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Prevalence and determinants of respiratory symptoms, asthma, chronic bronchitis and allergic sensitization in Helsinki

A comparison between
Finland, Sweden and Estonia
The FinEsS studies – Helsinki I

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ACADEMIC DISSERTATION

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To my family

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Abstract

Objectives: To assess the prevalence and risk factor profiles of respiratory symptoms, asthma and chronic bronchitis in Helsinki, and to compare these results with those for Sweden and Estonia. Other important aims were to evaluate the prevalence and determinants of type 1 sensitization in Helsinki.

Materials and methods: This presentation is a part of a large epidemiological study in Finland, Estonia and Sweden (FinEsS). The first part of the study consisted of a postal questionnaire in 1995–1996 distributed to subjects in eight study centres. The study population in each centre was a population-based random sample designed to be representative of the general population. The original study sample in Helsinki consisted of 8000 subjects aged 20–69 years, 6062 (76%) of whom participated. Comparisons between countries were based on a narrower age group, 20–64 years, since 64 years was the upper age limit used in the original study in Estonia. Thus, altogether 58 661 subjects aged 20–64 years were invited to participate in Finland, Sweden and Estonia, and 44 483 (76%) did so. The second part of the study was a clinical study with a structured interview, lung function measurements and skin-prick tests with 15 common allergens. This thesis reports only the results of the prick tests in Helsinki. Of the 1200 subjects invited to participate in Helsinki, 643 (54%) consented. Skin-prick tests were performed on subjects ≤ 60 years of age; thus, a total of 498 tests were done.

Results: In Helsinki, the prevalence of physician-diagnosed asthma was 6.6% and of physician-diagnosed chronic bronchitis 3.7% among subjects aged 20–69 years. Comparison of the results between Finland, Sweden and Estonia in subjects 20–64 years of age revealed the highest prevalence of physician-diagnosed asthma in Sweden, 7.8%, while the prevalence in Finland was 5.9% and in Estonia 2.0% ($p<0.001$). The prevalence of physician-diagnosed asthma among those aged 20–29 years was 7.9% in Stockholm, 6.3% in Helsinki and 2.8% in Tallinn. Asthma-related symptoms were most common in Estonia, and among those with typical asthma symptoms the diagnosis of asthma was least likely in Estonia. Physician-diagnosed chronic bronchitis was reported to be 10.7% in Estonia, 3.1% in Sweden and 2.9% in Finland among subjects aged 20–64 years ($p<0.001$). Among those aged 20–29 years, 7.6% in Tallinn reported physician-diagnosed chronic bronchitis, while the prevalence estimates were 1.4% in Stockholm and 1.3% in Helsinki. The prevalence of smoking was similar for women in all three countries, around 30%, but large differences in smoking habits were present among

men; 60% of Estonian, 39% of Finnish and 28% of Swedish men smoked. Skin-prick tests in Helsinki revealed a high prevalence of sensitization, 46.9%. For subjects aged 26–39 years, the prevalence was highest, 56.8%, and 23.7% were sensitized to at least four allergens. The most common sensitizing allergen was the dog. Sensitization to multiple allergens was associated with a high prevalence of asthma and allergic rhinitis.

Conclusions: Compared with earlier Finnish studies, a higher prevalence of asthma and a lower prevalence of chronic bronchitis were found in Helsinki. The prevalence of physician-diagnosed chronic bronchitis was low in Helsinki, with only one-fifth of subjects fulfilling the symptom criteria for chronic bronchitis reporting having a diagnosis of chronic bronchitis. The prevalences of asthma and chronic bronchitis were similar in Finland and Sweden, but in Estonia physician-diagnosed asthma was less common and physician-diagnosed chronic bronchitis more common, particularly among young subjects. Further analyses revealed that the diagnosis of asthma was favoured in Finland and Sweden, while the diagnosis of chronic bronchitis was more likely in Estonia for subjects with the same symptoms. Allergic sensitization was common in Helsinki. Our findings of multiple sensitization also speak in favour of evaluating the degree of sensitization when assessing allergies.

