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Occupation and subcategories of asthma: a population-based incident case–control study

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ABSTRACT

Background We hypothesised that occupational exposures differently affect subtypes of adult-onset asthma.

Objective We investigated potential relations between occupation and three subtypes of adult asthma, namely atopic asthma, non-atopic asthma and asthma–COPD overlap syndrome (ACOS).

Methods This is a population-based case–control study of incident asthma among working-age adults living in Pirkanmaa Hospital District in Southern Finland. The determinant of interest was occupation at the time of diagnosis of asthma or the job that the subject had quit due to respiratory symptoms. Asthma was divided into three mutually exclusive subtypes on the basis of any positive IgE antibody (atopic and non-atopic asthma) and presence of persistent airways obstruction in spirometry (ACOS). We applied unconditional logistic regression analysis to estimate adjusted OR (aOR), taking into account gender, age and smoking.

Results The following occupational groups showed significantly increased risk of atopic asthma: chemical industry workers (aOR 15.76, 95% CI 2.64 to 94.12), bakers and food processors (aOR 4.69, 95% CI 1.18 to 18.69), waiters (aOR 4.67, 95% CI 1.40 to 15.56) and those unemployed (aOR 3.06, 95% CI 1.52 to 6.17). The following occupations showed clearly increased risk of non-atopic asthma: metal workers (aOR 8.37, 95% CI 3.77 to 18.59) and farmers and other agricultural workers (aOR 2.36, 95% CI 1.10 to 5.06). Some occupational groups showed statistically significantly increased OR of ACOS: electrical and electronic production workers (aOR 30.6, 95% CI 6.10 to 153.35), fur and leather workers (aOR 16.41, 95% CI 1.25 to 215.85) and those retired (aOR 5.55, 95% CI 1.63 to 18.97).

Conclusions Our results show that different occupations are associated with different subtypes of adult-onset asthma.

Key messages

What is already known about this subject?
- Previous epidemiological studies have shown that among the working population an individual's occupation or job category is related to risk of asthma.
- Studies on the association between occupational exposures and subcategories of asthma have not addressed this more recent subcategorisation of adult-onset asthma.

What are the new findings?
- Occupations that were associated with risk of three subtypes of adult asthma, that is, atopic and non-atopic asthma and asthma–COPD overlap syndrome, differed from each other.
- Many significant relations between occupation and subtypes of asthma were identified mainly among men, while others were identified predominantly among women.

How might this impact on policy or clinical practice in the foreseeable future?
- Clinicians should take these relations between different occupations and three subtypes of adult-onset asthma into account in their clinical practice, for example in the diagnostics and management of asthma.

BACKGROUND

Previous epidemiological studies have shown that among the working population an individual's occupation or job category is related to risk of asthma.[1–5] This is likely explained by various occupational exposures with different types of asthmogenic compounds.[6 7] Selection from and to the workforce according to diseases and their symptoms or lack of such diseases, often denoted as the healthy worker effect, may contribute to occupation-specific differences.[8] In epidemiological studies the main emphasis has previously been on identification of the causal agents. A complementary approach is to elaborate potentially different underlying mechanisms responsible for occupation-related asthma. Based on a literature search that we conducted, there were no previous studies which had considered subtypes of asthma in the context of a study on a large spectrum of occupations and the risk of subtypes of adult-onset asthma.

We reported in 2018, from our population-based study of incident asthma among adults aged 21–63 years old in a geographically defined area in Southern Finland, that is, the Finnish Environment and Asthma Study (FEAS),[9] that more than 6% actually had asthma–chronic obstructive pulmonary disease (COPD) overlap syndrome (ACOS), which is an obstructive lung disease that has been identified and characterised recently.[10–12] ACOS cases showed less often any positive allergy findings in skin prick tests and in Phadiatop analyses than asthma-only cases.[11] In this study, we analysed the

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Table 1 Characteristics of the current study population, the Finnish Environment and Asthma Study 1997–2000

