

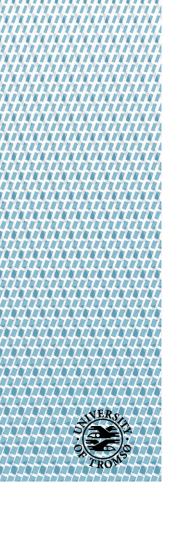
Faculty of health sciences / Department of community medicine

The Prevalence and Factors Associated with Decreased Oxygen Saturation in a GP Population of Adults: A Comparative Study in Northwest Russia and Northern Norway

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Roshmi Rayamajhi HEL-3950 Master's thesis in Public Health May 2016

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## **Acknowledgements**

Numerous people have been involved in the successful completion of this study. I warmly acknowledge all of them for their kind co-operation, tremendous effort, and suggestions.

First of all, I would like to thank my research supervisor Associate Professor Oleg Sidorenkov (MD, Ph.d.) for allowing me an immense opportunity to be the part of POMOR project, and giving me permission to carry out this study as partial fulfilment of the requirement for Master programme. He provided me with every prospect to explore and learn throughout this study period with his valuable suggestions and feedbacks.

Furthermore, I would like to express my sincere gratitude to co-supervisor researcher Ranjan Parajuli (MD, Ph.d.) for his constructive suggestions and continuous guidance; required during analysis, interpretation of data, and finalising the report.

My deepest appreciation to the student advisor of the Master's Degree program in Public Health, Mr Tor Gisle Lorentzen. I will be forever indebted for his generosity and co-operation. Further, I am thankful to the UiT-The Arctic University of Norway for granting me every chance to learn and expand my knowledge.

Also, I am grateful to my family for always believing in me and for their constant support. I extend special thanks to my friends Sujan Shrestha, Prasanna Karki and Sudip Shrestha for their helps and encouragements.

May 2016, Roshmi Rayamajhi Abstract

Objective: To explore the prevalence and contributing factors of lower oxygen

saturation in Northern Norway and Northwest Russia.

Methods: The descriptive cross-sectional study included 3833 respondents from

Northwest Russia (3215) and Northern Norway (618). All men and women aged 40

years or more, visiting general practitioners' (GPs) offices were the subjects. A

structured questionnaire, a digital handheld pulse oximeter for oxygen saturation

(SpO<sub>2</sub>) and pulse, and physical examination were used for data collection.

Independent sample t-test (continuous) and chi-square test (categorical) were used to

find a significant difference in two groups. The association between independent

variables and oxygen saturation was measured using logistic regression and was

reported as odd ratio (OR) with 95% confidence interval (CI).

**Results:** The prevalence of low SpO<sub>2</sub> (≤95%) was 4.4% in Northern Norway and

3.0% in Northwest Russia. In men and women, it was found to be 4.9% and 2.2%

respectively. A significant predictor of lower oxygen saturation in both genders was

'other heart disease'. In men, severe breathlessness problem (OR = 3.6; 95% CI = 1.4-

9.2) and current smoking habit (OR = 3.5; 95% CI = 1.6-7.3) showed statistically

significant association with lower oxygen saturation. In women, a significant

predictor of lower oxygen saturation was chronic obstructive pulmonary diseases

(COPD) (OR = 8.8; 95% CI = 4.2-18.8).

Conclusion: The contributing factors of lower oxygen saturation are other heart

diseases, COPD, severe breathlessness problem and smoking habit.

**Keywords:** *COPD*, prevalence, pulse oximetry, oxygen saturation

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#### **List of Abbreviations**

1. ARDS Acute Respiratory Distress Syndrome

2. BMI Body Mass Index

3. bpm Beats per minute

4. CHF Congestive Heart Failure

5. CI Confidence Interval

6. COPD Chronic Obstructive Pulmonary Diseases

7. COHb Carboxyhemoglobin

8. FEV Forced Expiratory Volume

9. FP Family Practitioner

10. GP General Practitioner

11. HBA1C Glycated Haemoglobin

12. LTOT Long Term Oxygen Therapy

13. SD Standard Deviation

14. SpO<sub>2</sub> Oxygen Saturation

15. SPSS Statistical Package for the Social Sciences

16. UK United Kingdom

17. WHO World Health Organisation



#### 1. Introduction

#### 1.1 Background

Oxygen saturation is a term referring to the concentration of oxygen in the blood. It measures the percentage of haemoglobin binding sites in the bloodstream occupied by oxygen. SpO<sub>2</sub> stands for peripheral capillary oxygen saturation; is an estimation of the oxygen saturation level (1).

A SpO<sub>2</sub> greater than 95% is considered normal and below 92% (at sea level) suggests hypoxemia (2). Low SpO<sub>2</sub> occurs due to hypoventilation, right-to-left shunts, reduced diffusion capacity, ventilation-perfusion mismatch, and reduced oxygen partial pressure in inspired air (3). Blood oxygen levels below 80% compromise the organ function, such as the brain and heart. Continued low oxygen levels lead to a respiratory or cardiac arrest and it needs to be addressed promptly (4).

Generally, to assess arterial oxyhemoglobin saturation an economical, non-invasive (5) hand-held (2) device; pulse oximetry is used. It is based on light absorbance of oxy- and deoxy-hemoglobin at 660 and 940 nm wavelengths (6). The accuracy of oximeters differs depending on how it is made, particularly at saturations below 70%. Finger probes compared to ear probes are found to have a significantly higher correlation with oxygen saturation. Furthermore, factors like deoxyhemoglobinemia, hypothermia, and skin pigmentation can decrease accuracy (7).

#### Application of pulse oximetry in general practice

Pulse oximetry is used to manage chronic obstructive pulmonary disease (COPD), acute exacerbations and a need for long-term oxygen therapy and grading the severity of asthma

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attack. Furthermore, it is used to assess the severity and oxygen requirements for patients with community-acquired pneumonia (8).

Additionally, the role of pulse oximetry is significant for patient assessment and monitoring in critical care, anesthesiology, and emergency departments (9). In emergency medicine, SpO<sub>2</sub> can relate mortality (10, 11) and is included in risk scores predicting prognosis together with other vital signs (12, 13). It rapidly detects changes in oxygen saturation thus, provides an early warning of hypoxemia (9, 14).

The choice to initiate oxygen therapy in acute COPD exacerbations based on an oxygen saturation value <90% is considered another possible application for pulse oximetry in primary care (15). A SpO<sub>2</sub> 92% indicates hypoxemia and the values between 93% and 95% are regarded as lower than normal (2, 14). A SpO<sub>2</sub> up to 95% has been found to predict hypoxia during exercise in COPD patients (16). Dutch family practice guideline for COPD recommends that in the case of an exacerbation of COPD, respiratory failure is unlikely to be present with an arterial oxyhemoglobin saturation measured by pulse oximetry SpO<sub>2</sub> >92% (17).

In a study by Giesen et al based on a retrospective medical record analysis of patients contacting family physicians (FPs) cooperative, the value of pulse oximetry was especially recognised for patients previously unknown to the FP who presented with acute medical problems (18). The occasions in which FPs in the United Kingdom (UK) most often use pulse oximetry is in patients who present with an exacerbation of COPD (19). Being a simple and valid screening test for systemic hypoxia (20), the use of pulse oximetry in general practice is suggested (21, 22). However, new guidelines

on the use of pulse oximetry are partly evidence-based and more research is accordingly required (2).

Asthma, a disease of the airways (23), is characterised by recurrent attacks of breathlessness and wheezing (24). The recent report (2014) estimated asthma to be prevalent among 334 million people worldwide. (23). COPD describes chronic lung diseases and leads to the persistent blockage of airflow from the lungs. World Health Organisation (WHO) estimates by 2030, COPD will likely to be the third leading cause of death worldwide (24).

Globally, COPD and asthma are common conditions observed in primary care; affecting more than 1 billion patients worldwide (2). The estimated prevalence in a population aged 40-69 years was 6.3% and 7.2% in COPD and asthma respectively (25). Although, asthma and COPD are two different and independent diseases, the range observed in clinical practice is complex, particularly in older people with factors of both diseases (26).

Other important causes of morbidity and mortality among older adults in western society besides COPD are cardiovascular diseases (CVD) (2). The majority of patients with COPD and congestive heart failure (CHF) get their diagnosis and treatment in general practice usually based on clinical symptoms (primarily, dyspnea) and physical examination. COPD and CHF are linked with reduced oxygenation of arterial blood in the lungs and, thereby, with low arterial oxyhemoglobin saturation (27).

In the developing world, COPD is understudied, underdiagnosed, and undertreated disorder (28, 29). In Russia, data available on the epidemiology of COPD is limited

and the prevalence is underestimated, as in the case in many other countries (28, 30). As per one of the population based studies in Krasnoyarsk region in Russia (2011), the true prevalence of COPD was estimated as approximately 21.2 per 1,000 which was two times more than the estimates based on medical diagnosis statistics (31). The respiratory disease showed higher premature mortality in Russian Arctic but the problem in Russia is disregarded (32).