List of original publications

This thesis is based on the following original publications, which are referred to in the text by their Roman numerals:

I Pallasaho P, Lundbäck B, Läspä SL, Jönsson E, Kotaniemi J, Sovijärvi ARA, Laitinen LA. Increasing prevalence of asthma but not of chronic bronchitis in Finland? Report from the FinEsS-Helsinki study. Respiratory Medicine 1999; 93: 798–809.

II Pallasaho P, Lundbäck B, Meren M, Kiviloog J, Loit H-M, Larsson K, Laitinen LA. Prevalence and risk factors for asthma and chronic bronchitis in the capitals Helsinki, Stockholm, and Tallinn. Respiratory Medicine 2002; 96: 759–769.

III Pallasaho P, Lindström M, Põlluste J, Loit H-M, Sovijärvi A, Lundbäck B. Low socio-economic status is a risk factor for respiratory symptoms: a comparison between Finland, Sweden and Estonia. The International Journal of Tuberculosis and Lung Disease 2004; 8: 1292–1300.

IV Pallasaho P, Meren M, Raukas-Kivioja A, Rönmark E. Different labelling of obstructive airway diseases in Estonia, Finland, and Sweden. European Journal of Epidemiology 2005; 20: 975–983.

V Pallasaho P, Rönmark E, Haahtela T, Sovijärvi ARA, Lundbäck B. Degree and clinical relevance of sensitization to common allergens among adults: a population study in Helsinki, Finland. Clinical Experimental Allergy 2006; 36: 503–509.

Paper II was also included in the dissertation of Mari Meren in Karolinska Institutet in 2005. All original communications are reproduced with the permission of their copyright holders.

Abbreviations

ATS	American Thoracic Society
BHR	Bronchial hyperresponsiveness
BMI	Body mass index
BTS	British Thoracic Society
CI	Confidence interval
COPD	Chronic obstructive pulmonary disease
EAACI	European Academy of Allergy and Clinical Immunology
ECRHS	European Community Respiratory Health Survey
ETS	Environmental tobacco smoke
FEV1	Forced expiratory volume in one second
FVC	Forced vital capacity
GINA	Global Initiative for Asthma
GOLD	Global Initiative for Chronic Obstructive Lung Disease
IgE	Immunoglobulin E
ISAAC	International Study of Asthma and Allergies in Childhood
IUATLD	International Union Against Tuberculosis and Lung Disease
OLIN	Obstructive Lung Disease in Northern Sweden
OR	Odds ratio
PEF	Peak expiratory flow
WAO	World Allergy Organization
WHO	World Health Organization

1 Introduction

Asthma and allergic sensitization have increased in prevalence during the second half of the last century. This increase has been well documented all over the world in Westernized communities. The highest prevalence estimates of asthma have been found in English-speaking countries. Two worldwide population studies have focused on this phenomenon: the ECRHS (European Community Respiratory Health Survey) in adults and the ISAAC (International Study of Asthma and Allergies in Childhood) in children.

A pandemia of chronic obstructive pulmonary disease (COPD) has also been predicted due to the increasing prevalence of smoking. However, the smoking habits in the Nordic countries show the opposite trend. WHO (World Health Organization) has predicted COPD to be the third commonest cause of death by the year 2020.

Many Nordic countries have long traditions of respiratory epidemiological studies. Denmark, Iceland, Norway and Sweden have participated in the ECRHS. Sweden participated in the ISAAC as well. Finland participated in the ISAAC, but not in the ECRHS. Major epidemiological studies on obstructive airway diseases in the Nordic countries consist of the OLIN (Obstructive Lung Disease in Northern Sweden) study in Sweden, the Bergen-Hordaland studies in Norway and the Copenhagen City Heart Study in Denmark. Estonia took part in both ECRHS and ISAAC.

In Finland, population-based large respiratory epidemiological studies in adults date back to the 1960s and 1970s, when Huhti (1965) performed his studies on chronic bronchitis, and Alanko (1970) on asthma. At that time, the prevalence of asthma was low, 1.4%, whereas the prevalence of chronic bronchitis was high, 27% among men and 5.5% among women. Since then cohort studies in farmers, conscripts, students and elderly population have been performed, but no large population-based cross-sectional or longitudinal studies have been carried out on obstructive airway diseases. Large changes in the epidemiology of obstructive airway diseases and allergic sensitization occurring between the 1960s and 1990s warranted an epidemiological study in Finland.