Characteristics	Atopic asthma cases (n=156)	Non-atopic asthma cases (n=187)	ACOS cases (n=25)	Controls (n=932)
Age, median (Q1, Q3)	32.5 (25.5, 45.0)	48.0 (39.0, 55.0)	53.0 (48.0, 60.0)	43.0 (34.0, 52.0)
Gender, n (%)				
Male	57 (36.5)	54 (28.9)	17 (68.0)	438 (47.0)
Female	99 (63.5)	133 (71.1)	8 (32.0)	494 (53.0)
Education, n (%)*				
No vocational schooling	23 (14.7)	42 (22.7)	10 (40.0)	154 (16.6)
Vocational course	17 (10.9)	36 (19.5)	8 (32.0)	104 (11.2)
Vocational institution	57 (36.5)	45 (24.3)	1 (4.0)	271 (29.2)
College level	36 (23.1)	43 (23.2)	3 (12.0)	261 (28.1)
University or corresponding	23 (14.7)	19 (10.3)	3 (12.0)	138 (14.9)
Smoking, n (%)†				
Never	79 (50.6)	93 (50.3)	2 (8.0)	485 (52.2)
Ex-smoker	30 (19.2)	47 (25.4)	7 (28.0)	205 (22.0)
Current smoker	47 (30.1)	45 (24.3)	16 (64.0)	240 (25.8)
Pets indoors sometimes, n (%)	121 (77.6)	125 (66.8)	15 (60.0)	616 (66.1)
Indoor mould exposure at work or at home, n (%)‡	36 (23.1)	38 (20.3)	6 (24.0)	193 (20.7)
Secondhand smoke exposure, n (%)				
Past 12 months exposure§	31 (19.9)	40 (21.4)	8 (32.0)	166 (17.8)
Cumulative lifetime exposure§¶				
No exposure	60 (39.7)	65 (36.5)	12 (52.2)	359 (40.3)
<100 cigarette-years	30 (19.9)	39 (21.9)	3 (13.0)	206 (23.2)
≥100 cigarette-years	61 (40.4)	74 (41.6)	8 (34.8)	325 (36.5)

*Education missing for 4 controls and 2 cases of non-atopic asthma.
†Smoking missing for 2 controls and 2 cases of non-atopic asthma.
‡Mould exposure missing (answered 'do not know') for 1 control.
§Combined home and workplace exposure.
¶Cumulative lifetime secondhand smoke exposure missing for 42 controls, for 19 cases of non-atopic asthma and for 5 cases of atopic asthma.
ACOS, asthma–COPD overlap syndrome.

FEAS to investigate the role of occupation in the development of three subtypes of adult asthma, namely atopic asthma, non-atopic asthma and ACOS. This approach provides new information on the link between occupation and asthma subtypes, which is important for asthma diagnosis and treatment.

METHODS

Study design

The study was a population-based case–control study of newly diagnosed asthma among working-age adults (21–63 years old) living in Pirkanmaa Hospital District in Southern Finland.[9] The study subjects had signed an informed consent.

Study population

The study population of the current analyses included adults 21–63 years old who were living in Pirkanmaa Hospital District in Southern Finland during the recruitment period of the FEAS from September 1997 to March 2000 (table 1). To be included in this part of the study the subjects also had to have serum Phadiatop measured, as we used specific IgE antibody results for subcategorisation of cases into atopic and non-atopic asthma.

Cases

Cases of asthma had received a new diagnosis of bronchial asthma fulfilling the national diagnostic criteria applied at the time of data collection.[9] The diagnostic criteria were the following:

- Occurrence of at least one asthma-like symptom: prolonged cough, wheezing, attacks of or exercise-induced dyspnoea, or nocturnal cough or wheezing AND
- Demonstration of significant reversibility in airways obstruction in lung function investigations through the following findings: (1) significant improvement in response to short-acting bronchodilating medication in a bronchodilator test after baseline spirometry or at the end of methacholine challenge—the criteria for significant changes were: forced expiratory volume in 1 s (FEV_1) ≥15%, forced vital capacity (FVC) ≥15% and peak expiratory flow (PEF) ≥23%; and/or (2) ≥20% daily variation and/or ≥15% improvement in response to short-acting bronchodilating medication during at least 2 days in a 2-week diurnal PEF monitoring; and/or (3) significant improvement in spirometric lung function (for % criteria see above) and/or ≥20% improvement in the average PEF level in response to a 2-week oral steroid treatment.

Cases were recruited between September 1997 and March 2000, first in the city of Tampere and since 1998 in the whole Pirkanmaa Hospital District in Southern Finland. Recruitment took place at the outpatient clinic of Tampere University Hospital, offices of private-practising pulmonary physicians and by general practitioners at the public health-care centres in the region. The response rate was 90%. In addition, the Finnish National Social Insurance Institution invited to our study all patients whose reimbursement right for asthma medication had begun in the Pirkanmaa District during the study recruitment period, but who had not yet participated. The participation rate through this route was 78%. A total of 521 cases of adult-onset asthma participated in the FEAS.

