Occupation, socioeconomic status and chronic obstructive respiratory diseases - The EpiLung study in Finland, Estonia and Sweden

Jalasto, Juuso

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Occupation, socioeconomic status and chronic obstructive respiratory diseases – The EpiLung study in Finland, Estonia and Sweden

Juuso Jalasto [a,*], Paul Lassmann-Klee [a], Christian Schyllert [b], Ritva Luukkonen [c], Mari Meren [d], Matz Larsson [e], Jaak Põlluste [d,1], Britt-Marie Sundblad [f], Ari Lindqvist [g], Steinar Krokstad [h], Hannu Kankaanranta [i,j,k], Paula Kauppi [g], Anssi Sovijärvi [a], Tari Haahtela [l], Helena Backman [b,m], Bo Lundbäck [i], Päivi Piirilä [a]

[a] *Department of Clinical Physiology, HUS Medical Diagnostic Center, Helsinki University Central Hospital and University of Helsinki, Helsinki, Finland*
[b] *Department of Public Health and Clinical Medicine, Section of Sustainable Health, The OLIN Unit, Umeå University, Umeå, Sweden*
[c] *Finnish Institute of Occupational Health, Helsinki, Finland*
[d] *National Institute for Health Development, Tallinn, Estonia and North Estonia Medical Centre Foundation, Tallinn, Estonia*
[e] *Clinical Health Promotion Centre, University of Lund, and Örebro University Hospital, Örebro, Sweden*
[f] *Institute of Environmental Medicine, Karolinska Institute, Stockholm, Sweden*
[g] *Department of Pulmonary Medicine, Heart and Lung Center, Helsinki University Hospital and Helsinki University, Helsinki, Finland*
[h] *HUNT Research Centre, Department of Public Health and Nursing, Norwegian University of Science and Technology, Norway*
[i] *Krefting Research Centre, Institute of Medicine, Department of Internal Medicine and Clinical Nutrition, University of Gothenburg, Gothenburg, Sweden*
[j] *Department of Respiratory Medicine, Seinäjoki Central Hospital, Seinäjoki, Finland*
[k] *Tampere University Respiratory Research Group, Faculty of Medicine and Health Technology, Tampere University, Tampere, Finland*
[l] *Skin and Allergy Hospital, Helsinki, Finland*
[m] *Department of Health Sciences, Luleå University of Technology, Luleå, Sweden*

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ABSTRACT

Objective: To study occupational groups and occupational exposure in association with chronic obstructive respiratory diseases.
Methods: In early 2000s, structured interviews on chronic respiratory diseases and measurements of lung function as well as fractional expiratory nitric oxide (F_{ENO}) were performed in adult random population samples of Finland, Sweden and Estonia. Occupations were categorized according to three classification systems. Occupational exposure to vapours, gases, dusts and fumes (VGDF) was assessed by a Job-Exposure Matrix (JEM). The data from the countries were combined.
Results: COPD, smoking and occupational exposure were most common in Estonia, while asthma and occupations requiring higher educational levels in Sweden and Finland. In an adjusted regression model, non-manual workers had a three-fold risk for physician-diagnosed asthma (OR 3.18, 95%CI 1.07–9.47) compared to professionals and executives, and the risk was two-fold for healthcare & social workers (OR 2.28, 95%CI 1.14–4.59) compared to administration and sales. An increased risk for physician-diagnosed COPD was seen in manual workers, regardless of classification system, but in contrast to asthma, the risk was mostly explained by smoking and less by occupational exposure to VGDF. For $F_{ENO,}$ no associations with occupation were observed.
Conclusions: In this multicenter study from Finland, Sweden and Estonia, COPD was consistently associated with manual occupations with high smoking prevalence, highlighting the need to control for tobacco smoking in studies on occupational associations. In contrast, asthma tended to associate with non-manual occupations requiring higher educational levels. The occupational associations with asthma were not driven by eosinophilic inflammation presented by increased F_{ENO}.

* Corresponding author.
E-mail address: juuso.jalasto@helsinki.fi (J. Jalasto).
[1] Deceased July 22, 2020.

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1. Introduction

Asthma and chronic obstructive pulmonary disease (COPD) cause significant burden to public healthcare. They are associated with many comorbidities, and especially COPD increases mortality [1]. They may also appear together, today commonly labelled asthma-COPD overlap. Occupational exposure may be important in the development of adult asthma or asthma symptoms [2–5]. Although smoking is the dominant cause of COPD, attention has also been given to occupational exposure to vapours, gases, dusts and fumes (VGDF) [4,6–10].

