støv med mer. Den rene KOLS kjenner seg ved en jevn reduksjon i lungefunksjonen pga en pågående
ødeleggelse av lungevev. Forskning har ikke kunnet påvise behandlingseffekt av en del av de legemidler som til nå har vært brukt. Myndighetene vil derfor ikke lenger gi refusjon til disse legemidler på blå resept.

En rekke pasienter har både astma og KOLS. Dersom man i journalen kan dokumentere dette, vil pasienten kunne fortsette å få sine legemidler på blå resept.

**Hva gjør du?**
Som pasient ved Lillestrøm legesenter som har fått Flutide, Pulmicort, Seretide eller Symbicort fem 1/1 2005 får du dette brevet. For å avklare om du fortsatt har rett til å få lungemedisinen på blå resept ber vi deg:

1. Ta kontakt med Lillestrøm legesenter for å bestille en kontrolltime.
2. Besvar vedlagte spørreskjema, og bring det med deg ved denne kontrollen.
3. Det er viktig at du ikke har tatt inhalasjonsmedisinen undersøkelsesdagen.

**Hva gjør vi?**
Ved klinisk undersøkelse og sykehistorie ønsker vi å dokumentere at du fortsatt fyller kravene til å få disse legemidler på blå resept. Ved å gjøre det på denne måten håper vi å unngå kaos på apoteket, i telefonen eller i luka på legesenteret ved neste reseptfornyelse.

Du kan lese om endringene i refusionsforskriftene på internett på følgende adresse:

[http://www.legemiddelverket.no/templates/InterPage_20108.aspx](http://www.legemiddelverket.no/templates/InterPage_20108.aspx)

I samarbeid med Universitetet i Oslo Institutt for samfunns- og allmenneledisin ønsker vi å bruke den innmatede informasjonen til en vitenskapelig undersøkelse, hvor alle informasjoner er **100 % anonyme.**

Vennlig hilsen

**Legene ved Lillestrøm legesenter**
<table>
<thead>
<tr>
<th>Nummer</th>
<th>Mann</th>
<th>Kvinne</th>
<th>Alder</th>
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</thead>
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</table>

1a Hvor mye røker du
- Rokerikke: 0-10 dag
- 10-20 dag
- Mere enn 20 dag

1b Hvor lenge har du røkt
- 0-10 år
- 10-20 år
- 20-40 år
- Mere enn 40 år

2 Hvor gammel var du da du fikk lungesykdom?
- Under 20 år
- 20-40 år
- 40-60 år
- Mere enn 60 år

2a Har du kjent allergisk sykdom?
- Ja
- Nei

2b Hadde du barne-eksem som liten?
- Ja
- Nei

3 Hoster du og i tilfelle hvordan?
- Høster ikke
- Tørnhøste
- Hoster oppslam

4 Varierer dine symptomer i løpet av døgnet?
- Ja
- Nei
### Påstand om din sykdom:

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<thead>
<tr>
<th></th>
<th>Ikke riktig</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>Delvis Riktig</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>Helt riktig</th>
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<td><strong>Dine medisiner:</strong></td>
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<td>Jeg føler at inhalasjonsmedisinen hjelper meg</td>
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<td>Jeg er engstelig for å miste mine medisiner</td>
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<td>Jeg føler at inhalasjonsmedisinen bedrer hossten min</td>
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<td>Jeg føler at inhalasjonsmedisinen reduserer slim og oppsytt</td>
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<td>Jeg har hyppige sykdomsforveiler</td>
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<td><strong>Din sykdom og livskvalitet</strong></td>
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<td>Lunge-sykkommen reduserer mine muligheter til fysisk livsutfoldelse, som trim, sykling, turer i fjell osv</td>
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<td>Lungermedisin bedrer mine muligheter til fysisk livsutfoldelse, som trim, sykling, turer i fjell osv</td>
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<td><strong>Endringer i refusjonsordninger for astma og KOLS:</strong></td>
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<td>Jeg viste ikke noe om dette før jeg fikk brev fra fastlegen</td>
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<td>Jeg forventer at min fastlege tar kontakt med meg om viktige endringer i minmedisinering</td>
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**Hvilke lungermedisin bruker du:**

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<tr>
<th></th>
<th>Seretide</th>
<th>Flutide</th>
<th>Pulmicort</th>
<th>Symbicort</th>
</tr>
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</table>

**Hvilken sykdom gjør at du bruker denne lungermedisinen:**

<table>
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<tr>
<th></th>
<th>Astma</th>
<th>KOLS</th>
<th>Astma + KOLS</th>
<th>Annet</th>
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</table>
Appendix 2

Letter of Invitation

Questionnaires

Registration forms from the DIOLUP study
Bakgrunn og hensikt
Vårt legekontor deltar i en landsomfattende undersøkelse om behandling av astma og KOLS hos fastlegen. Dette er et spørsmål til deg om å delta i en forskningsstudie for å belyse hvordan personer med astma og KOLS bør undersøkes og behandles når de får en akutt forverring av sin sykdom. Hvor raskt bør lege oppsøkes ved forverring av KOLS eller astma? Hvilke undersøkelsener bør fastlegene foreta? Bør pasienter ha medisiner hjemme og starte egenbehandling?

Hva innebærer studien?
Dersom du sier ja til å være med blir du innkalt til en undersøkelse i løpet av 3 måneder. Denne undersøkelsen bør foretas når din sykdom er i stabil fase. Du vil bli spurtrum din sykdom.


Dersom du blir innlagt på sykehus, skal du komme til kontroll hos fastlegen tre uker etter at du er skrevet ut. Du bør oppsøke ditt fastlegekontor i forbindelse med alle forverringer i året etter første undersøkelse, dersom det rent praktisk passer for deg. Alle undersøkelsene vil være gratis.

Mulige fordeler og ulemper
Du vil bli ekstra grundig undersøkt. Deltakelse innebærer ekstra besøk hos legen, og dermed bruk av din tid. Undersøkelsene medfører ikke fysisk ubehag utover et stikk i fingeren.

Hva skjer med data som blir samlet inn om deg?
Prøvene tatt av deg og informasjonen som registreres om deg vil bli oppbevart i din journal hos fastlegen. Disse opplysningene vil også bli overført i avidentisert form (uten navn og fødselsnummer eller andre direkte gjenkjennerende opplysninger) til en kvalitetssikret elektronisk database ved Universitetet i Tromsø. En kode knytter deg til dine opplysninger og prøver gjennom en navneliste som oppbevares på ditt fastlegekontor. Det er bare autorisert personell
ved fastlegekontoret som har tilgang til denne. Det vil ikke være mulig å identifisere deg i resultatene av studien når disse publiseres.

**Frivillig deltakelse**

Dersom du har spørsmål til studien kan du også kontakte prosjektsvarlig professor Hasse Melbye ved Allmennmedisinsk forskningsenhet, Institutt for samfunnsmedisin, Universitetet i Tromsø, telefon 77644816, e-post hasse.melbye@ism.uit.no
Samtykke til deltakelse i studien

Jeg er villig til å delta i studien

Dato og signatur

Navn med store bokstaver
Baseline, fylles ut av pasient.

Pasientkode:  

I hvor mange år har du hatt astma og/eller KOLS?  

- Astma  
- KOLS  

Hvilken diagnose fikk du først?  

- Astma  
- KOLS  

Hvilken diagnose har du nå?  

- Astma  
- KOLS  

I hvor mange år har du hatt den diagnosen du har nå?  

- <5 år  
- >5 år  

Hvem ga deg den diagnosen du har nå?  

- fastlegen  
- læge  
- annen lege  
- vet ikke  

Hvilken lege kontrollerer deg oftest?  

- fastlegen  
- læge  
- annen lege  
- vet ikke  

Hvem ble du sist undersøkt av? (for i dag)  

- fastlegen  
- læge  
- annen lege  
- vet ikke  

Har du vært innlagt på sykehus pga. astma eller KOLS?  

- Ja  
- Nei  

Hvis ja, hvor mange ganger siste 12 mån?  

- ganger  

Her er noen plattater som du kan si deg enig eller uenig i.

Det er nødvendig å opprette lege hver gang pusteproblemene forverrer seg  

- helt enig  
- nokså enig  
- verken enig eller uenig  
- nokså uenig  
- helt uenig  

Når pusteproblemene blir verre er det vankelig å vite om jeg trenger å bli undersøkt av lege  

- helt enig  
- nokså enig  
- verken enig eller uenig  
- nokså uenig  
- helt uenig  

Når pusteproblemene blir verre ville det være best om jeg kunne styre behandlingen selv  

- helt enig  
- nokså enig  
- verken enig eller uenig  
- nokså uenig  
- helt uenig  

Når pusteproblemene blir verre vil jeg helst bli undersøkt av lege i løpet av en dag eller to  

- helt enig  
- nokså enig  
- verken enig eller uenig  
- nokså uenig  
- helt uenig  

Det er betydelig å snakke med en lege når pusteproblemene blir verre  

- helt enig  
- nokså enig  
- verken enig eller uenig  
- nokså uenig  
- helt uenig  

Plages du med heste?  