The FinEsS studies started in 1995 in three neighbouring countries, **Fin**land, **Es**tonia and **S**weden. The primary objective was to assess the prevalence of respiratory symptoms, asthma, chronic bronchitis, and allergic sensitization. The first part of the study aimed to give a description of demographic data in order to calculate risk factors for symptoms and diseases by using a postal questionnaire. The second part consisted of a structured interview and clinical examinations to evaluate the prevalence of

obstructive airway diseases using clinical criteria, to measure the proportion and degree of impaired lung function in the general population, to assess the prevalence of allergic sensitization and to examine new methods for differential diagnosis as well as early detection of obstructive airway diseases. The use of validated questions and the same clinical methods allowed us to compare results between countries.

This thesis focuses on the first part of the FinEsS studies, describing the results for Helsinki and comparing Helsinki to both Stockholm and Tallinn. Pooled data of all centres are analysed, focusing on risk factors and diagnostic differences. Comparison of diagnostic practices is achieved by comparing respiratory symptoms with the diagnoses of asthma and chronic bronchitis obtained in different countries. Data on allergic sensitization in Helsinki are also presented.

2 Background

2.1 Epidemiology and diagnosis of asthma

2.1.1 Defining asthma in epidemiological studies

The aim in epidemiological studies on asthma is to reflect the clinical picture of asthma as accurately as possible. These studies are challenging due to the lack of a gold standard for asthma diagnosis. Asthma can be defined based on either symptoms or lung function measurements, or both. Several questionnaires have been developed since the launching of the first widely used respiratory questionnaire in 1960 by the Medical Research Council (MRC) of Great Britain. These other questionnaires include the ECSC (European Community for Coal and Steel, Brille 1962), the IUATLD (International Union against Tuberculosis and Lung Disease, Burney et al. 1989), the Tucson Study questionnaire (Lebowitz 1975), the ECRHS (European Community Respiratory Health Survey, Burney et al. 1994), The OLIN (Lundbäck et al. 1991), the Tuohilampi questionnaire (Kilpeläinen et al. 2001) and the FinEsS questionnaire used in this study.

When validated with regard to a clinical diagnosis of asthma, the question about physician-diagnosed asthma yields a high specificity (Tóren et al. 1993). The mean sensitivity is lower, 68%, with a range of 48–100% (Tóren et al. 1993). Sensitivity depends on many things, e.g. accessibility to medical services and diagnostic practices. Bronchial hyperresponsiveness (BHR) yields a high specificity (generally over 80%), but a low sensitivity (generally below 50%) for asthma in epidemiological studies (Peat et al. 2001). Similar results would be expected for a positive bronchodilatation test in spirometry. In other words, lung function measurements are often normal in asthma patients with proper medication, while obstructive lung function or mild BHR without symptoms does not necessarily mean asthma. Questions on symptoms related to asthma and diagnosis of asthma take into account that asthma is a disease with variable symptoms and lung function measures over time. Measurement of sensitization to relevant allergens is essential in risk factor assessment for asthma (Peat et al. 2000). Probably the best way of measuring asthma in epidemiological studies would be a combination of questions about symptoms and diagnoses with peak expiratory flow (PEF) measurements, spirometry, BHR assessment, and skin-prick tests along with a physician`s conclusion on the data, but this would be very expensive in large studies. When the purpose is to study differences in asthma prevalence, questions on asthma-related symptoms have been shown to yield a better combination of sensitivity and specificity than BHR alone or combined with symptoms data (Pekkanen and Pearce 1999).