In Norway, the annual incidence of COPD is 7 cases per 1000 adults (33). The prevalence of COPD among adults aged 40 years or more varies from 5 to 10% (34). The  $SpO_2$  levels  $\leq 95\%$  is associated with reduced lung function, dyspnea (27) and increased mortality in the Norwegian adult population (35).

COPD and CHF are resource-demanding medical conditions due to the cost of long-term treatment and frequent hospitalization and the expenses apt to increase in future. According to the Norwegian Directorate of Health, the prevalence of CHF is about 0.3-2 % and increases with age up to 10% among adults aged 80 years or more (36). The treatment of patients with COPD in Norway was calculated to cost about 24 billion Norwegian Kroner during the next 20 years and these expenses are related to disease exacerbations rate. In addition, the cost of treatment of COPD patients will be 200% higher if the rate of disease exacerbations in Norway will be the same as in Sweden (37).

Epidemiological data suggests long-term oxygen therapy (LTOT) delivered by oxygen concentrators in patients with severe hypoxic chronic COPD is underprescribed by General Practitioners (GPs) in England and Wales. Provision of a non-

invasive measure of oxygenation likely to improve detection of hypoxic subjects and enhance appropriate setting (35).

The information about low oxygen saturation and its association with mortality or morbidity in a general population is limited. In recent studies, the predictors for low oxygen saturation in an adult population were found to be increased body mass index (BMI) (either very high or very low), reduced lung function defined by forced expiratory volume in 1s (FEV<sub>1</sub>)% predicted (38), increasing age, gender male, smoking history - both smoking, former smoking and pack-years (former smoking often not significant when pack years included) (39), and history of cardiovascular disease (CVD). Those predictors were found associated to predict increasing mortality in general adult population studies (3).

During short-term respiratory compromise, pulse oximetry delivers a method for rapid assessment. In a patient with acute respiratory illness (example, influenza) or breathing difficulty (example, an asthma attack), SpO<sub>2</sub> of 92% or less may indicate a need for oxygen supplementation. In addition, in the patients with acute respiratory infection, it helps to determine the severity of the illness and, in conjunction with other criteria, determining whether and how to refer patients for further treatment (40). Moreover, it is also helpful in diagnosing diabetic peripheral arterial disease (41), in screening for congenital heart disease in children (42) and in predicting mortality risk in patients with a pulmonary embolus (43). Hence, it can be a useful aid to clinical decision-making, nevertheless, it is not a substitute for a clinical assessment nor sufficient for diagnosis by itself (40).

Despite the wide range of potential functions of pulse oximetry, very little research has been reported about its usage. The limited data reported have shown that the pulse oximetry can be beneficial to patients with acute respiratory insufficiency (including acute asthma attacks) and in the follow-up of patients with chronic respiratory conditions (22). To shed more light on the practicality of pulse oximetry, the aim of this study was to study associations between low oxygen saturation level (SpO<sub>2</sub>  $\leq$ 95%) and the variables.

# 1.1.1 Background of POMOR Project

Data for this study was collected from the POMOR project (2012).

The POMOR project was started in 2009 as a collaboration program in postgraduate education of general practitioners with the objective to exchange Norwegian experience in small group teaching with Russian colleagues. The project ended up in 2014.

The Pomor Project (2012) was financed by the Norwegian Ministry of Health and Care Services under the Northern Dimension Partnership in Public Health and Social Well-being. As a part of the scientific study in POMOR project, the data on pulse oximetry and its correlates were collected from the GP populations in Northern Norway and Russia (44).

#### 1.2 Statement of Problem

Primary care clinicians are the first point of contact for patients suffering from acute respiratory infections. These health care professionals need tools to help them evaluate, monitor, and decide when to refer patients with respiratory conditions (2).

Arterial blood gas measurement, obtained by arterial puncture is the gold standard for measurement of oxygen saturation. But it is invasive, painful, time-consuming, costly, provides only intermittent information on patient status, and is impractical in most primary care settings (2). Pulse oximetry in other hand, is simple to use, and useful in triaging potentially hypoxic patients to determine which patients should have arterial blood gas measurements (40).

Being non-invasive method of screening and when applied to all COPD patients seen in general practice can help reveal those fulfilling the criteria for long-term oxygen who would otherwise not be identified (35). Likewise, it is an important tool to evaluate, and monitor pulmonary diseases (6) together with assessing the severity of their patient's condition (35) and can be used for the management of acute and chronic respiratory disease in primary care. However, the research is limited (40).

Worsening of pulmonary diseases is associated with a decrease in oxygen saturation (SpO<sub>2</sub>). Such a decrease in SpO<sub>2</sub> and associated factors has not been previously evaluated in a general adult population (45). Pulse oximetry has been recommended for monitoring COPD patients, but the evidence for its usefulness is bare (2). The aim of this study is to describe the distribution of low pulse oximetry values in a general adult population and their association with certain predictors (45).

#### 1.3 Rationale of the Study

The low arterial oxyhemoglobin saturation is an objective proxy display of chronic respiratory failure and conditions like chronic heart failure and others, which a GP meets in his/her everyday practice. This knowledge is necessary for health authorities for planning health care in these groups of patients. Our study will be beneficial further to investigate the importance of using pulse oximetry in primary care settings.

Moreover, this study will be useful in finding the associated factors of lower oxygen saturation among GP populations. It will be helpful to provide the evidence of the importance of usage of pulse oximetry in clinical settings thus encouraging the clinical areas to introduce pulse oximetry in the health settings as a normal procedure.

In addition, this study can provide recommendations for the use of pulse oximetry in general practice for following-up the patients with chronic heart- or/and respiratory failure in Norway and Russia. Before introducing pulse oximetry in general practice on a larger scale in Norway and Russia, it is important to explore SpO<sub>2</sub> distribution in subgroups of GP patients.

This study can also be beneficial for other researchers to gain valuable information regarding the issue of interest. Besides, it can also be valuable to the organization working in pulse oximeter together with those working in the area of respiratory diseases and cardiovascular diseases.

#### 1.4 Objectives of the Study:

#### 1.4.1. General Objectives

To explore the factors associated with decreased oxygen saturation among GP populations of adults in Northern Norway and Northwest Russia.

# 1.4.2 Specific Objective

- To find the common factors associated with lower oxygen saturation among GP populations of adults in Northern Norway and Northwest Russia.
- To compare the prevalence of lower oxygen saturation between Northern Norway and Northwest Russia.
- To explore the significant association between gender and level of oxygen saturation.
- To provide information to the centers concerned which will be helpful to implement the usage of pulse oximetry for general practitioners.

## 1.5 Research Question/ Hypothesis

What is the prevalence of lower oxygen saturation among GP populations of adults in Northern Norway and Northern Russia?

What are the major factors associated with decreased oxygen saturation in GPs adult populations?

1.6 Operational Definitions of Variables

**Dependent variable** 

The participant's oxygen saturation was measured using digital handheld pulse

oximeter. Three readings were recorded and the highest value was used as the best

pulse oximetry value. The values were further classified into normal and lower:

Lower: <SpO<sub>2</sub> 95%

Normal: >SpO<sub>2</sub> 95%

**Independent variables** 

Baseline demographic characteristics: age, sex, measurements, self-reported cardiac

diseases, self-reported respiratory diseases, grading of breathlessness and smoking

were measured.

All men and women aged 40 years or more visiting a GP office of the doctor

participating in the study self-recorded their age. After filling in the questionnaire, and

rested for at least 15 minutes, the health personnel measured the arterial oxy-

hemoglobin saturation of patients with a digital handheld pulse oximeter. Three

measurements with intervals of 1 minute were recorded and the best one was used in

the analyses. Then height (without shoes), and weight (in light clothing) were

recorded. Body Mass Index (BMI) was categorized according to World Health

Organisation (WHO) criteria as normal, overweight and obese if BMI <25 kg/m<sup>2</sup>,

BMI = (25-29.99) kg/m<sup>2</sup> and BMI  $\geq 30$  kg/m<sup>2</sup> respectively.

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The participants themselves recorded any presence of myocardial infarction, arterial hypertension, and any other heart diseases. These were included as self-reported cardiac diseases. The participants recording presence of asthma, COPD, respiratory infection, chronic lung diseases were included as self-reported respiratory diseases. Self-reported breathlessness was classified as none, moderate and severe breathlessness categories. Smoking habits were reported as: never, ex-smoker, and current smoker.

# 2. Methodology

#### 2.1 Study Design

Descriptive cross-sectional study

#### 2.2 Study Site

Data collected from GP offices in Northern Norway and Northwest Russia. In Russia, the data were collected in the cities of Arkhangelsk and Murmansk and in the offices placed in the rural areas of Arkhangelsk region.

#### 2.3 Study Population

All men and women aged 40 years or more visiting GP offices of the doctor who voluntarily participated in the study.

#### 2.4. Sampling Technique

All men and women aged 40 years or more visiting a GP office of the doctor participating in the study.