Abbreviations

ARC	Allergic rhinitis or conjunctivitis
CI	95% confidence interval
COPD	Chronic obstructive pulmonary disease
F_{ENO}	Fractional exhaled nitric oxide
FEV_1	Forced expiratory volume in 1 s
FinEsS	Finland, Estonia and Sweden Nordic Epidemiological Study on Obstructive Lung Diseases
ICS	Inhaled corticosteroid
ISCO88	International Standard Classification of Occupations (1988 edition)
IQR	Interquartile range
Nordic EpiLung	A multidisciplinary research approach on obstructive airway diseases: socio-economical and life course perspectivesA multidisciplinary research approach on obstructive airway diseases: socio-economical and life course perspectives
NYK	Nordic Classification of Occupations
OLIN	Obstructive Lung Diseases in Northern Sweden
OR	Odds ratio
SEI	Swedish Socioeconomic Index
SPT	Skin pick test
SSYK	Swedish Standard Classification of Occupations (2012 edition)
VGDF	Exposure to vapours, gases, dusts and fumes

The Nordic EpiLung study, concerning the socioeconomic differences in Nordic countries, started in 2017. It gathered data from the previous Northern European epidemiological study (FinEsS = Finland, Estonia and Sweden Study) on obstructive pulmonary disease [11]. In early 2000s, 1669 randomly selected subjects were interviewed and clinically examined with measurements of lung function and of fractional exhaled nitric oxide (F_{ENO}). For the present paper, the data was used to evaluate how occupation, socioeconomic status, and smoking relate to the occurrence of respiratory diseases and symptoms [12–15]. At the time of data collection, Estonia had just become independent and was socio-economically at a lower level than Finland (Helsinki) and Sweden (Örebro and Stockholm).

Assessment of occupational exposure has been diverse with postal questionnaire surveys, interviews on exposure at workplace [3] or using Job-Exposure Matrixes (JEM). The latter comprises lists of exposure to a variety of potentially harmful agents for selected occupational titles [16–18]. There is no consensus on the optimal way to evaluate occupational exposure in epidemiology [3,16]. Furthermore, the classification of occupations has also an effect on the observed associations of occupation with respiratory diagnoses and symptoms [4]. In Nordic countries, commonly used occupational classifications include Swedish Socioeconomic Classification (SEI, Socioeconomic Index), Nordic Classification of Occupations (NYK) based on the International Standard Classification of Occupations (ISCO) and Swedish Standard Classification of Occupations (SSYK).

Fraction of exhaled nitric oxide (F_{ENO}) is used to assess bronchial eosinophilic inflammation [19,20]. In the recent Nordic EpiLung-study [21], we found lower F_{ENO} levels in Estonia, compared to Finland and Sweden, indicating an east-west disparity in the prevalence of eosinophilic inflammation. The asthma risk was increased in Helsinki, Narva, and Stockholm, compared to Saaremaa in Estonia.

In the present study, we asked whether occupation or socioeconomic status, assessed by job titles, associate with obstructive respiratory diseases and symptoms as well as indices of eosinophilic inflammation in the three countries.

2. Material and methods

The respiratory data originate from the FinEsS Study of Finland, Estonia and Sweden with five participating research centres (Supplementary, Fig. 1). They performed similar questionnaire surveys and clinical examinations of random adult cohorts.

2.1. The study cohort (FinEsS, Nordic EpiLung)

The FinEsS Study was started in 1995 to study the prevalence and symptoms of obstructive pulmonary disease in Finland, Estonia and Sweden [22–24]. The study began as a questionnaire survey posted to 8000 subjects in Stockholm, Örebro and Helsinki each, to 5519 subjects in Narva and to 5432 in Saaremaa. Cohorts in each research center were formed by randomization into 10-year-age cohorts. The postal questionnaire was based on the OLIN (Obstructive Lung Diseases in Northern Sweden) research project [11,25], which was developed mainly from the British Medical Research Council [26] and US Tucson [27] questionnaires.

The study continued in the early 2000s with structured interviews in 2658 randomly selected responders from the five centres. Of them 1669 were randomized for lung function testing including F_{ENO} measurements. Finally, 1498 subjects, aged 20–60 years with valid F_{ENO} measurements were included in the study cohort [21]. In 2017, the Nordic EpiLung study commenced in Nordic countries to find out how socio-economic differences affect chronic obstructive pulmonary diseases.

2.2. Clinical examinations

Structured interview. The structured interview and clinical tests were conducted in 1997–2003. The interview included 162 questions about respiratory diseases, medication, and risk factors for asthma and COPD. The interview, based on the former postal questionnaire, with some modifications, has been used in several Nordic studies [28–31]. The questions used in the present study were the following.