- Torgheste  
- slimbistle  
- ingen heste  

85
Ved sp. Ang. utfylling av spørreskjema vennligst kontakt Elin Drivenes, tlf 99 56 22 26, Tone Leinan eller Lene Dalbakk

<table>
<thead>
<tr>
<th>Yrkeserfaring</th>
<th>heltid</th>
<th>deltid</th>
<th>ufor</th>
<th>pensionist</th>
<th>Sykmeldt, rehabilitering, attføring</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yrkesaktiv</td>
<td>For det meste stillesittende arb. (f.eks skrivebordsarb. monstring)</td>
<td>Arbeid som krever at du går mye (f.eks ekspedisjonsarb., lett industriarb., undervisning)</td>
<td>Arbeid der du går og løfter mye (f.eks postbod, pleier, bygningsarb.)</td>
<td>Tungt kroppsarbeid</td>
<td></td>
</tr>
</tbody>
</table>

Har du arbeidet i et miljø med irriterende stov, gass eller røyk?  
Ja  Nei

Hvis ja, i hvor mange år?  
0-5 år  5-20 år  >20 år

Arbeider du eller har du arbeidet i helsevesenet?  
Ja  Nei

Har du eller har du hatt annet omsorgsyrke?  

Har du eller har du hatt en ledersjobb med personalansvar?  

Asthma og KOLS i familien  
Har en av dine foreldre hatt astma eller KOLS?  
Ja  Nei

Har du hatt samboer eller søsken med astma eller KOLS?  

Har du hatt barn med astma eller KOLS?  

Har du eller har du hatt daglig omsorg for barn?  

Røyking  
Røyker nå  
Ja  Nei

Røytet tidligere  

Hvis ja;
Antall år røykt

Hvis ja;
Gjennomsnittlig antall sigaretter pr dag i årene røykt

FYLLES UT AV HELSE SEKRETAER

Hb g/dl

CRP mg/L

PO₂ (best av 3 målinger)

Legerkode

Legg ved spirometri og reversibilitetstest.
**Registrierungsskjema i legejournalen for Baseline-undersøkelsen**

<table>
<thead>
<tr>
<th>Patientkode</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Alder</td>
<td></td>
</tr>
<tr>
<td>Kjønn</td>
<td>Kvinne</td>
</tr>
<tr>
<td>Varighet av den obstruktive lungesykdommen (år)</td>
<td></td>
</tr>
<tr>
<td>Antall eksaserbasjoner behandlet med antibiotika eller prednison siste 12 mndr.</td>
<td></td>
</tr>
<tr>
<td>Har pasienten fått resept på antibiotika eller prednison til egenbehandling siste 2 år?</td>
<td>Ja</td>
</tr>
<tr>
<td>Bruker pasienten forstøverapparat?</td>
<td></td>
</tr>
<tr>
<td>Har pasienten hjemmesurstoff</td>
<td></td>
</tr>
<tr>
<td>Medisinbruk (fast, inntak dgl eller minst hver uke)</td>
<td>Ja</td>
</tr>
<tr>
<td>Hurtigvirkende beta2agonist til inhalasjon (feks. Ventolin)</td>
<td></td>
</tr>
<tr>
<td>Oxis eller Serevent</td>
<td></td>
</tr>
<tr>
<td>Flutide eller Pulmicort</td>
<td></td>
</tr>
<tr>
<td>Seretide eller Symbicort</td>
<td></td>
</tr>
<tr>
<td>Atrovent eller Spiriva</td>
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</tr>
<tr>
<td>Singulaire eller annen leukotrienantagonist</td>
<td></td>
</tr>
<tr>
<td>Teofyllinpreparat</td>
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</tr>
<tr>
<td>Peroral beta2agonist</td>
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<tr>
<td>Lomudal</td>
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</tr>
<tr>
<td>Annen allergimedisin</td>
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</tr>
<tr>
<td>Blodtrykksmedisin</td>
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<tr>
<td>Statiner</td>
<td></td>
</tr>
<tr>
<td>Annen hjerte-kar-medisin</td>
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</tr>
<tr>
<td>Antidiabetika eller insulin</td>
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</tr>
<tr>
<td>Prednison mot obstruktiv lungesykdom</td>
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</tr>
<tr>
<td>Prednison mot annen sykdom</td>
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</tr>
<tr>
<td>Annen immunologisk beh. eller medisin mot kreft</td>
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</table>
Kroniske sykdommer

<table>
<thead>
<tr>
<th>Ja</th>
<th>Nei</th>
</tr>
</thead>
<tbody>
<tr>
<td>R96</td>
<td>R95</td>
</tr>
</tbody>
</table>

Hvilken av disse diagnose er sist journalført

<table>
<thead>
<tr>
<th>Ja</th>
<th>Nei</th>
</tr>
</thead>
<tbody>
<tr>
<td>Har pasienten annen kronisk lungesykdom?</td>
<td></td>
</tr>
<tr>
<td>Har pasienten koronar hjertesykdom</td>
<td></td>
</tr>
<tr>
<td>Har pasienten hatt hjerneslag eller drypp</td>
<td></td>
</tr>
<tr>
<td>Har pasienten annen hjerte-kar-sykdom</td>
<td></td>
</tr>
<tr>
<td>Har pasienten diabetes</td>
<td></td>
</tr>
<tr>
<td>Har pasienten blitt behandlet for kreft</td>
<td></td>
</tr>
<tr>
<td>Har pasienten atopisk eksem</td>
<td></td>
</tr>
<tr>
<td>Har pasienten allergisk rhinit eller konjunktivitt</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Høyre lunge</th>
<th>Venstre lunge</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ja</td>
<td>Nei</td>
</tr>
</tbody>
</table>

Perkusjon
Hyppersonor perkusjonslyd
Dempning

Auskultasjon
Svekket respirasjonslyd
Knatryler (eller kreptasjoner)
Pipeulyder (sibili, rhonki)
Appendix 3

Letter of invitation

Questionnaires from the 6th Tromsø study
Vil du være med i den 6. Tromsøundersøkelsen?
» viktig forskning
» undersøkelse av egen helse
» forebygging av helseproblemer
Hva er Tromsøundersøkelsen?
Tromsøundersøkelsen er et stort forskningsprosjekt. Opplysninger som samsles inne skal brukes til å gi oss kunnskap som kan bedre menneskers helse.

Den første Tromsøundersøkelsen ble gjennomført allerede i 1974, og dette er den sjette i rekken. Et viktig mål med undersøkelsen er å få kunnskap om hvorfor noen blir syke mens andre beholder god helse gjennom livet.

Visste du at ..?
Den som deltar på Tromsøundersøkelsen får også en enkel undersøkelse av sin egen helse.

Hva forskes det på i Tromsøundersøkelsen?
Tromsøundersøkelsen gjennomføres først og fremst for å kunne øke kunnskapen om de store folkehelseproblemene og forhold som påvirker disse, blant annet:

- Hjerte- og karsykdommer
- Lungesykdommer (f.eks. KOLS)
- Diabetes
- Stoffskiftesykdommer
- Kreftsykdommer
- Psykiske plager
- Demens
- Muskel- og skjelettplager

Undersøkelsen vil også bli benyttet til forskning om bruk og effekter av legemidler, trivsel, livskvalitet, livsstil, døgnryme, smerten, sosial ulikhet, fysisk aktivitet, kosthold, bruk av helsetjenester og alternativ behandling. Det vil også bli undersøkt om miljøgifter kan påvises i blodet og om disse innvirkende på helsen.

Videre vil det bli gjort forskning på kvinnesyksommer, sykdommer i fordøytelseorganer, allergi, nyrer og urinveier, nervesystemer, sanseorganer og hud. Det vil også bli forsket på arbeidsuferhet som følge av disse sykdommene eller tilstandene.

En del av prosjektene vil spesielt undersøke samspillet mellom arv, miljø, sykdom og helse. Til slike prosjekter vil det bli hentet ut DNA (arvestoff) fra blodprøvene.

Det er allerede planlagt mange forskningsprosjekter som skal benytte data fra Tromsøundersøkelsen. Du vil finne en liste over disse på vår internettseite:

http://www.troms06.no

Vil du delta?
Ved å delta på Tromsøundersøkelsen er du med på å bidra til forskning om hvordan sykdom kan forebygges og behandles, hva som fremmer god helse, og hva som er årsak til helseproblemer.

Hvorfor spør vi deg?
Alle som møtte til spesialundersøkelsene i Tromsøundersøkelsen i 1994 og 2001, og et tilfelldig uttrykket utvalg av personer som er over 30 år og som er innbyggere i Tromsø kommune, blir spurtt om å delta.

Alle er viktige!
Hver deltaker er like viktig, enten du er ung eller gammel, frisk eller syk. Det har vært stort framstøt til de tidligere Tromsøundersøkelsene. Godt oppmøte er viktig for gode forskningsresultater. Det er en styrke for forskningen at de som har vært med i tidligere Tromsøundersøkelser møter fram på nytt.

Frivillig
Visste du at ..?
Du kan delta på Tromsøundersøkelsen selv om det er deler av undersøkelsen du ikke ønsker å være med på.

Din helse
Cirka fire uker etter undersøkelsen vil du få et brev med resultatene fra målinger av kolesterol og blodtrykk. Dersom det er nødvendig, vil du bli anbefalt å ta kontakt med din fastlege. Det blir ikke gitt rutinemessig tilbakemelding om resultater av andre blodprøver eller målinger.

Dersom resultatet av prøvene viser at det er nødvendig med oppfølgning av lege eller henvisning til spesialist, vil du bli orientert om det. Ved behov for henvisning til spesialist, vil du sørge for at slik henvisning blir sendt.

Du kan reserveve deg mot å få vите resultatene av prøvene dine. Men hvis et prøveresultat er slik at det er nødvendig med rask legebehandling, vil du uansett bli kontaktet.