The case population for this part of the study included a total of 368 subjects with adult-onset asthma and acceptable post-bronchodilator spirometry. New cases of asthma also had to have measurements of serum Phadiatop antibodies available, as

the cases were divided into subcategories of atopic asthma and non-atopic asthma based on this measurement. Atopic asthma was defined among asthma cases using serum Phadiatop score, which was based on serum IgE antibodies to common aeroallergens, including birch, timothy grass, ragweed, cat, dog, horse, and moulds *Dermatophagoides pteronyssinus* and *Aspergillus fumigatus*. At least one positive finding in Phadiatop was required to define atopic asthma. Among the asthma cases, ACOS was defined as spirometry showing persistent airflow obstruction with a postbronchodilator FEV_1/FVC less than 70% of predicted.[10 11]

Controls

This FEAS study population included 932 controls, who represented a random sample of adults 21–63 years old living in the study area at the time of data collection.[9] The sample was identified through the national population registry. Controls were recruited at regular intervals throughout the study period. We excluded from the control population 76 subjects (7.5%) who reported previous or current asthma on the baseline questionnaire, 6 subjects who had been older than 63 years at recruitment and 2 subjects who had returned incomplete questionnaire. The response rate among the controls was 80% among those who were living in Pirkanmaa District at the time of data collection.

Occupational groups

The study subjects answered at the time of recruitment a self-administered questionnaire that was modified from the Helsinki Office Environment Study questionnaire for use in a general population.[1 9] It included six sections: (1) personal characteristics; (2) health information, including respiratory symptoms and current and some previous respiratory diseases, such as asthma and respiratory infections, and selected other diseases, such as allergic rhinitis and eczema; (3) active smoking and exposure to secondhand smoke (SHS); (4) occupational history and some details of current work environment; (5) current home environment; and (6) dietary questions.

The section on occupational history enquired about current occupation and previous occupations throughout the subject's working history, starting with the current one and recalling history backwards.[1] Additional questions were asked about some details of the current work environment, for example, indoor moulds and dampness problems, exposure to SHS, and some other specific occupational exposures. We also enquired if the subject had changed his/her work due to respiratory problems.

We applied the International Standard Classification of Occupations-88[13] to classify the reported occupations as ISCO-88 corresponding to the time of data collection.[1 9] To classify each subject into an occupational group, we used current job at the time of asthma diagnosis or up to 3 months prior to it, or the most recent job that the subject had quit due to respiratory symptoms.

Statistical methods

We compared the risk of the three subtypes of asthma between different occupational groups and the reference group. We used OR as the measure of the relation between an occupational group of interest and the risk of the subtype of asthma. The reference category included professionals, clerks and administrative personnel. We adjusted OR for age, gender and smoking in unconditional logistic regression analysis. The cumulative lifetime consumption of tobacco was estimated as cigarette-years, calculated as the average smoking rate (cigarettes/cigars/pipefuls per day) × duration of smoking. In addition, we conducted sensitivity analyses adjusting also for having pets indoors, exposure to dampness and moulds, exposure to SHS during the last 12 months, and lifetime cumulative SHS. We applied SAS V.9.4 (PROC LOGISTIC) in the multivariate analyses.

RESULTS

Characteristics of cases and controls

In the current analyses of the FEAS study population with Phadiatop results available, there were altogether 368 cases of new asthma, including 156 cases (42.4%) of atopic asthma, 187 cases (50.8%) of non-atopic asthma and 25 cases (6.8%) of ACOS, as well as 932 controls (table 1).

Risk of subtypes of adult asthma associated with occupational groups

Table 2 shows the adjusted OR (aOR) of having new asthma for each asthma subtype by occupation. Some occupational groups showed a statistically significantly increased risk of new asthma. Among those with atopic asthma, the following occupations showed increased risk: chemical industry workers (aOR 15.76, 95% CI 2.64 to 94.12), bakers and food processors (aOR 4.69, 95% CI 1.18 to 18.69), waiters (aOR 4.67, 95% CI 1.40 to 15.56) and the unemployed (aOR 3.06, 95% CI 1.52 to 6.17). Among those with non-atopic asthma, the occupations showing clearly increased risk were metal workers (aOR 8.37, 95% CI 3.77 to 18.59) and farmers and other agricultural workers (aOR 2.36, 95% CI 1.10 to 5.06). Increased aOR of non-atopic asthma was also identified among forestry workers (aOR 5.77), chemical industry workers (aOR 4.19), dentists and dental workers (aOR 3.48) and rubber and plastic workers (aOR 3.45), but their 95% CI included 1. Some of these occupations have previously been considered as risk factors for atopic asthma, so these new identified associations with non-atopic asthma should be taken into consideration when conducting diagnostic procedures or scientific research on work-related asthma.