2.1.2 Diagnosing asthma in clinical work

Numerous guidelines on asthma diagnosis and treatment exist worldwide, the most famous being the GINA guidelines (Global Initiative for Asthma). A Nordic consensus report on asthma management was published in 2000 (Dahl and Bjermer 2000). This report stresses the importance of early detection of asthma. PEF measurements and spirometry with a reversibility test for those with suspected obstruction are recommended. A positive reversibility test is defined as an improvement of >15% of PEF (or > 60 l/min) or >12% (or >200ml) of FEV1 (forced expiratory volume in one second). Further, a diurnal PEF variability [(highest PEF–lowest PEF) x 100/highest PEF)] of at least 15% during 2 or more out of 7 days is recommended to indicate asthma.

In the Finnish national asthma guidelines, however, the diagnostic requirements used to be more strict: an improvement of ≥15% of FEV1 or PEF in reversibility test, or a diurnal PEF variation of ≥20% [(highest PEF–lowest PEF) x 100/mean of the highest and lowest PEF] was required. The reversibility criteria for FEV1 changed into ≥12% in March 2006 (Haahtela et al. 2006). The Estonian diagnostic practices were influenced by the former Soviet Union criteria until the end of the 1980s. Asthma was defined as an allergic disease due to atopy or "infection allergy". Other types of variable bronchial obstruction resulted in different diagnoses (Meren et al. 2001). Further, asthma patients were not allowed to travel abroad, which might have influenced diagnostic practices (Meren et al. 2001).

In clinical work, the diagnosis of asthma consists of many components: assessment of symptoms and risk factors, clinical examination, lung function measurements, assessment of eosinophilic inflammation and allergy, and x-rays to exclude other diseases. Thus, the diagnosis is a summary of many components. It is sometimes difficult to discriminate between asthma and chronic obstructive pulmonary disease, and the two conditions can co-exist. The lack of any gold standard for diagnosing asthma and the complexity of making the diagnosis have led to different diagnostic practices. The national reimbursement criteria for asthma medication may also influence the diagnosis. The strict reimbursement criteria for COPD have resulted in many Finnish COPD patients with asthma-like reversibility in lung function measurements receiving an asthma diagnosis to assure higher reimbursement for inhalant medication. The large number of asthmatics has led to the recommendation that general practitioners set the diagnosis of asthma in health care centres in Finland instead of referring the patients to pulmonary specialists. The diagnostic tools in health care centres are different from those in outpatient clinics of hospitals, which use new diagnostic methods, enabling early diagnosis of asthma-like inflammation, further increasing differences in diagnostic practices. However, in most cases, the diagnosis of asthma can easily be made at health care centres. Furthermore, heightened awareness of asthma may have increased the activity of diagnosing asthma, thus influencing the figures of asthma prevalence and incidence over time

(Lundbäck et al. 2001). In recent years, however, reports of the prevalence of asthma reaching a peak have appeared after decades of an increasing trend (Flemming et al. 2000, Toelle et al. 2004, von Hertzen et al. 2005). In a study on schoolchildren in the British Isles, asthma-related symptoms and rhinoconjunctivitis decreased from 1995 to 2002, but the prevalence of asthma increased, which was explained by diagnosing increasingly milder disease (Anderson et al. 2004).

2.1.3 Asthma in Sweden

The prevalence of asthma in a Swedish population aged 16–64 years was only 2.0% in the 1960s (Julin and Wilhelmsen 1967). Asthma was associated with female gender, allergic disposition and family history of allergic diseases. At the beginning of the 1970s asthma was found in 2.6% of the Swedish adult population (Kiviloog et al. 1974). From 1971 to 1981, the prevalence of asthma increased among Swedish conscripts from 1.9% to 2.8% (Åberg 1989). In the ECRHS in 1990–1991, the prevalence of asthma in young adults aged 20–44 years had increased up to 5.5–6.8% (Björnsson et al. 1994). A similar prevalence, 5.5%, was shown for adults aged 20–69 years in a postal survey in southern Sweden in 1992 (Montnémery et al. 2001). Recently, a prevalence estimate of 6.5% was published (Masoli et al. 2004).