Slik foregår undersøkelsen

Unngå før undersøkelsen
For at resultatene skal bli mest mulig korrekt, er det en fordøl om du avstår fra alkohol og smertestillende medisiner 12 timer før undersøkelsen.

Påkledning
Vekt og høyde, liv- og hoftevidde måles med lett påkledning, men uten sko. For at det skal gå raskt å måle blodtrykk, er det en fordøl om du har plagg som ikke strammer over armen og benet. Ha gerne et kortermet plagg innerst.

Spørreskjema

Utfyler svar i spørreskjema er like viktig for forskningen som resultater fra blodprøver og undersøkelser.
Regelmessig bruk av legemidler

Undersøkelser

De måler høyde, vekt, hoitvidde og livvidde, de måler blodtrykket og tar blodprøve av deg. I tillegg vil følgende undersøkelsener bli gjort:

» Beintetthetsmåling (måling av beinmasse) i den ene armen med svake røntgenstråler. Målingene brukes til å undersøke risiko for beinskjørhet og brudd.

» Bakterieprøve fra nese og hals fra om lag halvparten av deltagerne, for å se etter gule stafylokoker, en bakterie som normalt finnes på hud og slinninger hos mennesker, men som i enkelte tilfeller kan forårsake alvorlige infeksjoner. Prøven gjøres med fuktet vattpensel.


» Hårprøve. Vi vil be om å få noen hårstrå for å undersøke forekomsten av spormetaller som kvikksølv.

Fysisk aktivitet og kosthold. Vi planlegger at utvalgte deltakere vil bli bedt om å registrere fysisk aktivitet (aktivitetsmåler som skritteltellere og lignende) og kosthold i en periode.

Blodprøver
Blodet fordeles på fem glass, men til sammen utgjør det ikke mer enn 45 milliliter, som er mindre enn en tidel av det en blodgiver gir. For de aller fleste vil det være tilstrekkelig med ett stikk. Disse analysene blir gjort:

» Måling av kolesterol og andre fettstoffer, blodsukker, blodlegemer, stoffskifteprøver, hormoner, markører for betennelsesreaksjoner, allergi, mage- og tarmfunksjon, lever- og nyrerefeksjon samt muskel- og beinmarkører.

» DNA (arvestoff) vil bli lagret til bruk i forskningsprosjekter som er omtalt i denne brosjyren og som kartlegger sammenhengen mellom av og miljø, sykdom og helse. DNA vil ikke bli brukt til andre formål enn forskning.

» Miljøgifter, blant annet sporstoff, spormetaller og organiske stoffer. Forekomsten i blodet skal sammenlignes med tilsvarende målinger i andre befolkninger. Forskere vil studere om miljøgifter kan påvirke helse vår.

Spesialundersøkelsen
Når første del av Tromsundersøkelsen er gjennomført, kan du bli forespurt om å delta i en eller flere deler av Spesialundersøkelsen noen uker senere. Over halvparten vil bli spurt om dette. Hele spesialundersøkelsen vil vare cirka en time, og
varigheten vil være avhengig av hvor mange deler du blir spurt om å være med på. Ved oppmøte til Spesialundersøkelsen vil det bli tatt ny blodprøve som skal brukes til samme formål som beskrevet for første del av undersøkelsen. Deler av blodprøven blir frosset ned for senere bruk i forskning som er beskrevet i denne brosjyren.

Hvilke undersøkelser gjøres i Spesialundersøkelsen?

» Ultralyd av blodårene (arteriene) på halsen. Undersøkelsen gjøres for å se etter forkalkninger og innsnevringer av årene. Undersøkelsen kartlegger også blodforsyningen til hjernen.

» Ultralyd av hjertet gjøres for å undersøke hjerternes form og funksjon.

» Måling av beintettethet i rygg/hofte og kroppens fettmengde. Målingene brukes til å undersøke risiko for beinskjærhet og brudd, og for studier om sammenhengen mellom kroppssett, beinmasse og brudd.


» Tester av hukommelse gjøres ved hjelp av enkle spørsmål og omfatter også evne til gjenkjenning av ord og grad av fingerbevegelselighet.


» Ny bakteriepróve fra nese og hals. Próven utføres på samme måte som i første del av undersøkelsen.


For å sikre høy kvalitet på forskningsdata ønsker vi å undersøke et litet utvalg som møter til undersøkelsen to ganger med circa en ukes mellomrom. De som er aktuelle vil bli forespurt om dette ved framme.

Nye prosjekter
Noen deltakere vil i ett vedbli spurt om å delta i videre undersøkelser. Hvis dette gjelder deg, vil du få en forespørsel i posten. Du er ikke forpliktet til å delta selv om du har deltatt i andre deler av Tromsøundersøkelsen. Omtale av alle delprosjektene finner du på nettsiden vår:

http://www.tromso6.no

Forskring og finansiering
Deltakere i Tromsøundersøkelsen er forsikret gjennom Norsk Pasientskadeestatutning. Tromsøundersøkelsen er finansiert av Universitetet i Tromsø, Helse Nord HF samt ulike forskningsfond.
Etikk, personvern og sikkerhet
Du kan være trygg på at informasjon som gis til Tromsøundersøkelsen vil bli behandlet med respekt for personvern og privatliv, i og samsvar med lover og forskrifter. Alle medarbeidere som jobber med undersøkelsen har taushetsplikt. Opplysninger som samles inn vil bare bli brukt til godkjente forskningsformål.


Den enkelte forsker får ikke tilgang til opplysninger som gjør det mulig å identifisere enkeltpersoner. Hver enkelt deltaker har en rett til å vite hvilke opplysninger som er lagret om en selv.

For alle prosjekter kreves det at prosjektlederen tilhører en kompetent forskningsinstinasjon.

Tromsøundersøkelsen har konsesjon fra Data- tilsynet og er godkjent av Regional komité for medisinsk forskningsetikk, Nord-Norge.

**Sammenstilling med andre registre**

Opplysninger om deg fra den sjette Tromsøundersøkelsen kan bli knyttet sammen med opplysninger fra tidligere Tromsøundersøkelser. For enkelte prosjekter kan det være aktuelt å sammenligne opplysninger om deg med opplysninger fra barn, søsken, foreldre og besteforeldre hvis disse har deltatt i Tromsøundersøkelsen.

For spesielle forskningsprosjekter kan det være aktuelt å sammenstille informasjon fra Tromsøundersøkelsen med nasjonale helseregister som Reopregistreret, Medisinsk fødselsregister, Krefregisteret, Norsk pasientregister og Dødsårsaksregisteret, og andre nasjonale registre over sykdommer som det forsegles på i Tromsøundersøkelsen.

I tillegg kan det være aktuelt å innhente helseopplysninger fra primær- og spesialisthelsetjenesten til bruk i forskning på sykdommer og helseproblemer som er nevnt i denne brosjyren, for eksempel hjerte-karsykdom, diabetes og beinbrudd. I slike tilfeller innhentes nytt samtykke, eller annen type godkjennelse (dispensasjon fra taushetsplikten).

Informasjon fra Tromsøundersøkelsen kan også bli sammenstilt med registre ved Statistisk sentralbyrå, for eksempel om miljø, befolkning, utdanning, inntekt, offentlige ytelser, yrkesdeltakelse og andre forhold som kan ha betydning for helsen.

Slike sammenstillinger krever noen ganger forhåndsgodkjennelse av offentlige instanser, for eksempel Regional komité for medisinsk forskningsetikk, Datatilsynet eller NAV.

**Bruk av innsamlede data i framtiden**

Data fra Tromsøundersøkelsen vil kun bli brukt til forskning og vil ikke kunne brukes til andre formål.

Opplysninger og prøver som du gir, blir oppbevart på ubestemt tid til bruk i forskning til formål som nevnt i denne brosjyren. I noen tilfeller kan det bli aktuelt å gjøre analyser av blodprøver ved forskningsinstinasjoner i utlandet. Hvis dette gjøres, vil det skje i en slik form at våre utenlandske samarbeidspartnere ikke kan knytte prøvene opp mot deg som person.

Hva som er aktuelle problemstillinger i medisinsk forskning forandrer seg hele tiden. I framtiden kan data bli brukt i forskningsprosjekter som i dag ikke er planlagt, forutsatt at det er i samsvar med gjeldende lover og forskrifter. For alle slike nye prosjekter kreves det at prosjektet er godkjent av Regional komité for medisinsk forskningsetikk og Datatilsynet.

Tromsøundersøkelsen informerer om nye forskningsprosjekter på: http://www.tromso6.no

Her kan du også lese om forskningsresultatene fra Tromsøundersøkelsen. Forskningsresultater vil ellers bli publisert i internasjonale og nasjonale tidsskrifter, på faglige konferanser og møter. Det vil ikke være mulig å identifisere enkeltpersoner når forskningsresultatene offentliggjøres.
Samtykke
Hvis du vil delta i den sjuette Tromsøundersøkelsen, må du gi skriftlig samtykke til dette. Personale på Tromsøundersøkelsen vil kunne gi mer informasjon om undersøkelsen, og kan svare deg dersom du har spørsmål i forbindelse med samtykket.

Hvis du vil trekke tilbake ditt samtykke, henvend deg til:
Tromsøundersøkelsen, Inst. for samfunnsmedisin
Universitetet i Tromsø
9037 Tromsø
telefon: 77 64 48 16
telefaks: 77 64 48 31
e-post: tromsous@ism.uit.no
internett: www.tromsø6.no

Hvis vi i framtiden ønsker å forske på nye spørsmål som ikke er beskrevet i denne brosjyren, kan det bli nødvendig å be deg om et nytt samtykke.