Among those with ACOS, some occupational groups showed high OR with statistically significant 95% CI, although the total amount of ACOS cases was rather small (table 3). These occupational groups included electrical and electronic production workers (aOR 30.6, 95% CI 6.10 to 153.35), fur and leather workers (aOR 16.41, 95% CI 1.25 to 215.85) and those retired (aOR 5.55, 95% CI 1.63 to 18.97). The unemployed also showed a high risk of ACOS with an aOR of 5.46, although its CI included 1.

Risk of subtypes of adult asthma with occupational groups according to gender

Many of the significant relations between occupational groups and the three subtypes of asthma were identified mainly among men (table 4A), while others were identifiable predominantly among women (table 4B). Among men, a high-risk atopic asthma was identified among bakers and food processors (aOR 28.90, 95% CI 2.39 to 349.36), textile workers (aOR 22.49, 95% CI 1.29 to 390.75) and the unemployed (aOR 7.94, 95% CI 2.31 to 27.31). In men, high-risk non-atopic asthma was found among metal workers (aOR 10.87, 95% CI 4.33 to 27.28) and students (aOR 14.90, 95% CI 2.91 to 76.19), as well as among chemical industry workers (aOR 19.9, 95% CI 0.90 to 442.67), although the last CI included 1. When analysing those who had developed ACOS among men, the following occupational groups showed a high risk: rubber and plastic workers (aOR 35.34, 95% CI 2.63 to 475.12), electrical and electronic production workers (aOR

Table 2 Adjusted OR of atopic and non-atopic asthma by occupation, the Finnish Environment and Asthma Study 1997–2000

	Atopic asthma cases (n=156)			Non-atopic asthma cases (n=187)*			Controls (n=932)*
Occupation	**n**	**OR†**	**95% CI**	**n**	**OR†**	**95% CI**	**n**
Bakers and food processors	4	**4.69**	**1.18 to 18.69**	1	0.53	0.06 to 4.49	7
Chemical industry workers	4	**15.76**	**2.64 to 94.12**	1	4.19	0.31 to 56.60	2
Cleaners	8	2.00	0.82 to 4.86	12	1.44	0.69 to 3.03	34
Construction and mining workers	2	0.69	0.15 to 3.15	4	1.58	0.51 to 4.89	31
Day-care workers	4	2.34	0.71 to 7.71	3	0.80	0.22 to 2.86	16
Dentists and dental workers	0	–	–	1	3.48	0.21 to 56.82	1
Drivers	2	0.97	0.21 to 4.47	2	1.09	0.24 to 4.92	23
Electrical and electronic production workers	2	1.03	0.22 to 4.96	2	1.47	0.31 to 6.87	14
Engine workshop workers	2	0.74	0.16 to 3.40	2	1.45	0.32 to 6.61	21
Farmers and agricultural workers	3	1.00	0.29 to 3.45	11	**2.36**	**1.10 to 5.06**	35
Forestry and related workers	1	4.21	0.31 to 57.31	1	5.77	0.49 to 67.58	2
Fur and leather workers	1	1.24	0.14 to 11.20	1	0.69	0.08 to 6.03	6
Glass, ceramic and mineral workers	2	3.11	0.56 to 17.40	0	–	–	6
Hairdressers	0	–	–	3	1.19	0.23 to 6.24	6
Housewives	3	0.93	0.25 to 3.47	0	–	–	18
Laboratory technicians	0	–	–	0	–	–	7
Metal workers	5	2.18	0.74 to 6.38	14	**8.37**	**3.77 to 18.59**	23
Maternity leave	1	1.05	0.12 to 9.12	0	–	–	7
Nurses and nursing associates	6	1.11	0.43 to 2.88	7	0.78	0.33 to 1.85	41
Painters	1	1.78	0.21 to 15.22	0	–	–	7
Physicians	0	–	–	2	1.97	0.38 to 10.23	8
Printers	0	–	–	1	0.69	0.08 to 5.84	8
Rubber and plastic workers	2	2.16	0.41 to 11.32	4	3.45	0.92 to 12.84	7
Retired	6	1.93	0.72 to 5.19	17	1.27	0.66 to 2.45	61
Sick leave	0	–	–	0	–	–	1
Storage workers	1	0.63	0.08 to 5.05	5	2.60	0.87 to 7.81	14
Students	12	1.45	0.65 to 3.24	7	2.36	0.89 to 6.23	29
Textile workers	3	2.36	0.62 to 9.03	4	1.20	0.37 to 3.92	13
Other occupations	14	1.5	0.77 to 2.94	12	0.93	0.47 to 1.85	73
Unemployed	16	**3.06**	**1.52 to 6.17**	5	0.64	0.24 to 1.72	42
Waiters	6	**4.67**	**1.40 to 15.56**	4	2.79	0.76 to 10.18	7
Wood and paper workers	3	1.50	0.39 to 5.77	2	1.48	0.31 to 7.14	14
Total	153	–	–	177	–	–	901
Occupation missing	3	–	–	10	–	–	31
Professionals, clerks and administrative	39	1.00	–	49	1.00	–	317