Allergic rhinitis or conjunctivitis (ARC). "Have you had hay fever (allergic rhinitis) or allergic eye inflammation?"

Asthma diagnosed by a physician. "Have you been diagnosed with asthma by a physician?"

Asthma symptoms. "Have you had any symptoms of asthma during the last 12 months?"

Asthma medication. "Have you used any asthma medicines in the last 12 months?" Furthermore, those who answered "yes" were asked about certain asthma medications.

COPD diagnosed by a physician. "Have you been diagnosed with chronic bronchitis or emphysema by a physician?" Synonym for COPD at the time [32].

Chronic cough or sputum. "Have you had longstanding cough during the last year?" or "Do you usually have phlegm when coughing or do you have phlegm on your chest, which is difficult to bring up?"

Inhaled corticosteroids (ICS). "Have you used inhaled corticosteroids during the last 12 months?"

Smoking. "Do you smoke?" Subjects who answered "yes" were classified as current smokers and "no" as not current smokers.

Pack years were calculated from a question of "How many cigarettes

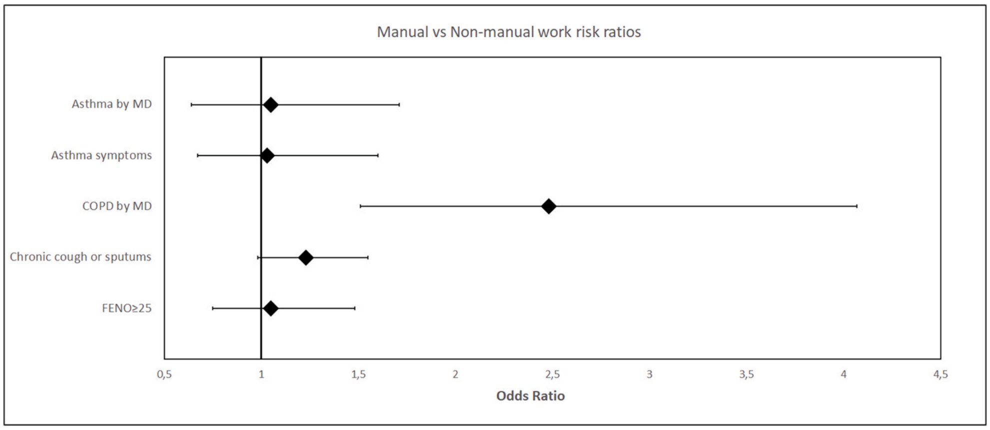

Fig. 1. The significantly increased risk for physician diagnosed COPD in Manual Workers (Industry and Service in SEI classification) compared with Non-manual Workers as a reference groups (combination of Professionals and Executives high, Non-Manual Workers intermediate and Non-Manual Workers low in SEI classification). A forest plot with values acquired from multinomial regression analysis.

per day have you been smoking on an average since you started smoking?" with options of "1–4, 5–14, 14–24 or >24". Similar questions were asked about cigars and pipe smoking. Participants who were smokers or ex-smokers were also asked at what age they began or stopped smoking. The pack year values obtained from this were then divided into four categories. Further details can be found in the statistics section.

2.3. Other definitions

Occupational exposure to vapours, gases, dusts and fumes (*VGDF*) was used both as a value acquired by summation from 4 separate Job-Exposure Matrix (JEM) components which was used to calculate a mean value for each group (*VGDF mean*), and as a cut-off variable (*any VGDF*). When the sum of the 4 VGDF components was least 1, the participant was considered having *any VGDF*. The component values were obtained from the list of occupations and have been explained earlier [5,7]. Determinants of this variable are further detailed in the supplementary section (Supplementary, Fig. 2a and b).

Atopy is defined as a positive result (wheal diameter ≥ 3 mm) caused by any common allergen in the skin prick test (SPT).

FENO ≥ 25 is defined as the group having standardized F_{ENO} (ppb) value of 25 ppb or higher. This is recommended as a cut-off value for a mild inflammation in risk analyses [19].

FEV_1% was acquired from the spirometry results [33].

2.4. Spirometry and F_{ENO} measurements

Different spirometers were used in the participating centres (in Helsinki SensorMedix Vmax22; in Stockholm, Ohio spirometer; in Örebro, Volugraph 2000 and Vitalograph; in Narva and Saaremaa,

Table 1
Subject characteristics, respiratory diseases, symptoms, occupational exposure, and smoking.