Vil du delta?
Følgende tekst er en kopi av dokumentet du blir bedt om å signere når du møter fram til undersøkelsen:

Samtykke til bruk av helseopplysninger i forskning - den 6. Tromsøundersøkelsen

I brosjyren jeg har fått tilsendt, har jeg lest om undersøkelsens innhold og formål, og jeg har hatt mulighet til å stille spørsmål. Jeg samtykker herved i å delta i undersøkelsen [dato/signatur].
Tromsøundersøkelsen
Institutt for samfunnsmedisin, Universitetet i Tromsø
9037 TROMSØ

telefon: 77 64 48 16
telefaks: 77 64 48 31
epost: tromsous@ism.uit.no
internett: www.tromso6.no
## Tromsø-undersøkelsen

**HELESE OG SYKDOMMER**

2007–2008 KONFIDENTIELT

- **Sjiktet skal leses oppskrift: Vennligst bruk blå eller sort penn.** Du kan ikke bude komma, bruk blanker, stavet av.

###はじめ

<table>
<thead>
<tr>
<th>Hvordan tenker du om di egen helset i alminnelig?</th>
<th>Ja</th>
<th>Nei</th>
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<tr>
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<tr>
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### spørsmål

<table>
<thead>
<tr>
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<th>Ja</th>
<th>Nei</th>
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</thead>
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<td>Avgrens.</td>
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<tr>
<td>Kravrel gjenfamly europeiske NAVO-</td>
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<tr>
<td>Måten</td>
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### vi antar

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| Måten |    |    |

### bruksav heilejene

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###Bruks av heilejene

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**Bruk av heilejene**

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**Bruk av heilejene**

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| Lignende klimater |    |    |
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**Bruk av heilejene**

| Avgrens. |    |    |
| Kravrel gjenfamly europeiske NAVO- |    |    |
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| Lignende klimater |    |    |
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**Bruk av heilejene**

| Avgrens. |    |    |
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| Lignende klimater |    |    |
| Måten |    |    |

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**Bruk av heilejene**

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| Kravrel gjenfamly europeiske NAVO- |    |    |
| Lengdel |    |    |
| Lignende klimater |    |    |
| Måten |    |    |

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**Bruk av heilejene**

| Avgrens. |    |    |
| Kravrel gjenfamly europeiske NAVO- |    |    |
| Lengdel |    |    |
| Lignende klimater |    |    |
| Måten |    |    |

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**Bruk av heilejene**

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| Lengdel |    |    |
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| Måten |    |    |

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**Bruk av heilejene**

| Avgrens. |    |    |
| Kravrel gjenfamly europeiske NAVO- |    |    |
| Lengdel |    |    |
| Lignende klimater |    |    |
| Måten |    |    |

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**Bruk av heilejene**

<p>| Avgrens. |    |    |
| Kravrel gjenfamly europeiske NAVO- |    |    |
| Lengdel |    |    |
| Lignende klimater |    |    |
| Måten |    |    |</p>
<table>
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<th>BRUK AV MEDISINER</th>
<th>FAMILIE OG VENNER</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 Bruker du, eller har du brukt, noen av følgende medisiner? (Sett ett kryss for hver linje)</td>
<td>13 Hvem bor du sammen med? (Sett kryss for hvert spørsmål og angi antall)</td>
</tr>
<tr>
<td>Aldri brukt</td>
<td>Ja</td>
</tr>
<tr>
<td>Nå</td>
<td></td>
</tr>
<tr>
<td>Før</td>
<td></td>
</tr>
<tr>
<td>Medisin mot høyt blodtrykk..</td>
<td></td>
</tr>
<tr>
<td>Kolesterolenkende medisin...</td>
<td></td>
</tr>
<tr>
<td>Medisin mot hjertesykdom...</td>
<td></td>
</tr>
<tr>
<td>Vanndrivende medisin...</td>
<td></td>
</tr>
<tr>
<td>Medisin mot beinskjørt (ostoporose)</td>
<td></td>
</tr>
<tr>
<td>Insulin</td>
<td></td>
</tr>
<tr>
<td>Diabetesmedisin (tabletter)</td>
<td></td>
</tr>
<tr>
<td>Stoffskiftemedisinene</td>
<td></td>
</tr>
<tr>
<td>Thyroxin/levaxin</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>11 Hvor ofte har du i løpet av de siste 4 ukene brukt følgende medisiner? (Sett ett kryss pr linje)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ikke brukt siste 4 uker</td>
</tr>
<tr>
<td>Smertestillende på resept</td>
</tr>
<tr>
<td>Smertestillende reseptfris</td>
</tr>
<tr>
<td>Sovemidler</td>
</tr>
<tr>
<td>Beroligende medisiner</td>
</tr>
<tr>
<td>Medisin mot depresjon</td>
</tr>
</tbody>
</table>

| 12 Skriv ned alle medisiner – både de med og uten resept – som du har brukt regelmessig i siste 4 ukers periode. (Ikke regn med vitaminer, mineraler, urter, naturmedisin, andre kosttilskudd etc.) |

<table>
<thead>
<tr>
<th>14 Kryss av for de slektningene som har eller har hatt</th>
</tr>
</thead>
<tbody>
<tr>
<td>Foreldre</td>
</tr>
<tr>
<td>Hjertefarkt</td>
</tr>
<tr>
<td>Hjertefarkt før fylte 60 år</td>
</tr>
<tr>
<td>Angina pectoris (hjertekomme)</td>
</tr>
<tr>
<td>Hjerneslag/hjernebløddning</td>
</tr>
<tr>
<td>Beinskjørt (ostoporose)</td>
</tr>
<tr>
<td>Magesår/tolvfingerarmsår</td>
</tr>
<tr>
<td>Astma</td>
</tr>
<tr>
<td>Diabetes</td>
</tr>
<tr>
<td>Dyremans</td>
</tr>
<tr>
<td>Psykiske plager</td>
</tr>
<tr>
<td>Rusproblemer</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>15 Har du nok venner som kan gi deg hjelp når du trenger det?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ja</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>16 Har du nok venner som du kan snakke fortrolig med?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ja</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>17 Hvor ofte tar du vanligvis del i foreningsvirksomhet som for eksempel syklubb, idrettslag, politiske lag, religiøse eller andre foreninger?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aldri, eller noen få ganger i året</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>18 Hva er din høyeste fullførte utdanning? (Sett ett kryss)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grunnskole, framhaldsskole eller folkehøyskole</td>
</tr>
<tr>
<td>Yrkesskole videregående, yrkesskole eller realskole</td>
</tr>
<tr>
<td>Allmenn videregående skole eller gymnas</td>
</tr>
<tr>
<td>Høyskole eller universitet, mindre enn 4 år</td>
</tr>
<tr>
<td>Høyskole eller universitet, 4 år eller mer</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>19 Hva er din hovedaktivitet? (Sett ett kryss)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yrkesaktiv heltid</td>
</tr>
<tr>
<td>Yrkesaktiv deltid</td>
</tr>
<tr>
<td>Arbeidsledig</td>
</tr>
</tbody>
</table>

Får du ikke plass til alle medisiner, bruk eget ark.

VED FRAMMØTE vil du bli spurt om du har brukt antibiotika eller smertestillende medisiner de siste 24 timer. Om du har det, vil vi be om at du oppgir preparat, styrke, dose og tidspunkt.
20 Mottar du noen av følgende ytelser?
☐ Alderstrygd, fartsiddepensjon (AFP) eller etterlatterpensjon
☐ Sykepenger (er sykemeldt)
☐ Rehabiliterings-/tjattføringspenger
☐ Uførelyebepensjon, hel
☐ Uførelyebepensjon, delvis
☐ Dagganger under arbeidstid
donot
☐ Overgangstnad
☐ Sosialhjelp/-stønad

21 Hvor høy var husholdningens samlede bruttoinntekt
siste år? Ta med alle inntekter fra arbeid, trygde,
sosialhjelp og lignende.
☐ Under 125 000 kr  ☐ 401 000-550 000 kr
☐ 125 000-200 000 kr  ☐ 551 000-700 000 kr
☐ 201 000-300 000 kr  ☐ 701 000-850 000 kr
☐ 301 000-400 000 kr  ☐ Over 850 000 kr

22 Arbeider du utdelers minst 25 % av tiden, eller i
lokaler med lav temperatur, som for eksempel
lager-/industrihallen?
☐ Ja  ☐ Nei

23 Hvis du er i lønnet eller ulønnet arbeid, hvordan vil
du beskrive arbeidet ditt?
☐ For det meste stillesittende arbeid
(t.eks. skrivebordarbeid, montering)
☐ Arbeid som krever at du går mye
(t.eks. ekspediterarbeid, lasteindustriarbeid, undervisning)
☐ Arbeid der du går og løfter mye
(t.eks postbud, pleier, bygningsarbeider)
☐ Tungt kroppsarbeid

24 Angi bevegelse og kroppsselig anstrengelse i din
fritid. Hvis aktiviteten varierer meget t.eks mellom
sommer og vinter, så ta et gjennomsnitt. Spørsmålet
gjelder bare det siste året. (Sett kryss i den ruta som
passer best)
☐ Leser, ser på fjernsyn eller annen stillesittende
beskjæftigelse
☐ Spaserer, sykler eller beveger deg på annen måte
minst 4 timer i uken (her skal du også regne med gang
eller sykling til arbeidstedet, søndagsturer med muse)
☐ Driver mosjonsidrett, tyngre hagearbeid, snømåling
e.l. (merk at aktiviteten skal være minst 4 timer i uka)
☐ Trener hardt eller driver konkurransesidrett
regelmessig og flere ganger i uka