Statistically significant effects are shown in bold.
*Smoking missing for 2 controls and for 2 cases with non-atopic asthma.
†Adjusted for age, gender and smoking.

29.51, 95% CI 3.74 to 233.03), those unemployed (aOR 24.69, 95% CI 3.14 to 194.38) and those who had retired (aOR 23.67, 95% CI 3.14 to 194.38).

In women, high-risk atopic asthma (table 4B) was found among chemical industry workers (aOR 32.14, 95% CI 2.96 to 348.70), waiters (aOR 5.34, 95% CI 1.53 to 18.63) and those retired (aOR 3.08, 95% CI 0.91 to 10.38) or unemployed (aOR 2.29, 95% CI 1.00 to 5.25). The risk of non-atopic asthma was increased among women in the following occupations: rubber and plastic workers (aOR 5.06, 95% CI 1.08 to 23.68), drivers (aOR 5.11, 95% CI 0.31 to 84.12) and dentists and dental workers (aOR 3.42, 95% CI 0.21 to 56.00), although the 95% CI for the latter two occupations included 1. Among women, a high risk of ACOS was identified among electrical and electronic workers (aOR 32.1, 95% CI 1.30 to 792.47) and among fur and leather workers (aOR 16.18, 95% CI 0.84 to 310.23).

DISCUSSION

As recently a more sophisticated categorisation of adult asthma has been introduced, we analysed our large population-based study of adult-onset asthma in Southern Finland[19] to investigate which occupations are associated with three subtypes of adult-onset asthma. We found that among those new asthma cases who had serum Phadiatop measurements of IgE antibodies available, 42.4% had atopic asthma, 50.8% had non-atopic asthma and 6.8% had ACOS. The latter is an obstructive lung disease that was discovered after data collection of the FEAS had been conducted, so the ACOS cases were diagnosed for this part of the study afterwards based on spirometry results.

The following occupational groups showed significantly increased risk of atopic asthma: chemical industry workers, bakers and food processors, and waiters. The last occupation is an interesting finding as waiters are not exposed to traditional

Table 3 Adjusted OR of ACOS by occupation

	ACOS Total (n=25)*†		
Occupation	**n**	**OR‡**	**95% CI**
Construction and mining workers	1	1.52	0.17 to 13.81
Drivers	1	2.83	0.30 to 26.42
Electrical and electronic production workers	3	**30.6**	**6.10 to 153.35**
Engine workshop workers	1	3.97	0.41 to 38.92
Fur and leather workers	1	**16.41**	**1.25 to 215.85**
Rubber and plastic workers	1	9.93	0.99 to 99.38
Retired	7	**5.55**	**1.63 to 18.97**
Other occupations	1	2.20	0.24 to 19.93
Unemployed	2	5.46	0.99 to 30.03
Professionals, clerks and administrative (reference category)	5	1.00	–

Statistically significant effects are shown in bold.
*1 control and 1 case with ACOS who were on sick leave are missing because the model including sick leave could not be fitted.
†Smoking missing for 2 controls.
‡Adjusted for age, gender and smoking.
ACOS, asthma–COPD overlap syndrome.

allergens in their work for longer time periods, unless they also participate in food preparation. They were at the time of data collection exposed to environmental tobacco smoke, which has been related to adult asthma.[14] In addition, those who were unemployed showed increased risk of atopic asthma, suggesting that it may be more difficult to get employment if the subject has allergic asthma.