## 2.5 Sample Size

The prevalence of low SpO₂ levels (≤95%) was expected about 10% and 12-14%, in the Norwegian and Russian samples respectively. The primary interest represents the subgroup of patients with known COPD, which was assumed to comprise around of 10% in both samples. Thus, initially, it was planned to recruit 2000 Norwegians and 2000 Russians so that it could report 200 participants with known COPD in each

country. However, it was not possible practically to recruit 2000 Norwegian samples thus we adjusted the sample size with 618 samples from Norwegian group and 3215 samples from Russian group.

#### 2.6 Exclusion and Inclusion Criteria

GP population who were less than 40 years old and did not want to respond to the questionnaire were excluded.

#### 2.7 Instrumentation

**Questionnaire:** Participants were asked to fill in a one-page questionnaire while he/she was waiting for admission to the doctor.

**Physical examination**: Health personnel examined the patient. The height (without shoes), and weight (in light clothing) were measured. The arterial oxyhemoglobin saturation and pulse were measured with a digital handheld pulse oximeter.

#### 2.8 Data Collection Tools

**Techniques:** Respondents were asked to read through a short information letter on the study's aim and methodology and then to think over the proposal for 10-15 minutes, returning of the fulfilled questionnaire was considered as agreement to participate. After filling up the questionnaire, and resting for at least 15 minutes, the health personnel measured arterial oxyhemoglobin saturation with a handheld pulse oximeter.

**Tools**: A structured questionnaire was used for the data collection. A digital handheld pulse oximeter was used for measuring SpO<sub>2</sub> and Pulse. Physical examination was

done to measure height, weight and waist circumference. BMI was calculated with the formula (46):  $BMI = \frac{\text{weight}(kg)}{[height(h)]^2}$ 

#### 2.9 Data Analysis

The information collected from the respondents were sorted, coded and entered in datasheet created in a statistical package for Social Science (SPSS) version 23. Data from Norway and Russia was merged. Differences between nationalities (Norway and Russia) and gender (men and women) were tested using chi-square and Independent Sample t-test for categorical and continuous explanatory variables, respectively. The association between independent variables and oxygen saturation were assessed using binary logistic regression and was reported as odds ratio (OR) with 95% confidence interval (CI). The dependent variable, oxygen saturation was assigned the value 0 and 1. Low oxygen saturation (SpO<sub>2</sub>) with the value SpO<sub>2</sub> <95% was coded 0 and normal oxygen saturation with the value SpO<sub>2</sub> >95% was coded 1.

First, the association of independent variables and oxygen saturation was measured in an unadjusted univariate model. Multivariate logistic regression was conducted. The variables adjusted in the final model for multivariate logistic regression was obtained using backward elimination (wald method). The criterion for statistical significance was  $p \le 0.05$ .

#### 2.10 Ethical Aspects

The application was considered by Regional Committee for Medical and Health Research Ethics (REK south-east) in the meeting 22/08/2013. The assessment was made pursuant to the Health Research Act (hfl.)10, ref. Ethics Act 4 project Review. Pursuant to the Health Research Act 9 ref. 33 approved the committee. Participants received an information sheet without consent form and completing the questionnaire was considered sufficient consent. Participants were ensured to maintain the confidentiality.

# 3. Study Findings

#### 3.1 Demographic and baseline characteristics of the respondents

# 3.1.1 Demographic and baseline characteristics of respondents in Northern Norway and Northwest Russia

The descriptive study was conducted in Northern Norway and Northwest Russia. Altogether there were 3833 respondents, 618 from Norway and 3215 from Russia. The comparison and significant difference between two nationalities: Norway and Russia as per explanatory variables are summarised in Table 1.

Out of 3833 respondents, the majority were from Russia (83.9%). The mean age in Norway and Russia were 58.6 years and 60.4 years respectively (p-value = 0.001). In Norway, majority of the respondents (27.9%) were from age group (40-49) years, 26.4% were from age group (50-59) years, 25.2% were from the age group (60-69) years, 16. 5% were from age group (70-79) years, and few 4% were from 80 years and above age group. However, in Russia, the majority (29%) were from age groups (50-59) years, followed by 27.9% in age groups of (60-69) years, 18.9% in (40-49) years age groups, 17.4% in (70-79) years and 5.9% in 80 years and above. The number of female respondents was more in both Norway and Russia, 55.5% and 63.7% (p-value <0.001). Mean pulse rate in Norway and Russia were 70.7 beats/minute (bpm) and 72.5 bpm respectively. The majority of the respondents had a normal pulse rate (60-100) bpm both in Norway (76%) and Russia (88.1%) (p-value <0.001). The mean body mass index in Northern Norway and Northwest Russia were 28.1 kg/m² and 28.5 kg/m² respectively (p-value <0.001). The proportion of

overweight; BMI > (25- 29.9) kg/m<sup>2</sup> was 42.7% and obesity (BMI >30 kg/m<sup>2</sup>) was 26.2% in Norwegian respondents. In Russia, the proportion of overweight and obesity was 36.4% and 36.6% respectively (p-value <0.001).

Among the self-reported cardiac diseases, arterial hypertension was found more common cardiac diseases in both countries with its prevalence rate of 31.1% and 69.8% in Norway and Russia respectively (p-value <0.001). The prevalence of MI in Norway and Russia was 4.7% and 9.4% respectively (p-value <0.001). Similarly, among self-reported respiratory diseases, asthma, and respiratory infection were more common respiratory problems found both in Norway and Russia. In Norway, 10.8% respondents had asthma while it was 6.1% in Russia (p-value <0.001). Overall, 46.8% respondents in Norway reported breathlessness problems; among them, 4.2% reported severe difficulty in breathing. Likewise, in Russia, 51.7% reported breathlessness, among them 4.1% reported severe difficulty in breathing. In Norway, the majority of people were ex-smoker (43.8%). In contrary, the majority of Russian respondents never smoked (63.7%). In both countries, the proportion of current smokers were almost similar i.e, 18.3% and 18.9% in Norway and Russia respectively.

Table 1: Baseline characteristics of respondents as per nationality (Norway and Russia)

Factors	Norway n (%)	Russia n (%)	p-value
Valid n (%)	618 (100.0)	3215 (100.0)	
Age, years, mean (SD)	58.6 (11.8)	60.4 (11.6)	0.001
Age, years (cat)			< 0.001
40-49	166 (27.9)	608 (18.9)	
50-59	157 (26.4)	958 (29.8)	
60-69	150 (25.2)	898 (27.9)	
70-79	98 (16.5)	561 (17.4)	
80 above	24 (4.0)	190 (5.9)	
Total	595 (96.3)	3215 (100.0)	
Gender			< 0.001
Male	272 (44.5)	1168 (36.3)	
Female	339 (55.5)	2047(63.7)	
Total	611(98.9)	3215 (100.0)	
Measurements			
Pulse rate, bpm, mean (SD)	70.7 (14.0)	72.56 (11.4)	0.004
Pulse rate, bpm			< 0.001
<u>≤</u> 60	131(21.2)	315 (9.8)	
60-100	469 (76.0)	2834 (88.1)	
>100	17 (2.8)	66 (2.1)	
Total	617 (99.8)	3215 (100.0)	
BMI kg/m <sup>2</sup> , mean (SD)	28.1 (14.1)	28.5 (5.4)	< 0.001
BMI kg/m <sup>2</sup> (cat)			< 0.001
<25	188 (31.0)	852 (26.9)	
≤25- 29.9)	259 (42.7)	1152 (36.4)	
<u>≥</u> 30	159 (26.2)	1158 (36.6)	
Total	606 (98.1)	3162 (98.4)	
SpO <sub>2</sub> , mean (SD)	97.7 (1.2)	97.9 (1.4)	< 0.001
SpO <sub>2</sub> ,% (cat)			0.074
$SpO_2 \leq 95$	27 (4.4)	96 (3.0)	
SpO <sub>2</sub> >95	591(95.6)	3119 (97.0)	
Self-reported cardiac diseases			
MI	28 (4.7)	303 (9.4)	< 0.001
Total	593 (96.0)	3213 (99.9)	
<b>Arterial hypertension</b>	186 (31.1)	2241 (69.8)	< 0.001
Total	599 (96.9)	3212 (99.9)	
Other heart diseases	56 (9.1)	386 (12.0)	0.071
Total	594 (96.1)	3214 (100.0)	

Table to be continued in next page

Table 1 continued

Factors	Norway n (%)	Russia n (%)	p-value
Self-reported respiratory diseases			
Asthma	65 (10.8)	197 (6.1)	< 0.001
Total	602 (97.4)	3204 (99.7)	
COPD	30 (5.0)	207 (6.4)	0.178
Total	600 (97.1)	3211 (99.9)	
Respiratory infection	57 (9.5)	280 (8.7)	0.509
Total	597 (96.6)	3214 (100.0)	
Chronic lung diseases	14 (2.3)	126 (3.9)	0.061
Total	596 (96.4)	3214(100.0)	
Self-reported breathlessness			0.054
None	291 (53.7)	1152 (48.3)	
Moderate	228 (42.1)	1531 (47.6)	
Severe	23 (4.2)	132 (4.1)	
Total	542 (87.7)	3215 (100.0)	
Smoking Habit			< 0.001
Never smokers	232 (37.9)	2048 (63.7)	
Ex-smokers	268 (43.8)	559 (17.4)	
Current smokers	112 (18.3)	607 (18.9)	
Total	612 (99.0)	3214 (100.0)	

Values are mean with standard deviation (SD) or number n with percentage of column (%); BMI (Body Mass Index);  $SpO_2$  (Oxygen Saturation); bpm (beats per minute); MI (myocardial infarction); COPD (Chronic Obstructive Pulmonary Disease); <sup>1</sup> Calculated by Pearson's chi – squared test and Independent Sample t-test

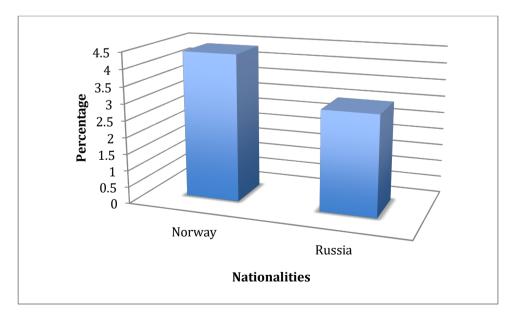


Figure 1: Prevalence of lower oxygen saturation based on nationalities

Figure 1 demonstrates the image about the prevalence of lower oxygen saturation in Northern Norway and Northwest Russia. The low oxygen saturation is prevalent higher in Northern Norway compared to Northwest Russia, ie, 4.4% and 3.0% respectively.