25 Hvor ofte driver du mosjon? (Med mosjon mener vi
at du f.eks går en tur, går på ski, svømmer eller driver
trening/idrett)
☐ Aldri
☐ Sjeldnere enn en gang i uken
☐ En gang i uken
☐ 2-3 ganger i uken
☐ Omtrent hver dag

26 Hvor hardt mosjonerer du da i gjennomsnitt?
☐ Tar det rolig uten å bli andopstilt eller svett.
☐ Tar det så hardt at jeg blir andopstilt og svett
☐ Tar meg nesten helt ut

27 Hvor lenge holder du på hver gang i fjernsyn?
☐ Mindre enn 15 minutter  ☐ 30 minutter – 1 time
☐ 15-29 minutter  ☐ Mer enn 1 time

28 Hvor ofte drikker du alkohol?
☐ Aldri
☐ Mænedlig eller sjeldnere
☐ 2-4 ganger hver måned
☐ 2-3 ganger pr. uke
☐ 4 eller flere ganger pr. uke

29 Hvor mange enheter alkohol (en øl, et glass vin, eller
en drink) tar du vanligvis når du drikker?
☐ 1-2  ☐ 5-6  ☐ 10 eller flere
☐ 3-4  ☐ 7-9

30 Hvor ofte drikker du 6 eller flere enheter alkohol ved
en anledning?
☐ Aldri
☐ Sjeldnere enn månedlig
☐ Mænedlig
☐ Ukentlig
☐ Daglig eller nesten daglig

31 Røyker du av og til, men ikke daglig?
☐ Ja  ☐ Nei

32 Har du røykt/røyker du daglig?
☐ Ja, nå  ☐ Ja, tidligere  ☐ Aldri

33 Hvis du har røykt daglig tidligere, hvor lenge er det
siden du sluttet?
Antall år

34 Hvis du røyker daglig nå eller har røykt tidligere:
Hvor mange sigaretter røyker eller røykte du vanligvis
daglig?
Antall sigaretter

35 Hvor gammel var da du begynte å røyke daglig?
Antall år

36 Hvor mange år til sammen har du røykt daglig?
Antall år

37 Bruker du, eller har du brukt, snus eller skrå?
☐ Aldri
☐ Nei, aldri  ☐ Ja, av og til
☐ Ja, men jeg har sluttet  ☐ Ja, daglig
### KOSTHOLD

38 Spiser du vanligvis frokost hver dag?
- [ ] Ja
- [ ] Nei

39 Hvor mange enheter frukt og grønnsaker spiser du i gjennomsnitt per dag? (Med enhet menes f.eks. en frukt, glass juice, potet, porsjon grønnsaker)
<table>
<thead>
<tr>
<th>Antall enheter</th>
<th></th>
</tr>
</thead>
</table>

40 Hvor mange ganger i uken spiser du varm middag?
<table>
<thead>
<tr>
<th>Antall</th>
<th></th>
</tr>
</thead>
</table>

41 Hvor ofte spiser du vanligvis disse matvarrene? (Sett ett kryss pr. linje)
<table>
<thead>
<tr>
<th>Poteter</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Pasta/ris</td>
<td></td>
</tr>
<tr>
<td>Kjøtt (om ikke kvernet)</td>
<td></td>
</tr>
<tr>
<td>Kvernet kjøtt</td>
<td></td>
</tr>
<tr>
<td>Gøtter, hamburger o.0</td>
<td></td>
</tr>
<tr>
<td>Grønnsaker, frukt, bær</td>
<td></td>
</tr>
<tr>
<td>Mager fisk</td>
<td></td>
</tr>
<tr>
<td>Fett fisk</td>
<td></td>
</tr>
</tbody>
</table>

42 Hvor mye drikker du vanligvis av følgende? (Sett ett kryss pr. linje)
| Melk, kefr, yoghurt |  |
| Fruktkjøtt |  |
| Brus/seskjedrikker med sukker |  |

43 Hvor mange kopper kaffe og te drikker du daglig? (Sett 0 for de typene du ikke drikker daglig)
| Filterkaffe |  |
| Kokkekaffe/presskanne |  |
| Annen kaffe |  |
| Te |  |

44 Hvor ofte spiser du vanligvis fiskelever?
- [ ] Sjelden/aldri
- [ ] 1-3 g i året
- [ ] 4-6 g i året
- [ ] 7-12 g i året

45 Bruker du følgende kosttilskudd?
<table>
<thead>
<tr>
<th>Daglig</th>
<th>Iblandt</th>
<th>Nei</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tran, trankapsler</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Omega 3 kapsler (fiskeolje, seloja)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kalktabletter</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### SPØRSMÅL TIL KVINNER

46 Er du gravid nå?
- [ ] Ja
- [ ] Nei
- [ ] Usikker

47 Hvor mange barn har du født?
<table>
<thead>
<tr>
<th>Antall</th>
<th></th>
</tr>
</thead>
</table>

48 Hvis du har født, fyll ut for hvert barn: fødselsår og vekt samt hvor mange måneder du ammet. (Angi så godt som du kan)
<table>
<thead>
<tr>
<th>Barn</th>
<th>Fødselsår</th>
<th>Fødselsvekt i gram</th>
<th>Ammet ant.med</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

49 Har du i forbindelse med svangerskap hatt for høyt blodtrykk?
- [ ] Ja
- [ ] Nei

50 Hvis Ja, i hvilket svangerskap?
- [ ] Første
- [ ] Senere

51 Har du i forbindelse med svangerskap hatt protein (eggehvide) i urinen?
- [ ] Ja
- [ ] Nei

52 Hvis Ja, i hvilket svangerskap?
- [ ] Første
- [ ] Senere

53 Ble noen av disse barna født mer enn en måned for tidlig (før termin) pga. svangerskapsforgiftning?
- [ ] Ja
- [ ] Nei

54 Hvis Ja, hvilket(t) barn
<table>
<thead>
<tr>
<th>Barn 1</th>
<th>Barn 2</th>
<th>Barn 3</th>
<th>Barn 4</th>
<th>Barn 5</th>
<th>Barn 6</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

55 Hvor gammel var du da du fikk menstruasjon første gang?
<table>
<thead>
<tr>
<th>Antall år</th>
<th></th>
</tr>
</thead>
</table>

56 Bruker du for tiden reseptpliktige legemidler som påvirker menstruasjonen?
| P-pille, hormonspiral eller lignende |  |
| Hormonpreparat for overgangs- alderen |  |

**VED FRAMMØTE** vil du få utfyllende spørsmål om menstruasjon og eventuell bruk av hormoner. Skriv gjerne ned på et papir navn på hormonpreparat du har brukt, og ta det med deg. Du vil også bli spurt om din menstruasjon har opphørt og eventuelt når og hvorfor.
SLIK FYLLER DU UT SKJEMAET:

Skjemaet vil bli lest maskinelt, det er derfor viktig at du krysser av riktig:
☐ Riktig
☒ Galt

Om du krysser feil, retter du ved å fylle boksen slik

Skriv tydelige tall 1 2 3 4 5 6 7 8 9 0
☒ 7 ✔ Riktig
☒ 7 ☒ Galt

Bruk kun sort eller blå penn, bruk ikke blyant eller tusj
1. BESKRIVELSE AV DIN HELSETILSTAND

Vis hvilke utsagn som passer best på din helsetilstand i dag ved å sette ett kryss i en av rutene utenfor hver av de fem gruppene nedenfor:

1.01 Gange
- Jeg har ingen problemer med å gå omkring
- Jeg har litt problemer med å gå omkring
- Jeg er sengeliggende

1.02 Personlig stell
- Jeg har ingen problemer med personlig stell
- Jeg har litt problemer med å vaske meg eller kle meg
- Jeg er ute av stand til å vaske meg eller kle meg

1.03 Vanlige gjøremål (f.eks. arbeid, studier, husarbeid, familie- eller fritidsaktiviteter)
- Jeg har ingen problemer med å utføre mine vanlige gjøremål
- Jeg har litt problemer med å utføre mine vanlige gjøremål
- Jeg er ute av stand til å utføre mine vanlige gjøremål

1.04 Smerte og ubeihag
- Jeg har verken smerte eller ubeihag
- Jeg har moderat smerte eller ubeihag
- Jeg har sterk smerte eller ubeihag

1.05 Angst og depresjon
- Jeg er verken engstelig eller deprimert
- Jeg er noe engstelig eller deprimert
- Jeg er svært engstelig eller deprimert

For at du skal kunne vise oss hvor god eller dårlig din helsetilstand er, har vi laget en skala (nesten som et termometer), hvor den beste helsetilstanden du kan tenke deg er markert med 100 og den dårligste med 0. Vi ber om at du viser din helsetilstand ved å trekke ei linje fra boksen nedenfor til det punkt på skalaen som passer best med din helsetilstand.
### 2. OPPVEKST OG TILHØRIGHET

**2.1. Hvor bodde du da du fylte 1 år?**
- [ ] I Tromsø (med dagens kommunegrenser)
- [ ] I Troms, men ikke i Tromsø
- [ ] I Finnmark fylke
- [ ] I Nordland fylke
- [ ] Annet sted i Norge
- [ ] I utlandet