The occupational groups that were associated with non-atopic asthma included metal workers, farmers and other agricultural workers, forestry workers, chemical industry workers, dental workers, rubber and plastic workers, and waiters. Some of these occupational groups are interesting from the perspective that occupational asthma diagnostics have traditionally searched for atopic asthma, but some occupations previously linked with occupational asthma were associated in our study with non-atopic asthma, for example, farmers and dental workers. One possible mechanism underlying these associations could be irritant-induced asthma.[15 16]

The rather recently identified obstructive lung disease ACOS was also strongly and significantly associated with some occupations, although its incidence was rather small. Such occupations included electrical and electronic production workers, fur and leather workers, and rubber and plastic workers. ACOS was also significantly related to being retired. The latter suggests that subjects with ACOS may have relatively heavy disability, leading to retirement, or that they are transferred to retirement rather fast when they develop respiratory symptoms, that is, this could be explained by the so-called healthy worker effect.

In summary, we found that some occupations were strongly linked to atopic asthma, others to non-atopic asthma and some to ACOS. Some of the latter occupations were predominantly male occupations, such as metal workers. However, some of the relations suggest that men and women perform different tasks at work even though their job category is the same, so their risk of developing subtypes of asthma may differ from each other. For example, work in electrical and electronic production was strongly related to ACOS among both men and women, while

Table 4A Adjusted OR of non-atopic asthma and atopic asthma by occupational groups in men

	Atopic asthma (n=57)			Non-atopic asthma (n=54)*			Controls (n=438)*
Occupation	**n**	**OR†**	**95% CI**	**n**	**OR†**	**95% CI**	**n**
Bakers and food processors	3	**28.90**	**2.39 to 349.36**	0			1
Chemical industry workers	1	3.62	0.21 to 63.61	1	19.9	0.90 to 442.67	1
Construction and mining workers	0	–	–	4	2.01	0.60 to 6.7	31
Drivers	2	1.46	0.31 to 7.00	1	0.83	0.10 to 6.76	22
Electrical and electronic production workers	2	2.54	0.48 to 13.41	1	1.88	0.22 to 16.34	10
Engine workshop workers	1	0.47	0.06 to 3.86	2	1.93	0.39 to 9.48	21
Farmers and agricultural workers	1	0.91	0.11 to 7.29	4	3.20	0.93 to 11.03	21
Forestry and related workers	1	6.20	0.44 to 86.75	1	7.24	0.59 to 89.33	2
Glass, ceramic and mineral workers	2	3.56	0.60 to 21.19	0	–	–	6
Metal workers	5	3.01	0.97 to 9.34	13	**10.87**	**4.33 to 27.28**	23
Painters	1	4.53	0.48 to 43.20	0	–	–	5
Physicians	0	–	–	1	5.06	0.49 to 52.72	4
Printers	0	–	–	1	5.31	0.48 to 59.39	3
Rubber and plastic workers	2	5.57	0.83 to 37.37	0	–	–	4
Retired	1	0.93	0.11 to 7.83	2	0.89	0.18 to 4.31	26
Students	2	1.02	0.19 to 5.54	4	**14.90**	**2.91 to 76.19**	9
Storage workers	1	1.92	0.21 to 17.45	2	4.38	0.81 to 23.71	8
Textile workers	1	**22.49**	**1.29 to 390.75**	0	–	–	1
Other occupations	6	2.54	0.88 to 7.33	2	1.63	0.34 to 7.88	26
Unemployed	5	**7.94**	**2.31 to 27.31**	1	1.57	0.18 to 13.59	11
Wood and paper workers	3	1.85	0.44 to 7.81	1	1.77	0.21 to 15.28	12
Professionals, clerks and administrative	15	1.00	–	11	1.00	–	164

Statistically significant effects are shown in bold.
*Smoking missing for 1 control and for 1 case with non-atopic asthma.
†Adjusted for age and smoking.