	All	Sweden	Finland	Estonia	P	Sex		p
						Female	Male	
n	*1498*	*570*	*295*	*633*		*824*	*674*	
Age (y)	41 (18)	41 (17)	42 (18)	41 (20)	0.734	41 (18)	**42** (19)	0.226
BMI categorized (kg/m^2)					**0.001**			< **0.001**
<25 (%)	51	**56**	49	47		**54**	47	
25.0–29.9 (%)	35	34	**36**	**36**		30	**41**	
≥30 (%)	14	10	15	**17**		**16**	12	
FEV_1 (l)	3.34 (1.14)	3.32 (1.10)	3.24 (1.27)	**3.45** (1.14)	**0.001**	3.00 (0.86)	**3.98** (1.09)	< **0.001**
FEV_1 (%)	96 (18.3)	92 (18)	94 (15)	**100** (18)	< **0.001**	**97** (18.6)	95 (18.1)	**0.042**
F_{ENO} (ppb)	14.0 (10.5)	**15.5** (9.3)	15.4 (13.7)	12.5 (9.6)	< **0.001**	13.6 (10.1)	**14.6** (10.8)	0.643
Skin prick test (SPT) (%)	36	34[a]	**49**	31	< **0.001**	35	**36**	0.643
Allergic rhinitis (ARC) (%)	32	37	**40**	24	< **0.001**	**37**	27	< **0.001**
Asthma diagnosed by MD (%)	6	**9**	7	4	**0.001**	7	7	0.481
Asthma symptoms last year (%)	8	11	**13**	4	< **0.001**	**9**	7	0.165
Inhaled corticosteroid use (ICS) (%)	4	**6**	5	1	< **0.001**	**4**	3	0.692
Currently smoking (%)	31	24	34	**37**	< **0.001**	26	**37**	< **0.001**
Any VGDF (%)	44	35	31	**59**	< **0.001**	35	**55**	< **0.001**
COPD diagnosed by MD (%)	7	2	3	**13**	< **0.001**	**8**	5	0.079
Chronic cough or Sputum (%)	51	37	55	**61**	< **0.001**	**52**	50	0.442

Age, FEV1 (l), FEV1 (%) and F_{ENO} are median values with Interquartile range (IQR).
The highest occurrence of each value is bolded.
BMI Body-mass index; *FEV1* Forced expiratory volume in 1 s (liters/percent); *F_{ENO}* Fraction of exhaled nitric oxide; *MD* Doctor of Medicine; *VGDF* Vapours, gas, dusts and fumes; COPD Chronic obstructive pulmonary disease.
[a] Lower amount skin prick test allergens were tested in Sweden.

Vicatest). We used only the values of forced expiratory volume in 1 s (FEV_1) (Table 1), as the values of forced vital capacity (FVC) were not available from Estonia and Örebro in Sweden [34].

F_{ENO} was measured according to the ERS guidelines [35]. All participating centres employed a chemiluminescent nitric oxide (NO) analyzer (Sievers 270B, Boulder,Co, USA). In each centre, a standardization method was used to obtain F_{ENO} to correspond the same expiratory flow level. F_{ENO} flow at 50 m/s was chosen as the standard flow [35, 36].

2.5. Skin prick tests

Skin prick tests (SPT) were used to determine atopic disposition, which was defined as having at least one positive test result (skin wheal ≥3 mm) caused by a common allergen (15 allergens were tested in Finland and Estonia, 10 in Sweden). The test method and allergens used have been described previously [21].

Classifications of occupation by the current title.

Three different classification systems were used and compared to the respiratory diseases and symptoms. These classifications were the Swedish Socio-economic Index (SEI) [37] Nordic Classification of Occupations (NYK) [38] and ISCO88 [39]. Their use and combinations are further explained in the Supplemental section (Supplementary, Fig. 3a–c).

2.6. Statistics

Multivariable logistic regression modelling was performed to calculate odds ratios (OR) with 95% confidence intervals (95%CI) for respiratory diseases and symptoms in association with the occupational categories according to the three classification systems (SEI, NYK and ISCO88). A separate model was estimated to calculate OR and 95%CI for any VGDF. The regression models were adjusted for age, atopy, sex and pack years. Reference categories were as follows: Professionals and Executives (high) for SEI, Administration and Sales for NYK, Professionals for ISCO88 and no exposure for any VGDF.

F_{ENO} data consisted of both continuous and categorical variables. Kruskal–Wallis and Wilcoxon's rank sum test were used to test the continuous variables (age, FEV1, F_{ENO}). For the categorical variables, the χ^2 test was applied. Significance was set at $p < 0.05$ for all tests.