**2.2. Hvordan var de økonomiske forhold i familien under din oppvekst?**
- [ ] Meget gode
- [ ] Gode
- [ ] Vanskelige
- [ ] Meget vanskelige

**2.3. Hvilken betydning har religion i ditt liv?**
- [ ] Stor betydning
- [ ] En viss betydning
- [ ] Ingen betydning

**2.4. Hva regner du deg selv som? (Kryss av for ett eller flere alternativ)***
- [ ] Norsk
- [ ] Samisk
- [ ] Kvensk/Finsk
- [ ] Annet

**2.5. Hvor mange søsken og barn har du/har du hatt?**
- Antall søsken: ___________
- Antall barn: ___________

**2.6. Lever din mor?**
- [ ] Ja
- [ ] Nei

Hvis NEI: hennes alder ved død: ___________

**2.7. Lever din far?**
- [ ] Ja
- [ ] Nei

Hvis NEI: hans alder ved død: ___________

**2.8. Hva var/er den høyeste fullførte utdanning til dine foreldre og din ektefelle/samboer?**

<table>
<thead>
<tr>
<th>(sett ett kryss i hver kolonne)</th>
<th>Mor</th>
<th>Far</th>
<th>Ektefelle/samboer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grunnskole 7-10 år, framhaldsskole eller folkehøyskole</td>
<td>[ ]</td>
<td>[ ]</td>
<td>[ ]</td>
</tr>
<tr>
<td>yrkesfaglig videregående, yrkesskole eller realskole</td>
<td>[ ]</td>
<td>[ ]</td>
<td>[ ]</td>
</tr>
<tr>
<td>Allmennfaglig videregående skole eller gymnas</td>
<td>[ ]</td>
<td>[ ]</td>
<td>[ ]</td>
</tr>
<tr>
<td>Høyskole eller universitet (mindre enn 4 år)</td>
<td>[ ]</td>
<td>[ ]</td>
<td>[ ]</td>
</tr>
<tr>
<td>Høyskole eller universitet (4 år eller mer)</td>
<td>[ ]</td>
<td>[ ]</td>
<td>[ ]</td>
</tr>
</tbody>
</table>
### 3. TRIVSEL OG LIVSFORHOLD

#### 3.01 Nedenfor står tre utsagn om tilfredshet med livet som et hele. Deretter står to utsagn om syn på din egen helse. Vis hvor enig eller uenig du er i hver av påstandene ved å sette et kryss i rubrikkene for det tallet du synes stemmer best for deg. (sett ett kryss for hvert utsagn)

<table>
<thead>
<tr>
<th>Helt uenig</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>Helt enig</th>
</tr>
</thead>
<tbody>
<tr>
<td>På de fleste måter er livet mitt nær idealett mitt</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mine livsforhold er utmerkede</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Jeg er tilfreds med livet mitt</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Jeg ser lyst på min framtidige helse</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ved å leve sunt kan jeg forhindre alvorlige sykdommer</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

#### 3.02 Nedenfor står fire utsagn om syn på forhold ved din nåværende jobb, eller hvis du ikke er i arbeid nå, den jobben du hadde sist (sett ett kryss for hvert utsagn)

<table>
<thead>
<tr>
<th>Helt uenig</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>Helt enig</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arbeidet mitt er for belastende, fysisk eller følelsesmessig</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Jeg har tilstrekkelig innflytelse på når og hvordan arbeidet mitt skal utføres</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Jeg blir mobbet eller trakassert på arbeidspllassen min</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Jeg blir rettferdig behandlet på arbeidspllassen min</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

#### 3.03 Jeg opplever at yrket mitt har følgende sosiale status i samfunnet: (dersom du ikke er i arbeid nå, tenk på det yrket du hadde sist)
- ☐ Meget høy status
- ☐ Ganske høy status
- ☐ Middels status
- ☐ Ganske lav status
- ☐ Meget lav status

#### 3.04 Har du over lengre tid opplevd noe av det følgende? (sett ett eller flere kryss for hver linje)

<table>
<thead>
<tr>
<th>Nei</th>
<th>Ja, som barn</th>
<th>Ja, som voksen</th>
<th>Ja, siste år</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blitt plaget psykisk, eller truet med vold</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>Blitt slått, sparket eller utsatt for annen type vold</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
</tbody>
</table>

Noen i nær familie har brukt rusmidler på en slik måte at dette har vært til bekymring for deg... ☐ ☐ ☐ ☐

Dersom du har opplevd noen av disse forholdene, hvor mye plages du av dette nå?
- ☐ Ingen plager
- ☐ Noen plager
- ☐ Store plager
4. SYKDOMMER OG PLAGER

4.1 Har du i løpet av den siste måneden følt deg syk eller hatt en skade?
- Ja
- Nei

Hvis JA: har du i den samme perioden?
(sett ett kryss for hver linje)
- Ja
- Nei

- Vært hos allmennlege/fastlege
- Vært hos spesialist
- Vært på legevakt
- Vært innlagt i sykehus
- Vært hos alternativ behandler (kiropraktor, homeopat eller lignende)

4.2 Har du merket anfall med plutselig endring i pulsen eller hjertetætmen siste året?
- Ja
- Nei

4.3 Blir du tungpustet i følgende situasjoner?
(sett ett kryss for hvert spørsmål)
- Ja
- Nei

- Når du går hurtig på flatmark eller svak oppoverbakke
- Når du spaserer i rolig tempo på flatmark
- Når du vasker deg eller klarer på deg
- Når du er i hvile

4.4 Hoster du omtrent daglig i perioder av året?
- Ja
- Nei

Hvis JA: Er hosten vanligvis ledsaget av oppsytt?
- Ja
- Nei

Har du hatt slik hoste så lenge som i en 3 måneders periode i begge de to siste årene?
- Ja
- Nei

4.5 Hvor ofte er du plaget av søvnløshet?
(sett ett kryss)
- Aldri, eller noen få ganger i året
- 1-3 ganger i måneden
- Omtrent 1 gang i uka
- Mer enn 1 gang i uka

Hvis du er plaget av søvnløshet månedlig eller oftere, når på året er du mest plaget?
(sett ett eller flere kryss)
- Ingen spesiell tid
- Mørketida
- Midnattsloftida
- Vår og høst

4.6 Har du i de siste par ukene hatt vansker med å sove?
- Ikke i det hele tatt
- Ikke mer enn vanlig
- Heller mer enn vanlig
- Mye mer enn vanlig

4.7 Har du de siste par ukene følt deg ulykkelig og nedtrykt (deprimert)?
- Ikke i det hele tatt
- Ikke mer enn vanlig
- Heller mer enn vanlig
- Mye mer enn vanlig

4.8 Har du i de siste par ukene følt deg ute av stand til å mestre dine vanskeligheter?
- Ikke i det hele tatt
- Ikke mer enn vanlig
- Heller mer enn vanlig
- Mye mer enn vanlig

4.9 Nedenfor ber vi deg besvare noen spørsmål om din hukommelse: (sett ett kryss for hvert spørsmål)
- Ja
- Nei

Synes du at din hukommelse har blitt dårligere?
- Glemmer du ofte hvor du har lagt tingene dine?
- Har du problemer med å finne vanlige ord i en samtale?
- Har du fått problemer med daglige gjøremål som du mestret tidligere?
- Har du vært undersøkt for sviktende hukommelse?

Hvis JA på minst ett av de fire første spørsmålene ovenfor: Er det et problem i hverdagen?
- Ja
- Nei
4.10 Har du i løpet av det siste året vært plaget med smerter og/eller stivhet i muskler og ledd som har vart i minst 3 måneder sammenhengende? (sett ett kryss i hver linje)

<table>
<thead>
<tr>
<th></th>
<th>Ikke plaget</th>
<th>En del plaget</th>
<th>Sterkt plaget</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nakke, skuldre</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>Armer, hender</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>Øvre del av ryggen</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>Korsryggen</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>Hofter, ben, føtter</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>Andre steder</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
</tbody>
</table>

4.11 Har du vært plaget med smerter og/eller stivhet i muskler og ledd i løpet av de siste 4 ukene? (sett ett kryss i hver linje)

<table>
<thead>
<tr>
<th></th>
<th>Ikke plaget</th>
<th>En del plaget</th>
<th>Sterkt plaget</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nakke, skuldre</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>Armer, hender</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>Øvre del av ryggen</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>Korsryggen</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>Hofter, ben, føtter</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>Andre steder</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
</tbody>
</table>

4.12 Har du noen gang hatt:

<table>
<thead>
<tr>
<th></th>
<th>Ja</th>
<th>Nei</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brudd i håndledd/underarm?</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>Lårhalsbrudd?</td>
<td>□</td>
<td>□</td>
</tr>
</tbody>
</table>

4.13 Hvilken grad har du hatt følgende plager i de siste 12 månedere?

<table>
<thead>
<tr>
<th></th>
<th>Aldri</th>
<th>Litt</th>
<th>Mye</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kvalme</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>Halsbrann/sure oppstøt</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>Diare</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>Treg mage</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>Veksledende treg mage og diare</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>Oppblåsthett</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>Smerter i magen</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
</tbody>
</table>

4.14 Hvis du har hatt smerter i eller ubehag fra magen siste året:

<table>
<thead>
<tr>
<th></th>
<th>Ja</th>
<th>Nei</th>
</tr>
</thead>
<tbody>
<tr>
<td>Er disse lokaliserat øverst i magen?</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>Har du hatt plagerne så ofte som 1 dag i uka eller mer de siste 3 måneder?</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>Blir plagerne bedre etter avføring?</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>Har plagerne sammenheng med hyppigere eller sjeldnere avføring enn vanlig?</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>Har plagerne noen sammenheng med læsere eller fastere avføring enn vanlig?</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>Kommer plagerne etter måltid?</td>
<td>□</td>
<td>□</td>
</tr>
</tbody>
</table>