#### 3.1.1.2 Baseline characteristics of men and women in the study population

Table 2 presents the baseline characteristics of the study population by men and women. The descriptive study conducted in Norway and Russia constitutes 3833 participants among which 3826 participants responded to their gender. Female constituted the majority in number 2386 (62.4%) of which 85.8% female participants were Russian. The mean age was 60.4 years for men and 59.9 years for female (p-value <0.001).

The Smoking habit was more prevalent among men than women. However, the prevalence of obesity (BMI  $\geq$ 30 kg/m²) was higher in women than men. The lower oxygen saturation  $\leq$ 95% was prevalent more in men in comparison to female. Similarly, cardiovascular diseases like MI and respiratory diseases like COPD, chronic lung diseases were prevalent more in men than women.

The Majority in (83.5%) men and women (87.8%) had normal pulse rate; (60-100) bpm (p-value <0.001). The mean body mass index was 27.7 kg/m² for men and 28.9 kg/m² for women (p-value <0.001). The prevalence of overweight was higher in men (39.3%) in comparison to women (36.3%). However, the proportion of obesity was higher in women (37.8%) in comparison to men (30.2%) (p-value <0.001). The mean

oxygen saturation (SpO<sub>2</sub>) was 97.7% for men and 97.9% for women (p-value <0.001). The prevalence of lower oxygen saturation is higher in men (4.9%) than women (2.2%) (p-value <0.001). Moreover, among the self-reported cardiac diseases, arterial hypertension was the most common cardiac disease prevalent both in men and women, which was respectively 61.8% and 64.9% (p-value = 0.056). Myocardial infarction was prevalent more in men (14.6%) than women (5.1%) (p-value <0.001).

Similarly, among self-reported respiratory diseases, 10.5% men and 3.6% women (p-value <0.001) had COPD. Likewise, chronic lung's diseases were present among 4.7% men and 3.0% women. The majority of the men were involved in the smoking habit in comparison to women. Among them, 36.8% men and 12.4% women were exsmokers. While the proportion of current smokers among men and women was 32.0% and 10.8% respectively (p-value <0.001).

Table 2: Baseline characteristics of men and women in the study population

Factors	Men n (%)	Women n (%)	$\mathbf{P}^1$
Total valid	1440	2386	
Nationality			
Norway	272 (18.9)	339 (14.2)	< 0.001
Russia	1168 (81.1)	2047 (85.8)	
Age, years, mean (SD)	60.4 (11.5)	59.97 (11.7)	< 0.001
Age, years (cat)			0.019
40-49	282 (19.7)	492 (20.7)	
50-59	387 (27.0)	726 (30.5)	
60-69	437 (30.5)	611 (25.7)	
70-79	246 (17.2)	413 (17.4)	
80 above	79 (5.5)	135 (5.7)	
Measurement			
Pulse rate, bpm, mean	72.1 (12.6)	72.2 (11.4)	0.890
(SD)			
Pulse rate, bpm (cat)			
<60	206 (14.3)	240 (10.1)	< 0.001
60-100	1201 (83.5)	2096 (87.8)	
>100	32 (2.2)	50 (2.1)	
BMI $kg/m^2$ (SD)	27.7 (5.01)	28.9 (8.7)	< 0.001
BMI kg/m <sup>2</sup> (cat)			< 0.001
<25	433 (30.6)	607 (25.9)	
= 25-29.9	556 (39.3)	852 (36.3)	
>30	427 (30.2)	886 (37.8)	
SpO <sub>2</sub> , %, mean (SD)	97.7 (1.5)	97.9 (1.2)	< 0.001
SpO <sub>2</sub> , % (cat)			< 0.001
<u>&lt;</u> 95	70 (4.9)	52 (2.2)	
>95	1370 (95.1)	2334 (97.8)	
<b>Self-reported cardiac diseases</b>			
MI	209 (14.6)	122 (5.1)	< 0.001
<b>Arterial hypertension</b>	887 (61.8)	1537 (64.9)	0.056
Other heart diseases	179 (12.5)	263 (11.1)	0.179

Table to be continued in next page

Table 2 continued

Factors	Men n (%)	Women n (%)	$\mathbf{P}^{1}$			
Self-reported respiratory diseases						
Asthma	90 (6.3)	170 (7.2)	0.294			
COPD	150 (10.5)	86 (3.6)	< 0.001			
Respiratory infection	125 (8.7)	212 (8.9)	0.813			
<b>Chronic lung diseases</b>	67 (4.7)	72 (3.0)	0.009			
Self-reported breathlessness						
None	711 (50.5)	1129 (48.2)	0.367			
Moderate	638 (45.3)	1117 (47.7)				
Severe	58 (4.1)	97 (4.1)				
Smoking habit						
Never	449 (31.9)	1828 (76.8)	< 0.001			
Ex-smoker	529 (36.8)	295 (12.4)				
Current smoker	460 (32.0)	258 (10.8)				

Values are mean with standard deviation (SD) or number n with percentage of column (%); BMI (Body Mass Index); SpO<sub>2</sub> (Oxygen Saturation); bpm (beats per minute); MI (Myocardial Infarction); COPD (Chronic Obstructive Pulmonary diseases); ¹Calculated by Pearson's chi-squared test and Independent Sample t-test

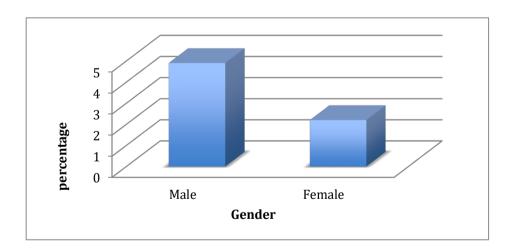


Figure 2: Proportion of lower oxygen saturation based on gender

Figure 2 displays the comparative image of lower oxygen saturation prevalent among male and female subgroups. It demonstrates the presence of lower oxygen saturation

more in the males compared to the females. It is found to be 4.9% among male while 2.2% among the female GP population.

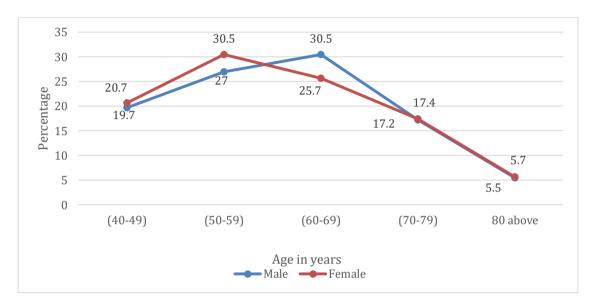


Figure 3: Age distribution according to gender

Figure 3 shows the distribution of different age groups among male and female subjects. The majority of the men (30.5%) belonged to the age group of (60-69) years, while in female (30.5%) were from (50-59) years age group. Only a few participants in both groups belonged to the age category of 80 years and above.

#### 3.2 Logistic Regression Analysis

# 3.2.1 Association between independent variables and lower oxygen saturation among GP female populations.

Table 3 presents the crude univariate analysis and (age) adjusted analysis of factors associated with lower oxygen saturation (normal/low:  $SpO_2 > 95\%/SpO_2 \le 95\%$ ) among GP female population of adults. The univariate analysis was performed with only a single independent variable included in the model at a time.

Among the GPs' female population, the independent variables associated with lower oxygen saturation (p-value <0.05) were age, BMI, self-reported cardiac diseases-(other heart diseases, arterial hypertension), self-reported respiratory diseases - (COPD, asthma, chronic lung diseases), and self-reported - breathlessness (severe).

The crude analysis in women population revealed statistically significant association between age and oxygen saturation. It showed the odds of having lower oxygen saturation increased with increasing age (OR = 1.04; 95% CI = 1.01-1.07). In univariate analysis, age group (51-60) years (OR = 2.9; 95% CI = 0.9-8.7), (71-80) years (OR = 3.6; 95% CI = 1.1-11.4) and 80 and above years (OR = 8.7; 95% CI = 2.6-28.7) were significantly associated with the lower oxygen saturation level.