The OLIN studies (Obstructive Lung disease in Northern Sweden) consist of well-conducted longitudinal studies of obstructive airway diseases and allergic sensitization among children and adults starting in1985. The OLIN studies showed an asthma prevalence of 5–6% among adults in 1986, an increase to 7–8% in 1992 and a further increase to nearly 10% in 1996 (Lundbäck 1991, 1993, 1998). The incidence of physician-diagnosed asthma in the OLIN studies was 4–5/1000/year (Rönmark et al. 1997), and when corrected for symptomatic subjects at baseline 2.3/1000/year (Lundbäck et al. 2001), with a remission of 6% in a ten-year period (Rönmark et al. 1999a). The Nordic part of the ECRHS found an incidence rate of similar magnitude in Sweden (Torén et al. 2004).

2.1.4 Asthma in Estonia

Epidemiological data on obstructive airway diseases from Estonia are scarce. Low asthma prevalences of 0.5% in Tallinn and 0.4% in Saaremaa were described in 1990 (Jannus-Pruljan and Loit 1994). A higher prevalence of asthma, 2.0%, was reported from Tartu in the ECRHS (ECHRS 1996). Recently, a prevalence rate of 5.4% for clinical asthma in Estonia was estimated (Masoli et al. 2004).

The FinEsS study has revealed a 2.0% prevalence of physician-diagnosed asthma and 2.7% of ever asthma in an Estonian population aged 15–64 years in 1996 (Meren et al. 2001). When clinical methods are used that combine common symptoms in asthma and BHR, the prevalence of asthma among adults in Estonia seems to be at least 5–8% (Meren et al. 2005).

2.1.5 Asthma in Finland

The prevalence of asthma in the 1970s was lower in Finland than in Sweden (1.4% vs. 2.6%) (Alanko 1970, Kiviloog et al. 1974). In the Finnish Twin Cohort study, physician-diagnosed asthma reported in a postal questionnaire was 1.35% in 1975 and 1.80% in 1981 (Vesterinen et al. 1988). In 1980, also based on a postal questionnaire, the prevalence of asthma was 4.1% in an urban population and 2.7% in a rural population (Heinonen et al. 1987). Haahtela et al. (1990) reported a steady prevalence of asthma, between 0.02% and 0.08%, from 1926 to 1961 based on statistics of the defence forces on Finnish conscripts, but a linear increase from the 1960s to the end of the 1980s. The rise was 20-fold from 1961 to 1989, reaching a prevalence of 1.79% in 1989. A further increase, with no signs of levelling off, was reported recently (3.45% in 2003) (Latvala et al. 2005). From 1986 to 1993, an increase in annual incidence of persistent asthma was shown for subjects aged 15–64 years based on register data (Reijula et al. 1996). The fastest increase was demonstrated among subjects with an age of less than 30 years. Women showed a rising trend in all age groups, while no increase was seen among men over 50 years of age. In the same time period, new cases of occupational asthma increased among both women and men. However, no significant rise in asthma prevalence was detected from 1975 to 1990 in the Finnish Twin cohort study (Huovinen et al. 1999). At the beginning of the 1990s, asthma in the elderly was assessed in a cross-sectional study, demonstrating current asthma in 2.9% of men and 3.8% of women aged more than 63 years (Isoaho et al. 1994). In 1996, a postal questionnaire survey performed in southern Finland showed a non-response-adjusted prevalence of asthma of 4.4% among adults aged 18–65 (Hedman et al. 1999). A lifetime occurrence of physician-diagnosed asthma was 4.6% among 10 667 first-year university students (Kilpeläinen et al. 2000). The highest prevalence estimate ever for asthma in the Finnish population, 8.0%, was recently published based on available data from different sources (Masoli et al. 2004).

The FinEsS study from northern Finland revealed a prevalence of physician-diagnosed asthma of 6.0% in adults aged 20–69, and a higher prevalence rate for ever-asthma, 6.4% (Kotaniemi et al. 2001).

2.1.6 Factors associated with asthma

Family history, atopy, smoking and obesity

Heredity and atopy have been considered to be main risk factors for asthma, as shown in the ECRHS as well as in other studies (Sunyer et al. 1997). In a Finnish study on university students, parental asthma or atopy was the strongest risk factor for asthma and allergic rhinoconjunctivitis (Kilpeläinen et al. 2000). However, in a Finnish study on elderly subjects aged at least 64 years, current asthma among women was associated with a history of having smoked at some time, with exposure to dust at work and with low social status (Isoaho et al. 1994).