4.15 Har du noen gang hatt:

<table>
<thead>
<tr>
<th></th>
<th>Ja</th>
<th>Nei</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sår på magesekken</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>Sår på tolfingertarmen</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>Magesår-operasjon</td>
<td>□</td>
<td>□</td>
</tr>
</tbody>
</table>

4.16 Har eller har du hatt noen av følgende:

<table>
<thead>
<tr>
<th></th>
<th>Aldri</th>
<th>Litt</th>
<th>Mye</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nikkelallergi</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>Pollenallergi</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>Andre allergier</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
</tbody>
</table>

4.17 Har du opplevd ufrivillig barnløshet i mer enn 1 år?

<table>
<thead>
<tr>
<th></th>
<th>Ja</th>
<th>Nei</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hvis JA, skyldes dette:</td>
<td>□</td>
<td>□</td>
</tr>
</tbody>
</table>

4.18 Bruker du glutenfri dietet?

<table>
<thead>
<tr>
<th></th>
<th>Ja</th>
<th>Nei</th>
<th>Vet ikke</th>
</tr>
</thead>
</table>

4.19 Til kvinner: Har du spontanabortert?

<table>
<thead>
<tr>
<th></th>
<th>Ja</th>
<th>Nei</th>
<th>Vet ikke</th>
</tr>
</thead>
</table>

4.20 Til mennene: Har din partner noen gang spontanabortert?

<table>
<thead>
<tr>
<th></th>
<th>Ja</th>
<th>Nei</th>
<th>Vet ikke</th>
</tr>
</thead>
</table>

4.21 Har du fått stilt diagnosen Dermatitis herpetiformis (DH)?

<table>
<thead>
<tr>
<th></th>
<th>Ja</th>
<th>Nei</th>
<th>Vet ikke</th>
</tr>
</thead>
</table>

4.22 Har du fått stilt diagnosen Dermatitis herpetiformis (DH)?

<table>
<thead>
<tr>
<th></th>
<th>Ja</th>
<th>Nei</th>
<th>Vet ikke</th>
</tr>
</thead>
</table>
4.22 Har du fått stilt diagnosen celiaki på bakgrunn av en vevsprøve fra tynnarmen tatt under en undersøkelse der du svelget en slange (gastroskopi)?

- Ja
- Nei
- Vet ikke

4.24 Har du egne tenner?

- Ja
- Nei

4.25 Hvor mange amalgamfyllinger har du/har du hatt?

- 0
- 1-5
- 6-10
- 10+

4.26 Har du vært plaget av hodepine det siste året?

- Ja
- Nei

Hvis NEI, gå til del 5, kosthold

4.27 Hva slags hodepine er du plaget av?

- Migrene
- Annen hodepine

4.28 Omtrent hvor mange dager per måned har du hodepine?

- Mindre enn 1 dag
- 1-6 dager
- 7-14 dager
- Mer enn 14 dager

4.29 Er hodepine vanligvis:

(sett et kryss for hver linje)

- Bankende/dunkende smerte
- Pressende smerte
- Ensidig smerte (høyre eller venstre)

4.30 Hvor sterk er hodepinen vanligvis?

- Mild (hemmer ikke aktivitet)
- Moderat (hemmer aktivitet)
- Sterk (forhinder aktivitet)

4.31 Hvor lenge varer hodepinen vanligvis?

- Mindre enn 4 timer
- 4 timer – 1 døgn
- 1-3 døgn
- Mer enn 3 døgn

4.32 Dersom du er plaget av hodepine, når på året er du plaget mest? (sett ett eller flere kryss)

- Ingen spesiell tid
- Mørketida
- Midnattsoilta
- Vår og/eller høst

4.33 Før eller under hodepinen, kan du da ha forbigående:

- Ja
- Nei

Synsforstyrrelse? (bakke ljer, flimring, tåkesyn, lyssmilt) ..............................................

Nummenhet i halve ansikt eller i hånden? ...........................................................

Forverring ved moderat fysisk aktivitet .........................................................

Kvalme og /eller oppskast ..............................................................................

4.34 Angi hvor mange dager du har vært borte fra arbeid eller skole siste måned på grunn av hodepine:

Antall dager ........................................................................................................

---

8
5. KOSTHOLD

5.1: Hvor ofte spiser du vanligvis følgende? (sett ett kryss i hver linje)

<table>
<thead>
<tr>
<th></th>
<th>0-1 g per mnd</th>
<th>2-3 g per mnd</th>
<th>1-3 g per uke</th>
<th>Mer enn 3 g per uke</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ferskvannsfisk (ikke oppdrett)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Saltvannsfisk (ikke oppdrett)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oppdrettetfisk (laks, røye, ørret)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tunfisk (forsk eller hermetisert)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fiskepålegg</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Skjell</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Den brune inmaten i krabbe</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hvalkjøtt/sel/kobbekjøtt</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inmat fra rein eller elg</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inmat fra rype</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

5.2: Hvor mange ganger i året spiser du/spiste du vanligvis følgende? (antall ganger)

<table>
<thead>
<tr>
<th>Antall ganger i året</th>
<th>Som voksen</th>
<th>I din barndom</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mølje</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Måsegg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reinsdyrkjøtt</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Selvplukket sopp og bær (blåbær/lytterbær/mulde)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

5.3: Hvor mange ganger i måneden spiser du hermetiske matvarer (fra metallboksene)?

<table>
<thead>
<tr>
<th>Antall ganger i måneden</th>
<th>Ja, daglig</th>
<th>Iblandt</th>
<th>Aldri</th>
</tr>
</thead>
</table>

5.4: Bruker du vitaminer og/eller mineraltilskudd?

<table>
<thead>
<tr>
<th>Antall ganger i mdr</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Mark sjokolade</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lys sjokolade/melkesjokolade</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sjokoladekake</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Andre søtsaker</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

5.5: Hvis du spiser sjokolade, hvor mye pleier du vanligvis å spise hver gang?

Tenk deg størrelsen på en Kvikk-Luns sjokolade, og oppgi hvor mye du spiser i forhold til den.

<table>
<thead>
<tr>
<th>¾</th>
<th>½</th>
<th>1</th>
<th>1½</th>
<th>2</th>
<th>Mer enn 2</th>
</tr>
</thead>
</table>

5.6: Hvor ofte drikker du kakao/varm sjokolade

<table>
<thead>
<tr>
<th>Antall ganger i mdr</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Mark sjokolade</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lys sjokolade/melkesjokolade</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sjokoladekake</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Andre søtsaker</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
## 6. ALKOHOL

<table>
<thead>
<tr>
<th>6.1 Hvor ofte har du det siste året:</th>
<th>Aldri</th>
<th>Sjeldner enn månedlig</th>
<th>Månedlig</th>
<th>Ukentlig</th>
<th>Daglig, eller nesten daglig</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ikke klart å stoppe og drikke alkohol når du først har begynt?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ikke klart å gjøre det som normalt forventes av deg fordi du har drukket?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trengt en drink om morgenen for å få komme i gang etter en rangel?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Felt skyld eller anger etter at du har drukket?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ikke klart å huske hva som skjedde kvelden før på grunn av at du hadde drukket?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>6.2 Har du eller andre noen gang blitt skadet på grunn av at du har drukket?</th>
<th>Aldri</th>
<th>Ja, men ikke det siste året</th>
<th>Ja, det siste året</th>
</tr>
</thead>
<tbody>
<tr>
<td>Har en slektning, venn, lege, eller annet helsepersonell vært bekymret for din drikking, eller foreslått at du reduserer inntaket?</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

## 7. VEKT

<table>
<thead>
<tr>
<th>7.1 Har du ufrivillig gått ned i vekt siste 6 måneder?</th>
<th>Ja</th>
<th>Nei</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hvis JA: Hvor mange kilo?</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>7.2 Anslå din vekt da du var 25 år gammel:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antall heke kg</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>7.4 Hvilken vekt ville du være tilfreds med (din trivselsvekt):</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antall kg</td>
</tr>
</tbody>
</table>

## 8. LOSEMIDLER

<table>
<thead>
<tr>
<th>8.1 Hvor mange timer i uka driver du med følgende fritids- eller yrkesaktiviteter:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bile reparasjoner/lakering, keramikkarbeid, måling/lakering/losemidler, frisør, glassmester, elektriker (Sett 0 om du ikke driver med slike fritids eller yrkesaktiviteter)</td>
</tr>
<tr>
<td>Antall timer per uke i gjennomsnitt</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>8.2 Bruker du hårfargemidler?</th>
<th>Ja</th>
<th>Nei</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hvis JA, hvor mange ganger per år?</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
9. BRUK AV HELSETJENESTER

9.01 Har du noen gang opplevd at sykdom er blitt mangelfullt undersøkt eller behandlet, og at dette har gitt alvorlige følger?
- Ja, det har rammet meg selv
- Ja, det har rammet en nær pårørende (barn, foreldre, ektefelle/samboer)
- Nei

Hvis JA, hvor mener du årsaken ligger?
(sett ett eller flere kryss):
- hos fastlege/allmennlege
- hos legevaktlege
- hos privatpraktiserende spesialist
- hos sykehuslege
- hos annet helsepersonell
- hos alternativ behandler
- hos flere på grunn av svikt i rutiner og samarbeid