Although in crude unadjusted analysis there was not significant association with lower oxygen saturation and BMI, however, adjusting the factor age, a significant association was observed between oxygen saturation level and BMI. Adjusting the factor age showed the odds of lower oxygen saturation increased with increasing BMI (OR = 1.01; 95% CI = 1.00-1.02). Also, according to self-reported cardiac disease, the

presence of heart diseases revealed the association with lower oxygen saturation (OR = 2.2; 95% CI = 1.1-4.2). Similarly, among self-reported respiratory diseases, COPD and lower oxygen saturation had a significant association with each other (OR = 10.1; 95% CI = 5.2-19.7). The odds of having lower oxygen saturation among those having chronic lung diseases was three times that of those without chronic lung diseases problems (OR = 3.3; 95% CI = 1.2-8.6). Similarly, women presented with asthma also had 3 times risk of having lower oxygen saturation. Likewise, the odds of having lower oxygen saturation among those reporting severe breathlessness problem was 4.4 times that of those without any breathlessness problems (reference group). Thus, severe breathlessness was significantly associated with the lower oxygen saturation level (OR = 4.4; 95% CI = 1.7-11.5).

Table 3: Univariate and age-adjusted analysis: Risk factors for lower oxygen saturation among female GP population

	Unadjusted	Adjusted for age		
Determinants	OR (95 % CI)	p*	OR (95% CI)	p**
Nationality				
Norway (ref)	1.0		1.0	
Russia	0.7 (0.3-1.6)	0.518	0.6 (0.3-1.4)	0.321
Age, years	1.04 (1.01-1.06)	0.001	-	
Age, years (cat)			-	
40-50 (ref)	1.0			
51-60	2.9 (0.9-8.7)	0.055		
61- 70	2.0 (0.6-6.5)	0.234		
71- 80	3.6 (1.1-11.4)	0.026		
Above 80	8.7 (2.6-28.7)	< 0.000		
Pulse rate, bpm	1.0 (0.9-1.0)	0.146	1.0 (0.9-1.0)	0.145
Pulse rate, bpm (cat)				
<60 (ref)	1.0		1.0	
= 60-100	0.6 (0.3-1.5)	0.383	0.6 (0.3-1.5)	0.386
>100	1.3 (0.2-6.8)	0.689	1.4 (0.2-7.0)	0.671
BMI, kg/m <sup>2</sup>	1.01(0.99-1.02)	0.066	1.01 (1.00-1.02)	0.029
BMI, (cat)				
<25 (ref)	1.0		1.0	
≤ 25- 29.9	0.9 (0.4-2.0)	0.806	0.7 (0.3-1.7)	0.580
<u>≥</u> 30	1.6 (0.8-3.3)	0.175	1.4 (0.7-3.0)	0.292
Self-Reported cardiac disea	ses			
MI				
No (ref)	1.0		1.0	
Yes	1.5 (0.5-4.3)	0.405	1.1 (0.3-3.0)	0.899
<b>Arterial Hypertension</b>				
No (ref)	1.0		1.0	
Yes	0.8 (0.4-1.5)	0.610	0.5 (0.2-0.9)	0.041
Other heart diseases				
No (ref)	1.0		1.0	
Yes	2.7 (1.4-5.2)	0.002	2.2 (1.1-4.2)	0.017

Table to be continued in next page

Table 3 continued

	Unadjusted for age		Adjusted for age	
Determinants	OR (95 % CI)	p*	OR (95 % CI)	p**
Self-reported respiratory dis	seases			
Asthma				
No (ref)	1.0		1.0	
Yes	3.2 (1.5-6.5)	0.001	3.2 (1.5-6.5)	0.001
COPD				
No (ref)	1.0		1.0	
Yes	11.4 (5.9-22.1)	< 0.001	10.1 (5.2-19.7)	< 0.001
Respiratory Infection				
No (ref)	1.0		1.0	
Yes	1.3 (0.5-3.1)	0.508	1.5 (0.6-3.6)	0.329
Chronic lung diseases				
No (ref)	1.0		1.0	
Yes	3.5 (1.3-9.2)	0.009	3.3 (1.2-8.6)	0.014
<b>Self-reported breathlessness</b>				
None (ref)	1.0		1.0	
Mild	1.5 (0.8-2.9)	0.150	1.2 (0.6-2.4)	0.471
Severe	7.1 (3.0-16.5)	< 0.001	4.4 (1.7-11.5)	0.002
Smoking habit				
Never (ref)	1.0		1.0	
Ex-smoker	0.5 (0.2-1.6)	0.332	0.7 (0.2-2.1)	0.627
Current smoker	1.2 (0.5-2.7)	0.638	1.7 (0.7-4.2)	0.178

OR (Odd Ratio); (ref) reference group; CI (confidence interval); BMI (Body Mass Index), COPD (Chronic Obstructive Pulmonary Disease); SpO<sub>2</sub> (Oxygen Saturation); bpm (beats per minute); MI (Myocardial Infraction); \*(crude); \*\* (adjusted for age)

# 3.2.2 Association between independent variables and lower oxygen saturation among GP male populations.

Table 4 summarizes the result of crude analysis and the result adjusted with age factor among GP male population. The analysis in men showed- age, pulse rate, self-reported cardiac diseases-arterial hypertension other heart diseases, self- reported

respiratory disease- COPD, self-reported breathlessness and current smoking habit as a statistically significant associative factors with oxygen saturation.

There was a significant association between lower oxygen saturation and age (OR = 1.05; 95% CI = 1.02-1.07). In univariate analysis, age group (51-60) years (OR = 14.5; 95% CI = 1.9-109.0), (60-70) years (OR = 14.1; 95% CI = 1.8-106.0), (70-80) years (OR = 24.8; 95% CI = 3.3-186.7) and 80 and above years (OR = 31.6; 95% CI = 3.8-257.2) were significantly associated with the lower oxygen saturation level.

With every unit rise in pulse rate, the odds of having lower oxygen saturation increased by 1.02 times (OR = 1.02; 95% CI = 1.01-1.04). According to self-reported cardiac disease, presence of heart diseases indicated the association with lower oxygen saturation (OR = 1.9; 95% CI = 1.1-3.5). Among self-reported respiratory diseases, COPD showed statistical significant association with lower oxygen saturation (OR = 2.7; 95% CI = 1.5-4.9). The trend of having lower oxygen saturation among those reporting breathlessness problem increased with increase in intensity. The odds of having lower oxygen saturation among those reporting mild breathlessness problem was almost twice (OR = 2.1; 95% CI = 1.1-3.9) and those reporting severe breathlessness problems was 7.1 times that of those without any breathlessness problems (reference group). The odds of having lower oxygen saturation among the current smokers was 4.0 times that of the nonsmokers, who never smoked (OR = 4.0; 95% CI = 2.0-8.0).

Table 4: Univariate and age-adjusted analysis: Risk factors for lower oxygen saturation among GP male population

Determinants	Unadjusted		Adjusted for age		
_	OR (95% CI)	p*	OR (95% CI)	p**	
Nationality					
Norway (ref)	1.0		1.0		
Russia	0.7 (0.4-1.2)	0.239	0.7 (0.3-1.2)	0.242	
Age, years	1.05 (1.02-1.07)	< 0.001	-		
Age, years (cat)			-		
40-50 (ref)	1.0		-		
51-60	14.5 (1.9-109.0)	0.009	-		
61- 70	14.1 (1.8-106.0)	0.010	-		
71- 80	24.8 (3.3-186.7)	0.002	-		
80 above	31.6 (3.8-257.2)	0.001			
Measurements	, , , ,				
Pulse rate, bpm	1.02 (1.01-1.04)	0.011	1.02 (1.01-1.04)	0.005	
Pulse rate, bpm (cat)	,		,		
<60 (ref)	1.0		1.0		
60-100	1.3 (0.6-2.8)	0.464	1.4 (0.7-3.2)	0.297	
>100	0.7 (0.1-6.6)	0.835	0.8 (0.1-7.2)	0.892	
BMI, kg/m2	1.0 (0.9-1.0)	0.253	1.0 (0.9-1.0)	0.221	
BMI, kg/m2 (cat)	,				
<25.0 (ref)	1.0		1.0		
<25.0-29.9	0.6 (0.3-1.2)	0.253	0.6 (0.3-1.2)	0.225	
>30.0	1.2 (0.7-2.2)	0.433	1.2 (0.7-2.2)	0.435	
Self-reported cardiac	diseases				
MI					
No (ref)	1.0		1.0		
Yes	1.1 (0.5-2.1)	0.790	0.7 (0.3-1.5)	0.464	
<b>Arterial hypertension</b>	,				
No (ref)	1.0		1.0		
Yes	1.8 (1.5-3.2)	0.030	1.2 (0.6-2.1)	0.502	
Other heart diseases	,		, ,		
No (ref)	1.0		1.0		
Yes	2.5 (1.4-4.5)	0.001	1.9 (1.1-3.4)	0.024	
Self-reported respirat					
Asthma	v				
No (ref)	1.0		1.0		
Yes	2.0 (0.9-4.3)	0.075	1.7 (0.7-3.7)	0.177	
COPD	,		, ,		
No (ref)	1.0		1.0		
Yes	3.3 (2.0-6.1)	< 0.001	2.7 (1.5-4.9)	< 0.001	