Table 4B Adjusted OR of non-atopic asthma and atopic asthma by occupational groups in women

	Atopic asthma (n=99)			Non-atopic asthma (n=133)*			Controls (n=494)*
Occupation	**n**	**OR†**	**95% CI**	**n**	**OR†**	**95% CI**	**n**
Bakers and food processors	1	1.37	0.14 to 13.57	1	0.56	0.07 to 4.89	6
Chemical industry workers	3	**32.14**	**2.96 to 348.70**	0	–	–	1
Cleaners	8	2.06	0.83 to 5.11	12	1.39	0.66 to 2.95	33
Day-care workers	4	2.28	0.68 to 7.62	3	0.76	0.21 to 2.73	16
Dentists and dental workers	0	–	–	1	3.42	0.21 to 56.00	1
Drivers	0	–	–	1	5.11	0.31 to 84.12	1
Electrical and electronic production workers	0	–	–	1	1.35	0.14 to 12.80	4
Farmers and agricultural workers	2	1.30	0.27 to 6.30	7	2.13	0.80 to 5.65	14
Fur and leather workers	0	–	–	1	0.63	0.07 to 5.57	6
Hairdressers	0	–	–	3	1.18	0.22 to 6.19	6
Housewives	3	0.96	0.25 to 3.64	0	–	–	18
Maternity leave	1	1.03	0.12 to 8.96	0	–	–	7
Nurses and nursing associates	6	1.15	0.43 to 3.04	7	0.77	0.32 to 1.84	38
Physicians	0	–	–	1	1.14	0.12 to 10.77	4
Rubber and plastic workers	0	–	–	4	**5.06**	**1.08 to 23.68**	3
Retired	5	3.08	0.91 to 10.38	15	1.39	0.66 to 2.95	35
Storage workers	0			3	2.08	0.50 to 8.73	6
Students	10	1.77	0.70 to 4.45	3	0.98	0.26 to 3.72	20
Textile workers	2	1.54	0.31 to 7.59	4	1.18	0.36 to 3.89	12
Other occupations	8	1.18	0.50 to 2.80	10	0.84	0.39 to 1.8	47
Unemployed	11	2.29	1.00 to 5.25	4	0.54	0.18 to 1.60	31
Waiters	6	**5.34**	**1.53 to 18.68**	4	2.71	0.72 to 10.15	6
Wood and paper workers	0	–	–	1	1.59	0.14 to 18.39	2
Professionals, clerks and administrative	24	1.00	–	38	1.00	–	153

Statistically significant effects are shown in bold.
*Smoking missing for 1 control and for 1 case with non-atopic asthma.
†Adjusted for age and smoking.

rubber and plastic work was related to ACOS only among men. Among women such work was linked to non-atopic asthma.

Having atopic asthma was a risk factor for unemployment among both men and women, while ACOS was linked to both unemployment and retirement among men. The relation of atopic asthma with unemployment may suggest that employers tend to avoid employing subjects with atopic diseases in occupations where it is well known that there are potential exposures to allergens. The linkage of ACOS with retirement may indicate either that having ACOS is a risk factor for greater disability or that workers with ACOS are transferred to retirement quite fast when they start to experience symptoms. There seems to be a need to emphasise active measures to promote workability even among those who have chronic respiratory diseases.

Validity issues

The identification of the asthma cases in this study was based on clinical diagnostic criteria which followed the Finnish National Guidelines.[16] There are today no internationally or nationally established diagnostic criteria for the subtypes of asthma. We applied two clinical measurements, specific IgE antibodies (Phadiatop test) and persistent obstruction on spirometry, to define the three subtypes of asthma for the purpose of the study. We used three operationally defined labels for the subtypes, atopic asthma, non-atopic asthma and ACOS. We emphasise that these operational subtypes do not represent any established clinical diagnoses.

The likelihood of selection bias was reduced with the design of the study as well as when conducting statistical analyses. Our focus on incident rather than prevalent cases improved the validity of the effect estimates, as occupational exposures were known to precede the onset of asthma. We enquired about any change in job after the onset of respiratory symptoms in order to reduce potential selection bias due to avoidance of occupational exposures after having developed symptoms.

This study was introduced to participants as a study on environmental factors and asthma in general, without emphasising occupational exposures, which diminishes potential information bias. We collected exposure information from cases and controls using the same questionnaire. To reduce information bias concerning the outcome, we verified the diagnoses of asthma by applying a rigorously defined diagnostic procedure and for cases recruited through the National Social Insurance Institution by reviewing the medical records of each potential case, so we were able to verify that their diagnosis was compatible with our criteria.

We adjusted for age, gender and smoking in the multivariate statistical analyses. We also conducted sensitivity analyses by fitting models with additional covariates, such as having pets indoors, exposure to dampness and moulds, exposure to SHS at the time of diagnosis, and lifetime cumulative SHS. The additional covariates did not have substantial influence on effect estimates, but they created instability in some of the models. Therefore we presented in the text the results of the main analyses.