9.02 Har du noen gang følt deg overtalt til å godta undersøkelse eller behandling som du selv ikke ønsket?
- Ja
- Nei

Hvis JA, mener du dette har hatt uheldige helsemessige følger?
- Ja
- Nei

9.03 Har du noen gang klaget på behandling du har fått?
- Har aldri vært aktuelt
- Har vurdert å klage, men ikke gjort det
- Har klaget muntlig
- Har klaget skriftlig

9.04 Hvor lenge har du hatt din nåværende fastlege/annen lege?
- Mindre enn 6 måneder
- 6 til 12 måneder
- 12 til 24 måneder
- Mer enn 2 år

9.05 Ved siste legebesøk hos fastlegen, snakket legen(e) til deg slik at du forsto dem? Svar på en skala fra 0 til 10, hvor 0=de var vanskelige å forstå og 10=de var alltid enkle å forstå
- 0
- 1
- 2
- 3
- 4
- 5
- 6
- 7
- 8
- 9
- 10

9.06 Hvordan vil du karakterisere behandlingen eller rådgivningen du fikk siste gang du var hos lege? Svar på en skala fra 0 til 10, hvor 0=meget dårlig behandling og 10=meget god behandling
- 0
- 1
- 2
- 3
- 4
- 5
- 6
- 7
- 8
- 9
- 10

9.07 Har du i løpet av de siste 12 måneder opplevd at det har vært vanskelig å bli henvist til spesialle versjonen?
- Ikke aktuelt
- Intet problem
- Noe problem
- Stort problem

9.08 Har du i løpet av de siste 12 måneder opplevd at det er vanskelig å bli henvist til fysiotherapeut, kiropraktor eller liknende?
- Ikke aktuelt
- Intet problem
- Noe problem
- Stort problem

9.09 Alt i alt, har du opplevd at det er vanskelig eller enkelt å bli henvist til spesialisttjenesten?
- Ikke aktuelt
- Meget vanskelig
- Noe vanskelig
- Rimelig enkelt
- Meget enkelt
9.10 Har du i løpet av de siste 12 måneder vært til undersøkelse eller behandling i spesialist-helsetjenesten?

☐ Ja    ☐ Nei

Hvis JA, snakket legen(e) til deg slik at du forstod dem? Svar på en skala fra 0 til 10, hvor 0=de var vanskelige å forstå og 10=de var alltid enkle å forstå

☐ 0 ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ 9 ☐ 10

9.11 Hvordan vil du karakterisere behandlingen eller rådgivningen du fikk siste gang du var hos spesialist? Svar på en skala fra 0 til 10, hvor 0=meget dårlig og 10=meget god

☐ 0 ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ 9 ☐ 10

9.13 Har du noen gang før 2002 gjennomgått en operasjon på sykehus eller spesialist-klinikk?

☐ Ja    ☐ Nei

9.14 Har du i løpet av de siste 12 måneder brukt urtemedisin, naturmidler eller naturlegemidler?

☐ Ja    ☐ Nei

9.16 Har du i løpet av de siste 12 måneder brukt meditasjon, yoga, qi gong eller thai chi som egenbehandling?

☐ Ja    ☐ Nei
## 10. Bruk av Antibiotika

### 10.01 Har du brukt antibiotika i løpet av de siste 12 måneder? (All penicillinliknende medisin i form av tabletter, mikstur eller sprayter)

- Ja
- Nei
- Husker ikke


<table>
<thead>
<tr>
<th>Kur 1</th>
<th>Kur 2</th>
<th>Kur 3</th>
<th>Kur 4</th>
<th>Kur 5</th>
<th>Kur 6</th>
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</table>

- Urinvesinfeksjon (blærebetennelse, blærekatarr)..............
- Luftvesinfeksjon (are-, bikule-, hals- eller lungebetennelse, bronkitt)
- Annet

Antall dagers antibiotika kur

<table>
<thead>
<tr>
<th>Kur 1</th>
<th>Kur 2</th>
<th>Kur 3</th>
<th>Kur 4</th>
<th>Kur 5</th>
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</table>

Hvordan skaffet du deg antibiotikakuren? Har du tatt flere kurser, sett ett kryss for hver kur.

- Etter resept fra lege/tannlege
- Uten kontakt med lege/uten resept:
  - Kjøp direkte fra apotek i utlandet
  - Kjøp gjennom Internett
  - Rest fra tidligere kur tilgjengelig hjemme
  - Fått av familie/venner
  - Andre måter

### 10.02 Har du antibiotika hjemme?

- Ja
- Nei

Hvis JA, er dette etter avtale med lege for å behandle kronisk eller hyppig tilbakevendende sykdom?

- Ja
- Nei

Hvis Nei, hvordan skaffet du deg dette legemiddelet? (Fleres kryss er mulig)

- Kjøpt direkte fra apotek i utlandet
- Kjøpt over Internett
- Rest fra tidligere kur
- Fått av familie/venner
- Andre måter

### 10.03 Kan du tenke deg å bruke antibiotika uten å kontakte lege først?

- Ja
- Nei

Hvis JA, hvilke tilstander vil du i så fall behandle? (Fleres kryss er mulig)

- Forkjøvelse
- Hoste
- Bronkitt
- Halsbetennelse
- Bikulebetennelse
- Feber
- Influensa
- Ørebetennelse
- Diaré
- Blerebetennelse
- Andre infeksjoner
11. DIN DOGNRYTME

Vi vil stille deg noen spørsmål som handler om dine savnvaner.

11.01 Har du hatt skiftarbeid de tre siste månedene?
    □ Ja    □ Nel

11.02 Antall dager i løpet av uken hvor du ikke kan velge fritt når du vil sove (f.eks arbeidsdager)?
    □ 0 □ 1 □ 2 □ 3 □ 4 □ 5 □ 6 □ 7

    Da går jeg til sengs klokken
    Jeg gjør meg klar til å sove klokken
    Antall minutter jeg trenger på å sovne
    Jeg våkner klokken
    Ved hjelp av: □ Vekkeklokke □ annen ytre påvirkning (støy, familie etc) □ av meg selv
    Antall minutter jeg trenger på å stå opp

11.03 Antall dager i løpet av uken hvor du fritt kan velge når du vil sove (f.eks helger eller fridager)
    □ 0 □ 1 □ 2 □ 3 □ 4 □ 5 □ 6 □ 7

    Da går jeg til sengs klokken
    Jeg gjør meg klar til å sove klokken
    Antall minutter jeg trenger på å sovne
    Jeg våkner klokken
    Ved hjelp av: □ Vekkeklokke □ annen ytre påvirkning (støy, familie etc) □ av meg selv
    Antall minutter jeg trenger på å stå opp
12. HUD OG HUDSYKDOMMER

12.01 Hvor ofte dusjer eller bader du vanligvis? (sett ett kryss)
- 2 eller flere ganger daglig
- 1 gang daglig
- 4-6 ganger per uke
- 2-3 ganger per uke
- 1 gang per uke
- sjeldnere enn 1 gang per uke

12.02 Hvor ofte vasker du vanligvis hendene med såpe i løpet av en dag? (sett ett kryss)
- 0 ganger
- 1-5 ganger
- 6-10 ganger
- 11-20 ganger
- Mer enn 20 ganger

12.03 Har du noen gang fått antibiotikakur (penicillin og liknende medisin) på grunn av en hudlidelser, for eksempel betent eksem, kviser, leggsår som ikke vil heale, tilbakevendende verkebyll?
- Ja
- Nei

Hvis JA, hvor mange ganger i gjennomsnitt per år fikk du antibiotika i den perioden du var mest plaget (sett ett kryss)
- 1-2
- 3-4
- Mer enn 4 ganger

12.04 Har du eller har du noen gang hatt følgende hudlidelser? (sett ett kryss for hver linje)
- Psoriasis
- Atopisk eksem (barneeksem)
- Tilbakevendende håndeksem
- Tilbakevendende kviser over flere måneder
- Leggsår eller fotsur som ikke ville heale i løpet av 3-4 uker

Hvis JA på spørsmål om leggsår/eller fotsur, har du leggsår i dag?
- Ja
- Nei

12.05 Har du ofte eller bestandig noen av følgende plager? (sett ett kryss for hver linje)
- Ja
- Nei
  - Hevelse i ankler og legger, særlig om kvelden
  - Åremutter
  - Eksem (rødt, klørende utslitt) på leggene
  - Smerte i beina når du går, men som forsvinner når du står stille

12.06 Har du noen gang fått følgende diagnoser av lege? (sett ett kryss for hver linje)
- Psoriasis
- Atopisk eksem
- Rosacea
- Ja
- Nei

12.07 Har du tilbakevendende store kviser/verkebyll som er ømme/smerterfule og som ofte tilhører med ar på følgende steder? (sett ett kryss for hver linje)
- Armhulene
- Under brystene
- Magefolden/navlen
- Rundt kjønnsmangatur
- Rundt endetarmslåpningen
- Lyskene
- Ja
- Nei

Hvis JA, har du noen gang oppsøkt lege på grunn av verkebyll?
- Ja
- Nei

Hvis JA, fikk du da noen av følgende behandlinger? (sett ett kryss for hver linje)
- Antibiotika salve/krem
- Antibiotika tabletter
- Kirurgisk åpning/tamming
- Større kirurgisk ingrep med fjerning av hud
- Kirurgisk laserbehandling
- Ja
- Nei
Takk for hjelpen!
Tromsø-undersøkelsen

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