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Table 4 continued

Determinants	Unadjusted		Adjusted for age		
_	OR (95% CI)	p*	OR (95% CI)	p**	
<b>Respiratory infection</b>					
No (ref)	1.0		1.0		
Yes	1.3 (0.6-2.9)	0.411	1.6 (0.7-3.6)	0.182	
<b>Chronic lung diseases</b>					
No (ref)	1.0		1.0		
Yes	1.9 (0.8-4.7)	0.121	2.0 (0.8-4.8)	0.123	
<b>Self-reported breathles</b>	sness				
None (ref)	1.0		1.0		
Mild	2.5 (1.4-4.5)	0.001	2.1 (1.1-3.9)	0.012	
Severe	10.0 (4.5-22.1)	< 0.001	7.1 (3.0-16.6)	< 0.001	
Smoking habit					
Never (ref)	1.0		1.0		
Ex-smoker	1.5 (0.8-3.1)	0.184	1.4 (0.7-2.9)	0.263	
Current smoker	2.5 (1.3-4.9)	0.004	4.0 (2.0-8.0)	< 0.001	

OR (Odd ratio); (ref) reference group; CI (Confidence Interval); BMI (Body Mass Index), COPD (Chronic Obstructive Pulmonary Disease); SpO<sub>2</sub> (Oxygen Saturation); bpm (beats per minute); \*(unadjusted p-value); \*\* (adjusted for age)

# 3.2.3 Multivariate logistic regression analysis: An association between independent variables and lower oxygen saturation among male and female GP population

Table 5 summarises the multivariate analysis among male and female GPs population. Multivariate analysis was performed with the significant predictors observed through backward (wald) method. Nationality, age, gender, self-reported cardiac diseases – other heart diseases, self-reported respiratory diseases- COPD, self-reported breathlessness, and smoking habit were adjusted in multivariate regression analysis. The factors- age, BMI, and COPD were included in multivariate analysis in men as priori. In the women, as priori, age and smoking variables were also added for multivariate analysis.

According to the multivariate analysis in table 5, the association between oxygen saturation level and nationalities was statistically significant in male population. The prevalence of lower oxygen saturation among the Russian participants was less compared to the participants from Norway (OR = 0.3; 95% CI = 0.1-0.7). Moreover, the odds of lower oxygen saturation among men increased with increasing pulse rate (OR = 1.02; 95% CI = 1.01-1.04).

According to self-reported cardiac disease, the presence of other heart diseases revealed the association with lower oxygen saturation in both male and female. The odds of having lower oxygen saturation among men and women with other heart diseases was two times more than those without other heart diseases. The odds of having lower oxygen saturation among female with arterial hypertension was 0.3 times that of the female with no arterial hypertension. Similarly, among self-reported respiratory diseases, the odds of having lower oxygen saturation among COPD female was 8.8 times than that without COPD.

In addition, the odds of having lower oxygen saturation among men with self-reported breathlessness is 3.6 times then that without breathlessness problem. Current smoking habit had an association with lower oxygen saturation in men (OR = 3.5; 95% CI = 1.6-7.3). However, multivariate analysis in the women does not show a statistical significant association between smoking habits and lower oxygen saturation.

Table 5: Multivariate adjusted odds ratio estimates for lower oxygen saturation with 95% confidence interval among male and female GP population

	Men		Women		
Factors	<b>Multivariate</b> <sup>a</sup>	p-value	Multivariate <sup>b</sup>	p-value	
_	Adjusted OR (95% CI)		Adjusted OR (95% CI)		
Nationality					
Norway (ref)	1.0		-		
Russia	0.3 (0.1-0.7)	0.003	-		
Age, years	1.03 (0.93-1.13)	0.511	1.03 (0.93-1.14)	0.485	
Age, years (cat)					
40-50 (ref)	1.0		1.0		
51-60	9.64 (1.04-89.34)	0.046	2.3 (0.4-10.7)	0.289	
61-70	6.8 (0.4-102.4)	0.162	1.2 (0.1-12.0)	0.859	
71-80	8.5 (0.2-256.3)	0.214	1.7 (0.07-39.7)	0.738	
Above 80	11.0 (0.1-778.4)	0.269	2.8 (0.1-170.0)	0.614	
Pulse measurement, bpm	1.02 (1.01-1.04)	0.012	-		
BMI	1.0 (1.0-1.1)	0.155	1.01(1.01-1.03)	0.006	
Self-reported cardiac diseases					
<b>Arterial hypertension</b>	-				
No (ref)	-		1.0		
Yes	-		0.3 (0.1-0.7)	0.007	
Other heart diseases					
No (ref)	1.0		1.0		
Yes	1.9 (1.1-3.5)	0.035	2.09 (1.03-4.21)	0.040	
Self-reported respiratory disea	ses				
Asthma	-				
No	-		1.0		
Yes	-		2.0 (0.9-4.5)	0.078	
COPD					
No (ref)	1.0		1.0		
Yes	1.6 (0.8-3.1)	0.118	8.8 (4.2-18.8)	< 0.001	
<b>Self-reported breathlessness</b>					
None (ref)			-		
Mild	1.6 (0.8-3.0)	0.114	-		
Severe	3.6 (1.4-9.2)	0.007	-		
Smoking habit					
Never (ref)	1.0		1.0		
Ex-smoker	1.1 (0.5-2.3)	0.749	0.3 (0.1-1.2)	0.111	
Current smoker	3.5 (1.6-7.3)	0.001	1.2 (0.5-3.0)	0.643	

<sup>&</sup>lt;sup>a</sup>Adjusted for nationality, age in years (continuous), age in years (categorical), pulse measurement, BMI, self-reported cardiac diseases-other heart diseases, self-reported respiratory diseases-COPD, self-reported breathlessness, smoking; <sup>b</sup>Adjusted for age in years (continuous),

age in years (categorical), BMI, self-reported cardiac diseases-arterial hypertension, other heart diseases, self-reported respiratory diseases- asthma, COPD, smoking; OR (Odd Ratio); ref (reference group); CI (Confidence Interval); COPD (Chronic Obstructive Pulmonary Disease); SPO<sub>2</sub> (Oxygen Saturation); bpm (Beats per minute); BMI (Body Mass Index)

#### 4. Discussion

#### 4.1 Methodological Consideration

#### 4.1.1 Selection bias

The comparison between two countries may vary because of their difference in socioeconomic status, mortality, co-morbidity, and the distribution of prevalence of several chronic diseases (47). Non-participants and participants might be different (47). The result can be generalized in Scandinavian countries (47); yet, the generalization to the entire world is questionable because of the sample number and the site limitation in Northern Norway and Northwest Russia.

#### 4.1.2 Information bias

It can be introduced as a result of measurement error in the assessment of both exposure and diseases (48). In our study, some variables were obtained from the self-reported questionnaire thus recall bias could exist which might influence the sensitivity and/or specificity of the questions. The data can be misclassified, leading to a nondifferential error. Moreover, answers to the stigmatized condition or habits, sometimes can be misleading. The answers towards smoking habit could be controversial. But our questionnaire was self-reporting, anonymous and answers were straightforward; limited to- ex-smoker, current smoker and never smoked. Thus, the results might not be misleading.

#### 4.1.3 Measurement errors

The sensitivity and specificity may differ between different ranges of the scale that leads to a differential error (49). In this study, weight and height were measured and BMI was calculated. In addition, SpO<sub>2</sub> and pulse were measured in resting subjects using pulse oximetry. Thus, measurements done in participants are valid. However, there are conditions which result in false SpO<sub>2</sub> reading; either lower or higher (50). For example, overestimation in darkly pigmented skin (51). Also, nail polish, dirt, artificial nails, and bright artificial light can cause falsely low readings or no readings (14). Additionally, carbon monoxide poisoning can result in inadequate oxygen transport despite normal pulse oximeter readings (14). Likewise, certain antiretroviral medications affect oxygen affinity for haemoglobin (52). Also, normal oxygen saturation levels in older patients may be slightly lower than in younger people (14). In addition, the presence of COHb in chronic heavy smokers (53, 54), and high glycohemoglobin (HbA1c) level in people with type 2 diabetes may also overestimate SpO<sub>2</sub> (55). There could be overestimated readings in heavy smokers and high COHb, or in people with type 2 diabetes and high HbA1c level.

#### 4.1.4 Confounding

Confounding is extraneous factor/ variable which distort the association between the exposure and disease of interest or the effect of the exposure of interest to the disease is distorted because of the extraneous factor (48). It is possible to control by randomization and matching while designing the study or by stratification, or by statistical modelling during analysis stage (56). Also, there is a possibility of

occurring type I error (false –positive) with an increase in the number of statistical analysis and can be solved by lowering the significance level. Similarly, type II error (false-negative) can occur with the increasing number statistical hypothesis testing which can be minimised by increasing the power of the study (57).