Atopy is a strong risk factor for asthma (Burrows et al. 1989). Pearce et al. (1999) have calculated a population attributable risk of 37% for asthma in adults with allergic sensitization. In a study on Spanish centres of ECRHS, asthma among young adults was likewise associated with allergic sensitization to perennial and seasonal allergens (Sunyer et al. 1997). In the Swedish part of ECRHS, however, cats and dogs were the allergens most closely associated with asthma (Plaschke et al. 1999). Similarly in northern Sweden, cats and dogs were the most important allergens, while sensitization to house dust mites and moulds was rare (Rönmark et al. 1998).

In the longitudinal follow-up of the OLIN studies, the following risk factors were reported (OR, odds ratio) for incident asthma in adults: family history of asthma 5.53 (95% CI 3.50–8.75), being an ex-smoker 2.30 (95% CI 1.29–4.11), current smoking 2.17 (95% CI 1.25–3.79) and female gender 1.78 (95% CI 1.12–2.84) (Lundbäck et al. 2001). The OLIN studies have also shown an additive effect of smoking and having a family history of asthma; a family history of asthma without smoking yielded a 4-fold increase in asthma, and smoking history alone without a family history of asthma a 2-fold increase, while together smoking history and having a family asthma history increased the risk to nearly 7-fold (Lundbäck 1998). Among non-smokers, exposure to environmental tobacco smoke outside the home for more than 5 hours daily was found to increase the risk for asthma (OR 1.79, 95% CI 1.02–3.16) in Estonia (Larsson ML et al. 2003). The benefits of smoking cessation on remission of asthma-related symptoms were clearly demonstrated in a recent Norwegian study (Eagan et al. 2004), although some asthmatics may report worsening of their symptoms (Hillerdahl and Rylander 1984). In a study on Finnish university students, tobacco smoke exposure during the first 2 years of life was a significant risk factor for asthma (Kilpeläinen et al. 2000). A recent study from Finland showed an increased risk for developing asthma among smokers and ex-smokers compared with non-smokers, and the conclusion was that smoking causes asthma in adulthood (Piipari et al. 2004).

Weight loss in obese asthmatics has been shown to reduce airway obstruction and PEF variability both short-term (Hakala et al. 2000) and long-term (Stenius-Aarniala et al. 2000). Further, better control of asthma symptoms and less need of rescue medication were achieved by weight loss (Stenius-Aarniala et al. 2000). Overweight, increased waist circumference and increased body mass index (BMI) have been associated with an elevated risk of developing asthma (Ford et al. 2004, Kronander et al. 2004). Increased BMI as a risk factor for incident asthma occurs in both men and women, as well as among both allergic and non-allergic subjects (Rönmark et al. 2005). Obesity is associated with reduced lung volumes in both genders and subsequent airway narrowing, which is greater in men (King et al. 2005).

Occupational exposure

Register data on adult-onset persistent asthma covering the entire employed population aged 25–59 years in Finland showed that the age-adjusted attributable fraction of occupation was 29% (95% CI 25–33%) for men and 17% (95% CI 15–19%) for women, indicating an increased risk, especially in agricultural, manufacturing and service work (Karjalainen et al. 2001). Similarly, in a Swedish study, exposure to welding fumes, man-made mineral fibres, solvents and textile dust were associated with an increased risk for asthma, with an attributable fraction of 11% adjusted for gender, smoking and age (Torén et al. 1999). Occupational airborne exposures to quartz, metal gases, aluminium production and processing, and welding were significantly associated with asthma and chronic obstructive airway disease in a study from Norway (Bakke et al. 1991).

Occupational risks were assessed in the ECRHS in a large sample of 15 637 subjects from 12 countries, and the highest risks for asthma were found for farmers (OR 2.62 [95% CI 1.29–5.35]), painters (2.34 [1.04–5.28]), plastic workers (2.20 [0.59–8.29]), cleaners (1.97 [1.33–2.92]), spray painters (1.96[0.72–5.34]) and agricultural workers (1.79 [1.02–3.16]) (Kogevinaas 1999). The proportion of asthma among young adults that was attributed to occupation was 5–10%. In a recent study from Norway, the attributable fraction of exposure to dust or fumes was 14.4% for the 11-year incidence of asthma in a population-based study of adults after adjusting for gender, age, educational level and smoking (Eagan et al. 2002). Dust or fume exposure combined with smoking yielded an attributable fraction of 26.2%.