To calculate the pack years, a yearly smoking amount in cigarette packs was evaluated. 1–4 cigarettes per day was considered as 1/3 of a pack, 5–14 as 2/3 of pack, 15–24 as a single cigarette pack and >24 as 4/3 of a pack. One cigar was equivalent to four cigarettes and 25 g of pipe tobacco weekly 50 cigarettes per week. Smoking parameters were summed to get daily amount of cigarette packs for an average year, which was multiplied by the years of smoking. The individual pack year values were then categorized withing 4 categories: None, < 10 pack years, 10-<20 pack years and ≥20 pack years to be used in the multinomial regression analysis.

All analyses were carried out using IBM SPSS Statistics version 25 (IBM Corp, New York, NY, USA).

3. Results

Subject characteristics are given in Table 1. Allergic rhinitis, atopic disposition, asthma and asthma symptoms were much more common in Sweden and Finland than in Estonia, while COPD, smoking and occupational exposure were more common in Estonia. Allergic rhinitis was more prevalent in women.

Manual labor was more common in Estonia than in Sweden or Finland (Table 2). Finland had the highest prevalence of non-manual occupation titles.

The prevalence of current smoking in all subjects was 31% and peaked to 40–50% in manual workers in Industry (SEI), Transportation and Communications (NYK) and Plant and Machine Operators and Assemblers (ISCO88) (Supplementary Table 1). The amount of pack years was also higher in manual than in non-manual work. F_{ENO} was significantly lower in the current smoking group. Prevalence of atopic disposition (positive SPT) did not differ between occupations.

Prevalence of asthma symptoms and asthma diagnosed by a physician were the highest in occupations classified as non-manual workers (SEI), healthcare & social work (NYK) and Legislation as well as in senior officials and managers (ISCO88) (Supplementary Table 2). COPD was most common in occupations classified as manual workers, the highest prevalence being in manual workers in Industry (SEI), Agriculture (NYK) and workers in Skilled Agricultural and Fishery (ISCO88).

Occupational exposure was more common in older age groups than in younger age groups (Supplementary Table 3). In addition, socioeconomic differences between age groups were more pronounced in men than in women (Supplementary Table 3).

In the adjusted multivariable logistic regression model (Table 3), there was a significant risk for asthma in the non-manual workers

Table 2
Distribution of occupations (%) in Sweden, Finland and Estonia according to the three classifications.

	All	Sweden	Finland	Estonia	
SEI (*n*)	*1339*	*524*	*240*	*575*	
Professionals and Executives (high)	11	10	**18**	8	
Non-Manual Workers (intermediate)	20	25	**30**	12	
Non-Manual Workers (low)	18	18	**21**	15	
Manual Workers Service	24	**30**	19	21	
Manual Workers Industry	26	15	8	**44**	
Self-employed	2	2	**5**	0	
P					< **0.001**
NYK (*n*)	*1426*	*542*	*278*	*606*	
Science & arts	19	22	**25**	13	
Health care & social workers	13	**19**	16	5	
Administration and Sales	27	30	**38**	20	
Agriculture	4	2	0	**8**	
Transportation and Communication	7	6	4	**9**	
Manufacturing	20	14	10	**31**	
Service	10	7	7	**14**	
P					< **0.001**
ISCO88 Major Groups (*n*)	*1394*	*510*	*277*	*607*	
Legislation, Senior Officials, Managers	4	**5**	1	4	
Professionals	17	19	**22**	13	
Technicians and Associate Professionals	21	23	**37**	12	
Clerks	9	**12**	8	7	
Service, Shop and Market Sales Workers	17	**20**	18	14	
Skilled Agricultural and Fishery Workers	3	1	0	**5**	
Craft and Related Trades Workers	13	9	6	**20**	
Plant, Machine Operators and Assemblers	10	7	5	**14**	
Elementary Occupations	7	5	4	**11**	
P					< **0.001**

The highest prevalence of occupational category in the three countries is bolded. *SEI* Swedish socioeconomic-index; *NYK* Nordic classification of occupations; *ISCO88* International standard classification of occupations (1988 edition).

Table 3
Multivariable risk analysis of diseases, symptoms and elevated F_{ENO} (FENO≥25 ppb).