In this study, stratification was done to explore the differences between men and women; in addition, age was adjusted while doing logistic regression. Men and women had different SpO<sub>2</sub> values (higher in men), even after adjusting for other known factors. Moreover, backward elimination (wald) was used to select variables to include in the final model for multivariate logistic regression. Known priori was also adjusted during multivariate analysis.

## 4.1.5 Statistical power and validity

The sample was taken from 40 years and above which reflects the general adult population in Northern Norway and Northwest Russia. The population is similar to the Norwegian population or other Caucasian northern European populations with respect to age and sex distribution or the prevalence of risk factors (58, 59). Hence, the results could be applicable to similar Caucasian northern European populations (47). The participation rate was high (more than 95%) and thus internally valid. However, external validity, the degree to what the result of a study is applicable to another population (48), ability to generalize with another population is questionable because of the limitation of subjects within in Northern part of Norway and Northwest Russia.

#### 4.2 Findings

According to this study, the lower oxygen saturation,  $SpO_2 \le 95\%$ ; measured at a single-point measurement with pulse oximetry was associated with nationality, age, gender, self-reported cardiac diseases-other heart diseases, self-reported respiratory diseases-COPD, self-reported breathlessness in the severe stage and current smoking habit.

We observed the distribution of lower oxygen saturation prevalent more among the Norwegian group (4.4%) compared to Russian (3.0%). The distribution of lower oxygen saturation is quite parallel with the Tromso study (2005/07) presenting the prevalence of decreased SpO<sub>2</sub> to be 4.9% among the subjects. Similarly, a cross-sectional population-based survey performed in Tromsø, Norway, in 2007-2008 showed the prevalence of SpO<sub>2</sub>  $\leq$ 95% as 6.3%.

The main reason for such difference in the Norwegian and Russian groups is due to a higher percentage of subjects in Norwegian group involving in the smoking habit (former and current smokers) compared to the Russian group ie, almost twice times higher rate in Norwegian group. In addition, the difference in health care system could be another possible reason for the difference in comorbidity among GP Populations in two countries. In Russia, usually, the patients with chronic diseases and low SpO<sub>2</sub> are treated by a specialist in the out patient departments (pulmonologists, cardiologist). Thus, the prevalence observed in Russian groups is underestimated or under-represented. However, the situation in Norway is inverse; GPs are responsible for treating chronically ill patients. The baseline characteristics in

our study had also shown the unhealthier group higher among Norwegian GP populations.

Further, the risk factors present with age accelerate lower oxygen saturation level. Ageing could be associated with physiological changes and increasing comorbidity. Consequently, it can be difficult to assess all confounding factors related to age in multivariable analyses (47).

As per this study, smoking was associated with low  $SpO_2$ . Smoking is associated with the development of emphysema, COPD, and chronic lung diseases which is responsible for lower oxygen saturation. Current smoking habit in men had shown a significant association with low  $SpO_2$  (27).

The prevalence of lower oxygen saturation was twice times more in male GP population compared to the female population in the study. The disparity in the distribution of risk factors such as co-morbidity, lifestyle pattern, and smoking habits can be the reason for this difference. The study showed that almost three-fourth of men were involved in smoking habits; almost twice times more than female GP populations. In addition, the presence of self-reported cardiac diseases and self-reported respiratory disease was common more among male compared to female subjects. Thus, it indicates that the male population attending general practitioners were unhealthier compared to female.

There was an association between BMI and lower oxygen saturation only in female groups. Correspondingly, the presence of COPD in female presented eight folds more risk of having lower oxygen saturation. Surprisingly, the study exhibited the risk of

having lower oxygen saturation among female with arterial hypertension as almost half that of the female with no arterial hypertension due to the unknown confounding factors.

Similarly, the male population of Russia showed almost half the risk of having lower oxygen saturation compared to Norwegian male. Likewise, in men, increase in pulse rate showed statistical significance with lower oxygen saturation. Also, the presence of self-reported breathlessness showed four times more risk of having lower oxygen saturation among the male population. The current smoking habit showed thrice times the risk of having lower oxygen saturation in the male GP populations.

A cross-sectional population-based survey performed in Tromsø, Norway, in 2007-2008, showed the similar pattern of result which showed with BMI, increased age, male gender, and smoking (p-value <0.001) as the predictor variables.

#### 4.3 Strength of the Study

- It is the comparative study showing the prevalence of lower oxygen saturation in Norway and Russia.
- This study tests the association between variables and lower oxygen saturation.
- It provides plans for advanced statistical analysis
- It represents a pilot project, trying to create a network of scientifically engaged general practitioners in Arkhangelsk and Murmansk regions in Russia to ensure their participation in more complicated and ambitious data collections in the future.

# 4.3 Limitation of the Study

- The study may not represent the overall situation throughout the world.
- Measurement error, recall bias, selection bias as explained above in methodological consideration parts.
- In general, Russian GP population are "healthier" than Norwegian GP population
  as most of the chronically ill patients in Russia are treated by the specialist only.
  Thus, the prevalence observed in Russian groups is the underestimation and under representative.

## 5. Conclusion

In conclusion, the lower oxygen was prevalent more in Northern Norway compared to Northwest Russia. Similarly, the proportion of lower oxygen saturation is present more among male groups compared to female groups. According to this study, lower oxygen saturation was related to gender, pulse rate, BMI, self-reported heart diseases, self-reported COPD, self-reported chronic and current smoking habit. Adjusting for confounders, a statistically significant predictor of lower oxygen saturation was self-reported cardiac disease, which was significant both in male and female groups. In men, self-reported breathlessness in severe stage, and current smoking habit showed statistically significant association with lower oxygen saturation. While in women, BMI and COPD were predictive factors associated with oxygen saturation.

## 6. Recommendation

Pulse oximetry is easy, safe, convenient and useful in risk assessment. It helps in providing some level of risk stratification and the findings can be used to evaluate further. Being a simple and valid screening test, the use of pulse oximetry in general practice is recommended.

Despite the wide potentials of pulse oximetry in primary care settings, there are only a few researches reported about the usage and application. Moreover, the information about low oxygen saturation and its association with mortality or morbidity in a general population is limited. Hence, it is also recommended to conduct more research on the application of pulse oximetry in nearby future.

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# **APPENDICES**

#### **Appendix I: Ethical Approval Letter**



Region: RFK sør-øst Saksbehandler: Giøril Bergva Telefon: 22845529

Vår dato:

Vår referanse: 2013/1273/REK sør-øst

Deres referanse

Deres dato: 25.06.2013

iato:

Vår referanse må oppgis ved alle henvendelser

Til Oleg Sidorenkov

2013/1273 Forekomst av og faktorer assosiert med lav surstoffmetning i en voksen populasjon i allmenn praksis, en sammenlignende studie i Norge og Russland

Forskningsansvarlig: Universitetet i Tromsø

Prosjektleder: Oleg Sidorenkov

Vi viser til søknad om forhåndsgodkjenning av ovennevnte forskningsprosjekt. Søknaden ble behandlet av Regional komité for medisinsk og helsefaglig forskningsetikk (REK sør-øst) i møtet 22.08.2013. Vurderingen er gjort med hjemmel i helseforskningsloven (hfl.) § 10, jf. forskningsetikklovens § 4.

#### Prosjektomtale

Prosjektet stiller følgende forskningsspørsmål: 1) Hvordan er surstoffsmetning målt med pulsoksymetri fordelt blant pasienter over 40 år i norsk og russisk allmennpraksis? 2) Hva er hyppigheten av lave verdier i forskjellige pasientgrupper, slik som pasienter med astma, KOLS og hjertesykdom, blant de som har tung pust uten kjent diagnose og blant antatt friske i Norge og Russland? Studien kan belyse i hvilken grad pasienter med lav surstoffmetning er diagnostert og behandlet for hjerte- og lungesykdom. Det vil dreie seg om 2.000 personer i Norge og 2.000 personer i Russland. De som deltar vil bi bedt om å utfylle et spørreskjema. Det vil også bli tatt målinger av høyde, vekt, omkrets rundt midje, samt surstoffmetning i kapillært blod. Helseopplysninger skal overføres til Arkhangelsk, Russland.

#### Vurdering

I søknaden bes det om fritak fra å innhente skriftlig samtykke. Deltagerne får et informasjonsskriv uten samtykkeerklæring, og utfylling av spørreskjemaet anses som tilstrekkelig samtykke. Begrunnelsen for ønsket om fritak fra skriftlig samtykke er at det ikke skal lagres personidentifiserbare data, og at det ikke skal foretas koblinger til andre datakilder. Derfor er det, ifølge prosjektleder, ikke hensiktsmessig å lagre samtykkeerklæringer påført navn.

Komiteen kan ikke se at det er vektige grunner, annet enn bekvemmelighetshensyn, til å fravike hovedregelen i helseforskningsloven § 13 om at samtykket skal være dokumenterbart, dvs. skriftlig. I dette tilfellet kan samtykke innhentes og lagres separat fra spørreskjema, som kan utfylles uten kjennetegn og mulighet for kobling til samtykkeerklæringene.