Socio-economic conditions

In Scotland, low socio-economic status doubled the risk for adult-onset wheeze, with other risk factors being current smoking, atopy and having a family history of atopy (Bodner et al. 1998). In the OLIN studies, incident asthma was associated with manual workers and assistant non-manual employees, and a significant association was found between incident asthma and being a manual worker in industry (Lundbäck et al. 2001). However, Montnémery et al. (2001) could not show any association between socio-economic condition and asthma in southern Sweden. No significant association of educational level with asthma was found in Norway during the 1980s (Bakke et al. 1995), but an association between low socio-economic status and increased incidence of asthma was recently demonstrated in a follow-up of the Hordaland County Cohort study in western Norway (Eagan et al. 2004). The steepest increase in asthma prevalence was noticed among those conscripts with a low socio-economic status in Sweden (Bråbäck et al. 2005). A 6-fold prevalence of asthma compared with the national rate was found among homeless children in New York (McLean et al. 2004), and inner city children have the highest prevalence of asthma in the US (Call et al. 1992).

Environmental factors

Large differences in prevalence of asthma and allergic sensitization among children have been documented between former West and East Germany (von Mutius et al. 1992, 1994). The first of these two papers reported a higher lifetime prevalence of bronchitis in East Germany, but no difference in prevalence of asthma. The latter reported a higher prevalence of asthma in the West compared with the East based on BHR in cold air challenge and questionnaire data. However, significantly higher prevalences for wheeze and coughing were found among children living in East Germany. Further, a higher prevalence of allergic sensitization to house dust mites, grass, birch, hazel, cats and dogs was found in the West. An explanation for the bronchitic symptoms in the East was sought from high levels of different pollutants (von Mutius et al. 1995). In a study with similar methods on another sample of schoolchildren, an increased prevalence of hay fever and allergic sensitization in the former East Germany was reported in 1998, but no change was observed in prevalence of asthma, asthma-related symptoms or BHR (von Mutius et al. 1998). Since then, differences in early childhood environment have been explored, and attention has been directed to living on a farm in early childhood, which has been found to prevent the development of allergic sensitization and asthma in many studies (Braun-Fahrländer et al. 1999, von Ehrenstein et al. 2000, Ernst and Cormier 2000, Kilpeläinen et al. 2000, Riedler et al. 2000). In the ECRHS pooled data on Belgium, France, Netherlands, Sweden and New Zealand, living on a farm during childhood did not protect against asthma in adulthood, but did protect against allergic sensitization (Leynaert et al. 2001). Interestingly, the farm environment was associated with a higher prevalence of allergic rhinitis and asthma among children in New Zealand (Wickens et al. 2002). In the ECRHS data from Belgium, asthma, asthma symptoms and house dust mite allergy were shown to be more frequent in urban Antwerp than suburban Antwerp (Wieringa et al. 1997). Differences as large as between former East and West Germany were demonstrated, but the reasons remained unidentified. The rural environment was also associated with a lower prevalence of asthma and allergic sensitization among children in Kenya (Perzanowski et al. 2002), as well as among adults in Mongolia (Viinanen 2004).

In a study from Norway, exposure to fungi and endotoxins was associated with a lower risk for atopic asthma, but a higher risk for non-atopic asthma in farmers (Eduard et al. 2004). Endotoxin levels in dust samples from the mattress were inversely related to occurrence of hay fever, atopic asthma and atopic sensitization in schoolchildren (Braun-Fahrländer et al. 2002). Endotoxin is a lipopolysaccharide of the Gram-negative bacterial wall. Past or present pet ownership has also been shown to reduce the risk of development of asthma in pre-teenage children (Rönmark et al. 1998, Perzanowski et al. 2002). House dampness and mould growth have been linked to an increased risk of asthma in both children (Åberg et al. 1996, Nafstad et al. 1998) and adults (Zock et al. 2002).