	Asthma by MD			Asthma symptoms			COPD by MD			Chr. cough or Sputum			FENO≥25		
	OR	(95%	CI)	OR	(95%	CI)	OR	(95%	CI)	OR	(95%	CI)	OR	(95%	CI)
SEI															
Professionals and Executives (high)	1	ref		1	ref		1	ref		1	ref		1	ref	
Non-Manual Workers (intermediate)	**3.18**	**(1.07**	**9.47)**	1.08	(0.50	2.31)	0.86	(0.29	2.61)	1.07	(0.69	1.65)	0.64	(0.36	1.15)
Non-Manual Workers (low)	1.11	(0.33	3.81)	0.57	(0.24	1.35)	1.01	(0.33	3.04)	0.97	(0.62	1.52)	**0.47**	**(0.25**	**0.88)**
Manual Workers Service	2.46	(0.81	7.41)	1.25	(0.60	2.62)	1.43	(0.51	3.99)	1.11	(0.72	1.70)	0.76	(0.43	1.33)
Manual Workers Industry	1.55	(0.50	4.80)	0.55	(0.24	1.24)	**3.51**	**(1.33**	**9.25)**	1.41	(0.93	2.15)	0.63	(0.36	1.09)
Self-employed	2.60	(0.43	15.7)	0.88	(0.17	4.47)	X[a]	(X[a]	X[a])	0.67	(0.25	1.79)	1.47	(0.50	4.34)
NYK															
Science & arts	1.09	(0.53	2.24)	1.16	(0.61	2.22)	1.12	(0.52	2.44)	1.04	(0.74	1.45)	0.95	(0.60	1.52)
Healthcare & social workers	**2.28**	**(1.14**	**4.59)**	2.24	**(1.18**	**4.24)**	0.22	(0.05	0.98)	1.05	(0.72	1.54)	1.18	(0.69	2.02)
Administration and Sales	1	ref		1	ref		1	ref		1	ref		1	ref	
Agriculture	0.67	(0.15	2.99)	0.27	(0.04	2.08)	**2.75**	**(1.01**	**7.53)**	1.70	(0.99	3.26)	0.33	(0.10	1.10)
Transportation and Communication	0.72	(0.23	2.22)	0.59	(0.20	1.81)	2.44	(0.98	6.09)	0.92	(0.57	1.48)	1.41	(0.77	2.59)
Manufacturing	0.78	(0.35	1.72)	0.85	(0.42	1.74)	**2.97**	**(1.50**	**5.85)**	**1.43**	**(1.02**	**2.00)**	0.78	(0.48	1.26)
Service	1.40	(0.61	3.23)	**2.39**	**(1.18**	**4.62)**	**2.23**	**(1.03**	**4.82)**	**1.80**	**(1.19**	**2.73)**	1.26	(0.72	2.19)
ISCO88 Major Groups															
Legislation, Senior officials, Managers	2.42	(0.78	7.45)	1.56	(0.53	4.55)	0.50	(0.06	4.04)	1.59	(0.84	2.99)	0.46	(0.15	1.37)
Professionals	1	ref		1	ref		1	ref		1	ref		1	ref	
Technicians and Associate Professionals	1.33	(0.60	2.93)	1.09	(0.56	2.14)	1.18	(0.48	2.94)	0.99	(0.68	1.44)	0.85	(0.50	1.43)
Clerks	1.09	(0.39	3.09)	0.89	(0.37	2.16)	0.88	(0.29	2.71)	0.86	(0.54	1.37)	0.77	(0.39	1.55)
Service, Shop and Market Sales Workers	1.37	(0.60	3.15)	1.20	(0.60	2.40)	0.69	(0.25	1.90)	1.24	(0.84	1.83)	1.50	(0.89	2.51)
Skilled Agricultural and Fishery Workers	1.13	(0.24	5.42)	X[a]	(X[a]	X[a])	**5.18**	**(1.69**	**15.9)**	1.52	(0.74	3.12)	0.51	(0.15	1.79)
Craft and Related Trades Workers	0.85	(0.31	2.30)	0.81	(0.35	1.88)	**3.71**	**(1.56**	**8.80)**	1.37	(0.90	2.09)	0.88	(0.49	1.59)
Plant, Machine Operators and Assemblers	0.68	(0.20	2.26)	0.55	(0.19	1.60)	**3.76**	**(1.46**	**9.71)**	1.29	(0.81	2.06)	1.14	(0.61	2.12)
Elementary Occupations	2.12	(0.84	5.37)	1.71	(0.76	3.87)	**4.32**	**(1.77**	**10.5)**	1.29	(0.78	2.13)	0.51	(0.23	1.17)
Any VGDF															
No exposure	1	ref		1	ref		1	ref		1	ref		1	ref	
Exposure	1.11	(0.70	1.77)	1.09	(0.72	1.65)	**1.70**	**(1.08**	**2.66)**	**1.37**	**(1.09**	**1.71)**	0.96	(0.70	1.31)
Any VGDF (not current smoker)															
No exposure	1	ref		1	ref		1	ref		1	ref		1	ref	
Exposure	1.35	(0.80	2.27)	1.01	(0.63	1.63)	1.58	(0.90	2.78)	1.13	(0.86	1.48)	1.14	(0.81	1.61)
Any VGDF (current smoker)															
No exposure	1	ref		1	ref		1	ref		1	ref		1	ref	
Exposure	0.68	(0.24	1.99)	1.87	(0.73	4.77)	1.84	(0.83	4.08)	**1.75**	**(1.14**	**2.71)**	0.58	(0.26	1.30)