Komiteen legger merke til at spørreskjemaet er på engelsk, og ber om at dette oversettes til norsk.

I søknaden opplyses det om at datamaterialet skal avidentifiseres etter prosjektslutt. Komiteen gjør oppmerksom på at hovedregelen er at data skal anonymiseres eller slettes etter prosjektslutt. Er det behov for forlengelse av prosjektet, må prosjektendringssøknad sendes til REK.

På denne bakgrunn setter komiteen følgende vilkår for godkjenning av prosjektet:

- Det skal innhentes skriftlig samtykke fra deltagerne Spørreskjemaet skal oversettes til norsk

#### Vedtak

Med hjemmel i helseforskningsloven § 9 jf. 33 godkjenner komiteen at prosjektet gjennomføres under forutsetning av at ovennevnte vilkår oppfylles.

I tillegg til vilkår som fremgår av dette vedtaket, er godkjenningen gitt under forutsetning av at prosjektet gjennomføres slik det er beskrevet i søknad og protokoll, og de bestemmelser som følger av helseforskningsloven med forskrifter.

Tillatelsen gjelder til 31.12.2014. Av dokumentasjonshensyn skal opplysningene likevel bevares inntil 31.12.2019. Opplysningene skal lagres avidentifisert, dvs. atskilt i en nøkkel- og en opplysningsfil. Opplysningene skal deretter slettes eller anonymiseres, senest innen et halvt år fra denne dato.

Forskningsprosjektets data skal oppbevares forsvarlig, se personopplysningsforskriften kapittel 2, og Helsedirektoratets veileder for «Personvern og informasjonssikkerhet i forskningsprosjekter innenfor helse og omsorgssektoren».

Dersom det skal gjøres vesentlige endringer i prosjektet i forhold til de opplysninger som er gitt i søknaden, må prosjektleder sende endringsmelding til REK.

Prosjektet skal sende sluttmelding på eget skjema, senest et halvt år etter prosjektslutt.

#### Klageadgang

Du kan klage på komiteens vedtak, jf. forvaltningslovens § 28 flg. Klagen sendes til REK sør-øst D. Klagefristen er tre uker fra du mottar dette brevet. Dersom vedtaket opprettholdes av REK sør-øst D, sendes klagen videre til Den nasjonale forskningsetiske komité for medisin og helsefag for endelig vurdering.

Vi ber om at alle henvendelser sendes inn på korrekt skjema via vår saksportal: http://helseforskning.etikkom.no. Dersom det ikke finnes passende skjema kan henvendelsen rettes på e-post til: post@helseforskning.etikkom.no.

Vennligst oppgi vårt referansenummer i korrespondansen.

Med vennlig hilsen

Finn Wisløff Professor em. dr. med Leder

> Gjøril Bergva Rådgiver

Kopi til: postmottak@ub.uit.no

# Appendix II: Questionnaire

Oxygen Saturation in North-West Russia A study of patients aged 40 year or older in general practice	
Name of practice:	
Gender Man Woman	Age years
Do you have or have you had any of the following diseases?	? (tick "yes" or "no")
Lung diseases: Asthma COPD, emphysema, or chronic bronchitis Pulmonary tuberculosis Lung Cancer Other chronic lung disease	Yes No No If yes, which?
Cardiovascular diseases Arterial hypertension Angina pectoris Myocardial infarction Other heart disease	Yes No
Diabetes	
Respiratory infection going on now	
Other disease bothering you now	If yes, which?
Do you take medication daily for a heart or lung disease?	
Smoking habit (one tick)  I have never smoked I am an ex-smoker	I smoke now
How do you in general consider your health to be (one tick)  Very bad Bad Neither good or bad	Good Very good
Breathlessness (one tick)  - I only get breathless with strenuous exercice - I get short of breath when hurrying on level ground - On level ground, I walk slower than people of the sor have to stop for breath when walking at my ow - I stop for breath after walking about 100 yards or - I am too breathless to leave the house or I am bre	same age because of breathlessness, in pace. after a few minutes on level ground
When did you last time visit a doctor? (several tics are poss Within the last month Within	ible) n the last 3 months Within the last year

Measurements			
Weight	kg		
Height	cm		
Abdominal Circumference	cm		
Pulse oximetry		Pulse	
First measurement	%		per minute
Second measurement	%		per minute
Third measurement	%		per minute
			perminute

# **Appendix III: POMOR Project**

Since 1998 the NPUC has been accumulating an experience to administrate Norwegian-Russian joint projects and to act as a project manager and financial manager, contact link, communication link and arena for projects realization with Norwegian and Russian co-partners.

The topic of social interaction received increasing attention to public debates in both countries that time. The social sphere development was not in a focus of Russian politicians that time, meanwhile the transformation of economics and lifestyles resulting from the reforming altered the conditions shaping world social sphere. A number of factors influenced an appearance of a new international project in the field of social work between Arkhangelsk and Bodo in 1998:

- Transformation of social sphere in Russia and in Arkhangelsk region;
- Availability of funds for Norwegian-Russian cooperation: Cooperation
   Program with Central and Eastern Europe in the field of higher education and research, Barents Secretariat;
- Mutual interest on behalf of researchers and staff on a institutional level in both countries:
- Accumulated experience within international projects by Russian and Norwegian universities

The project started in 1998 and turned out with a long-term cooperation between Arkhangelsk and Bodo:

- Pomor I 1998-2001 Participants: Bodo University College, Faculty of social sciences
- Pomor II 2001-2002 Pomor State University, Faculty of social work
- Pomor III 2002-2006 Norwegian-Pomor University Centre

The Pomor I took as its point of departure the objectives:

- to accomplish a program of institution-building at the faculty of social work,
   Pomor State University, and the Norwegian-Pomor University Centre in
   Arkhangelsk;
- to accomplish a program for improving and qualifying social work students in Bodo and Arkhangelsk;
- to strengthen the international perspectives of both institutions and develop democratic and human values in social work education.

The intention of the first Pomor project was students and staff exchange, conferences on various themes connected to the field of social work, curriculum and study program development, video-conferences, translation and editing of literature, development of comparative research projects.

The second Pomor project was closely related to the penalty system, and developing methods and programs for social workers in the penitentiary system.

The third cooperation project - the Pomor III that started in 2002 - continued previous activities. Over the past four years the Pomor III indicated major activities of research, education, de-centralized courses, training programs, translation and publishing books and paper collections, thematic excursions, seminars and conferences on such contemporary problems as prevention work on criminality and substance abuse, prevention work with child protection and family welfare, violence against women, mediation, democratization of social institutions, penitentiary system and NGO-s.

The development of the Pomor III worked out with a variety of forums and disseminated in various ways. Discussions have taken place in working meetings, seminars and international conferences. Publications included books, collections of contributions and articles. In addition, a series of thematic manuals and handbooks examining a number of central issues within the project, have been released during the process.

In May 2004 Arkhangelsk welcomed over 80 people to the international conference "Prevention strategies in social work". The conference became the crucial meeting within the project by providing an opportunity for Russian and Norwegian researchers, teachers and practical social workers to present their views to an audience of prevention strategies from social work perspective. The conference obtained to better understanding of the role of prevention work and disseminated among practical workers and academicians those strategies that would enhance local services and social work and social policy education development.

During the period of 2002-2005 a series of seminars have been held in Arkhangelsk. The seminars provided practical social workers, administrators from social sphere and academicians with knowledge and new approaches on mediation, penalty system and empowerment.

By means of cooperation with Mediation Board in Trondheim and thanks to enthusiasm and experience of Iren Sorfjordmo, the leader of Konfliktradet in Trondheim, about 20 Russians - officers of social services from Arkhangelsk - have got Norwegian diplomas as mediators. The program that based on learning an experience of Mediation Boards in Norway seems to be essential and useful for Russian environment where social situation hardly could be called as a stable one, and where courts are overloaded by administrative offences.

Mikaela Bengtsson from Sweden did much for the project development in 2002-2003 in democratization and prevention within penitentiary system aspect. The Brattsbrytet program led by Mikaela involved prison officers from Arkhangelsk and Murmansk, who were to learn new approaches and to get todays' competence on a penalty system development and rehabilitation of inmates. Implementation of the program in several colonies and prisons in Arkhangelsk county was a success.

Helping people in solving life problems by means of empowerment has received increasing attention in the program "VINN" (Victory"). The project has been initiated jointly by Norwegian Ministry of Justice and educational centre KRUS from Oslo. Torunn Hojdahl and Marna Storksen have been the leaders for the TOT (training of

trainers) seminar in Arkhangelsk and shared knowledge with Russian participants on empowerment strategies.

The closing conference for the Pomor III was held in Bodo in June 2006. One of the most significant results of the conference and of the Pomor cooperation as well, as a sign of a really successful cooperation, was the establishing of a network where all members can continue to share ideas on relevant subjects, to cooperate directly person-to-person, to involve new members and to initiate new cooperation proposals. Such a network between Arkhangelsk and Bodo is a today's' reality.