Although the new cases of asthma were from a dynamic cohort representing approximately 500 000 person-years, the small numbers of exposed cases limited the statistical inference when

the prevalence of exposure was small, especially with ACOS. This led to two sources of potential error. First, the accuracy of the effect estimates was limited, as indicated by broad CIs. Second, the power to detect a true association was limited and thus lack of association was not always informative. The generalisability of our findings is limited by the role of chance in the statistical inference, as well as by differences in the actual occupational exposures in different populations. We recommend that new studies pool relevant existing cohorts to verify our findings with more accurate and generalisable effect estimates.

Synthesis with previous knowledge

The present study focused on the incidence of asthma and its three operationally defined subtypes in different occupations. It is important to note that these cases were not verified cases of occupational asthma, although workers in the occupations with a high incidence of asthma are likely to be exposed to asthmogenic agents. Occupational asthma is currently categorised into sensitiser-induced occupational asthma and irritant-induced occupational asthma.[16] Sensitiser-induced occupational asthma is caused by a specific workplace sensitiser which induces asthma with a mechanism that is associated with a specific immunological response. High-molecular-weight agents can cause production of specific IgE antibodies and typical allergic responses. Tarlo and Lemiere[16] list examples of occupations where workers are at risk of exposure to high-molecular-weight agents: farmers, laboratory workers working with animals, greenhouse workers, latex glove makers, grain workers, bakery workers, food production workers, office workers, printers and carpet makers. Also low-molecular-weight occupational chemicals can cause sensitisation and eventually asthma. Some of them cause production of specific IgE antibodies, including salts of nickel, chrome and cobalt.[17] However, majority of low-molecular-weight sensitising chemicals, such as diisocyanates, acid anhydride and acrylic monomers, may cause sensitisation through poorly understood mechanisms. Further, there is increasing evidence that there are airway irritants which cause occupational asthma in the absence of sensitisation.[16]

The observed differences in the association of occupation and different subtypes labelled as 'atopic' and 'non-atopic asthma' and 'ACOS' in the present study could reflect differences in the underlying mechanisms, although inference on the underlying mechanisms with given data is speculative. Nevertheless it is plausible to suggest that asthma cases with evidence of specific IgE positivity would at the population level be associated with the mechanisms of 'sensitizer-induced asthma', whereas asthma cases with lack of IgE positivity could represent mechanisms of 'irritant-induced asthma'.

To our knowledge our study is the first to investigate the role of different occupational exposures in the development of ACOS. We measured the persistent airways obstruction at the time of the diagnosis of asthma, which suggests a concurrent development of both asthma and restrictive obstruction which could over time lead to COPD. Trupin and coworkers[18] reported in 2003 that among a random sample of more than 2000 US residents 55–75 years old, the OR for COPD related to self-reported occupational exposure to vapours, gas, dust or fumes was 2.0 (95% CI 1.6 to 2.5). In addition, a recent longitudinal study of occupational exposures and incidence of COPD reported some results that may be relevant to the occurrence of ACOS in our study.[19] Occupational exposures that were associated with development of COPD in the European Respiratory Health Survey included exposure to biological dust (risk ratio (RR) 1.6, 95% CI 1.1 to 2.3), exposure to gases and fumes (RR 1.5, 95% CI 1.0 to 2.2) and exposure to pesticides (RR 2.2, 95% CI 1.1 to 3.8).

CONCLUSIONS

In this population-based study of new asthma among working-age adults in a geographically defined Pirkanmaa area in South Finland, among subjects having Phadiatop measurements available, 42.4% had atopic asthma, 50.8% had non-atopic asthma and 6.8% had ACOS. Our main finding was that the occupations that were associated with the three subtypes of adult asthma were different. In addition, the relations between occupational groups and subtypes of asthma differed between men and women. This suggests that men and women working in the same industry may perform different tasks. In conclusion, it is important to diagnose the obstructive lung disease subcategory when suspecting adult-onset asthma in different occupational groups. These different asthma subcategories are likely to require different approaches to diagnosis and management.

Contributors MSJ and JJKJ designed the study and interpreted the data. MSJ wrote the first draft of the manuscript and is the guarantor of the manuscript. MSJ and JJKJ have full access to data, and MSJ had the final responsibility to submit the manuscript. JJKJ, TKL, BH, Y-CW and C-HL interpreted the data and assisted in drafting the manuscript. TKL and JJKJ were responsible for the analysis. All authors approved the final version of the manuscript.

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Patient consent for publication Not required.

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