The calculations were adjusted for **age, atopy, pack years and sex**. Any VGDF in groups not current smoker and current smoker was adjusted similarly. Statistically significant results are bolded.
Chr. Chronic; *MD* Doctor of medicine; *VGDF* Vapours, gas, dusts and fumes; *COPD* Chronic obstructive pulmonary disease*; FENO* Fraction of exhaled nitric oxide; *Ref* reference value; *OR* Odds ratio; *CI* Confidence interval *SEI* Swedish socioeconomic index; *NYK* Nordic classification of occupations; *ISCO88* International standard classification of occupations (1988 edition).
[a] Results that could not be calculated due to small group sizes are marked with an X.

compared to professionals and executives in the SEI classification. Healthcare & social work and service work were shown to have a higher risk of asthma symptoms. There was no significant risk group for asthma or asthma symptoms in the ISCO88 classification.

A risk for COPD was seen in the multivariable model, adjusted for age, atopy, sex and pack years, with the manual labor groups in all three classification systems (SEI, NYK, ISCO88) (Table 3). Healthcare & social workers seemed to be protected from COPD (NYK). Fig. 1 shows the major risk for COPD, but not for other conditions, in the manual workers compared with combined non-manual workers in the SEI classification.

For the eosinophilic inflammation marker, $F_{ENO,}$ the analysis did not reveal any significant risk group for elevated values. The lowest F_{ENO} values among the current smokers were found in Estonia compared to Finland and Sweden ($p < 0.001$), although the reported pack years were the lowest in Estonia ($p = 0.006$) (Supplementary Figure 4-5).

4. Discussion

As several occupational classifications are used in Nordic countries, we chose to use three of them to get comprehensive analyses of the association between chronic lung diseases and occupational or socioeconomic status of the participants. The classifications differed from each other in some aspects. The Swedish Socioeconomic Index (SEI) and Nordic Yrkesklassificering (NYK) were superior for identifying associations between occupation and obstructive respiratory diseases and symptoms.

The results showed that all the three classifications associated significantly with COPD in the manual workers. They also smoked more and were more exposed to vapours, gases, dusts or fumes (VGDF) at work. Smoking was by far the most important risk factor, but occupational exposure also increased slightly the risk for chronic cough and sputum production. In an earlier study of a Finnish population, COPD was associated with occupational exposure yielding an additive effect of smoking [5]. The present results are in line with that in terms of COPD and symptoms, but our study did not find any association between occupational exposure and asthma. In fact, the non-manual workers, not much exposed at work, had increased risk for asthma and asthma symptoms in two of the occupational classifications. Our results are similar with previous observations indicating the increased risk for asthma in healthcare & social workers [40]. Regarding age groups and differences in socioeconomic status between them and sexes, occupational exposure was more common in older than younger age groups and socioeconomic differences between the age groups were greater in men than in women. These both are reflective for COPD being more common in men than in women and changes in occupational structure in Nordic countries with the shift from manual occupations to non-manual during the latter part of 20th century.

Elevated F_{ENO} levels are signs of eosinophilic inflammation [19] and were associated with occupations requiring higher education and with little occupational exposure. The F_{ENO} levels, the prevalence of allergic rhinitis and of atopic disposition were the lowest in Estonia, where manual professions and occupations not requiring high education were most common. F_{ENO} levels were the lowest in Estonian noncurrent smokers. Smoking is well known to lower F_{ENO} levels [19–21], and this was seen also here in all three countries. Estonian current smokers had the lowest F_{ENO} levels but, surprisingly, the Estonians reported the lowest pack years.

In earlier studies, the east-west disparity has been apparent in increase of sensitization to common allergens and allergic diseases. Most of the reports are from children, but the difference has pertained in adult populations as well [21,41,42], and also the level and pattern of allergic sensitization among adults is different in Estonia compared with Finland and Sweden, storage mites and cockroach being the most common sensitizers in Estonia (43). In earlier studies, the east-west disparity has been apparent in more common sensitization to common allergens and allergic diseases, including asthma in westernized countries. The disparity has been associated with reduced exposure to biodiverse natural environment with rich microbiota in westernized countries [21,41, 43–45]. The participants from Finland and Sweden had higher levels of F_{ENO} and had more often atopic disposition than those from Estonia. Estonians from Saaremaa and Narva were less likely to show mild eosinophilic inflammation, which here was suggested by lower F_{ENO} levels in both noncurrent and current smoking Estonians compared to Finns and Swedes. Ambient air pollution is a major global health risk, but its effect on the prevalence of allergies and asthma is controversial [46].

Our study did not indicate any association of occupational exposure to eosinophilic inflammation. Consequently, we suggest that differences in lifestyle and environmental changes (urbanization) are more important determinants than occupation explaining disposition to atopy, allergic diseases and asthma at population level. However, in specific working environments exposure to allergens or irritants may cause occupational or work-related asthma and rhinitis.

4.1. Strengths and limitations

The present material is large and includes data from three countries and five study centres. The participants represent variable socioeconomic status, lifestyle, environment and east-west location. The Estonians were recruited shortly after independency of the country. We also used the same structured interview for each center, and the cohorts were selected similarly randomized and stratified for age and sex. Therefore, the material is ideal for comparison of the risk factors of chronic respiratory diseases and symptoms.

One limitation was that the occupational exposure was not inquired from the subjects but assessed from the reported occupations with JEM-based occupational exposure levels. However, in earlier applications the used exposure assessment has given valid results [5]. The association with F_{ENO} and exposure in the occupational categories were logical although F_{ENO} levels remained usually low. ISCO88 was approximated from NYK and SEI as it was not used in the original FinEsS-study. It should also be noted that the classifications were done based on the title of the occupation. This approach does not always reflect the actual working conditions, which may differ with the same occupational title. There is also another problem in the assignment of occupation category from the current occupation title, as it does not take in to account the healthy worker effect [47] in which people change their occupation due to symptoms that have begun during their work. This effect could in some part explain the poor correlation between occupational exposure and asthma diagnose and symptoms. Further, the use of self-reported COPD diagnoses by a physician instead of spirometry-verified COPD is another weakness due to the known under-diagnosis and misclassification of COPD.

5. Conclusions

In summary, the three occupational classifications gave similar results on associations with COPD but non-uniform ones with asthma. COPD was associated with manual labour where the smoking prevalence was high. This combination was especially seen in Estonia, where also COPD was more common. In contrast to this asthma was more common in non-manual occupations requiring higher educational levels which were more common in Finland and Sweden.

Occupational exposure to vapours, gases, dusts or fumes was associated with symptoms common in bronchitis, but not with asthma. The F_{ENO} levels were higher in Sweden and Finland than in Estonia, and tended to be higher in non-manual occupations requiring high education, but significant occupational associations were lacking. Thus, occupational associations with asthma seem at least not mainly be driven by eosinophilic inflammation with elevated F_{ENO} levels, although lower F_{ENO} levels suggested on more favorable biodiversity in Estonia compared to Finland and Sweden. The results further highlight the importance of controlling for tobacco smoking in studies on occupational exposures and obstructive respiratory diseases, especially regarding COPD.

Ethics approval

The study was approved by the ethics committee of the Department of Medicine, Helsinki University Central Hospital and Tallinn Ethics Committee, Estonia and Swedish Ethical Review Authority. The subjects filled in a written informed consent form.

Consent for publication

Not applicable.

Data availability

The datasets used are not publicly available due to the laws of the study countries.

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CRediT authorship contribution statement

Juuso Jalasto: Formal analysis, Writing – original draft, Writing – review & editing, Visualization. **Paul Lassmann-Klee:** Formal analysis, Writing – original draft. **Christian Schyllert:** Writing – original draft. **Ritva Luukkonen:** Writing – original draft, Writing – review & editing. **Mari Meren:** Investigation. **Matz Larsson:** Investigation. **Jaak Põlluste:** Investigation. **Britt-Marie Sundblad:** Investigation. **Ari Lindqvist:** Resources, Writing – review & editing. **Steinar Krokstad:** Writing – original draft, Writing – review & editing. **Hannu Kankaanranta:** Writing – original draft, Writing – review & editing. **Paula Kauppi:** Writing – original draft, Writing – review & editing. **Anssi Sovijärvi:** Conceptualization, Writing – review & editing, Resources.

Tari Haahtela: Writing – original draft. **Helena Backman:** Writing – original draft. **Bo Lundbäck:** Conceptualization, Writing – original draft. **Päivi Piirilä:** Conceptualization, Supervision.

Declaration of competing interest

The authors declare that they have no competing interests.

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Appendix A. Supplementary data

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