2.1.7 Control of asthma

How are different guidelines for asthma applied in real life? In a study of asthmatics referred to a US university hospital emergency department for treatment, 60% of asthmatics were under-treated with respect to medication recommended by the guidelines and nearly 90% had no written instructions in case asthma worsened (Taylor et al. 1999). Asthma knowledge was poor, and only 60% of patients were seen by a physician yearly to control asthma. The AIRE (Asthma Insights and Reality in Europe) survey showed suboptimal asthma control in seven European countries with Sweden among these (Vermeire et al. 2002). This study revealed an insufficient monitoring of asthma. Less than half of adults had a written asthma management plan. The use of inhaled corticosteroids was not according to the guidelines in any of the countries. Of the adults, 15–25% had severe persistent asthma symptoms and 20–28% moderate persistent symptoms. In a French study, 85% of patients with severe asthma in Paris and 60% in Montpellier did not receive anti-inflammatory treatment (Bousquet et al. 1996). The national Asthma Programme in Finland showed improved treatment of asthma patients, with reduced hospital days and mortality due to asthma, during the 10-year programme that was initiated in 1994 (Haahtela et al. 2001).

2.2 Allergic sensitization in adults

Allergic sensitization has been a growing burden in Western countries (von Mutius et al. 1998, Linneberg et al. 2000). An increase in prevalence of atopic diseases, as well as a shift towards stronger sensitization, has been shown among children in Eastern Germany (Heinrich et al. 2002). Recent data on specific IgE for trees, grass and cats of middle-aged men showed that the proportion of those with specific IgE was significantly lower in earlier born cohorts (Law et al. 2005). While the precise reason for this rise in allergic sensitization remains unknown, the leading theory since the 1980s has been the hygiene hypothesis (Strachan 1989, Braun-Fahrländer et al. 1999, von Hertzen and Haahtela 2004). However, some challenges to the hygiene hypothesis exist, e.g. the very high prevalence of allergy and asthma among children living in very poor conditions in inner cities of North America (McLean et al. 2004). Different immunoresponse profiles have been demonstrated depending on the exposure to different allergens such as house dust mites and cats (Platts-Mills et al. 2001).

2.2.1 Definitions

The EAACI (European Academy of Allergy and Clinical Immunology) position paper gives the following definition for atopy: "*Atopy is a personal or familial tendency to produce IgE antibodies in response to low doses of allergens, usually proteins, and to develop typical symptoms such as asthma,*

rhinoconjunctivitis, or eczema/dermatitis" (Johansson et al. 2001). The term atopy is recommended to describe a tendency or trait, but not a disease. Allergy is defined as follows: "*Allergy is a hypersensitivity reaction initiated by immunologic mechanisms*". A positive skin-prick test should be referred to as "skin-prick test-positive". We have followed these recommendations, but also refer to positive responses in skin-prick tests as allergic sensitization.

2.2.2 Sweden and Estonia

As part of the ECRHS, atopy was studied by measuring IgE antibodies against *Dermatophagoides pteronyssinus*, birch, timothy, cats, and *Cladosporium* in young adults of Uppsala, Sweden, and Tartu, Estonia (Jõgi et al. 1998). The prevalence of IgE sensitization was lower in Tartu (19.1%) than in Uppsala (32.3%). Sensitization to birch, timothy, cats and *Cladosporium* was more common in Uppsala, while sensitization to mites occurred more frequently in Tartu.

The first FinEsS report on allergic sensitization described data from Tallinn, where sensitization was surprisingly common, with a prevalence of 34.5% among subjects aged 17–66 years, and 39.3% among those aged 20–44 years (Raukas-Kivioja et al. 2003). The prevailing allergen was the cockroach, followed by the mugwort, dog and two storage mites. This cockroach sensitization could be in part a cross-sensitization to dust mites and storage mites.

2.2.3 Finland

In 1978, a study comprising adolescents and conscripts from southeastern Finland showed single prick test-positive reactions in nearly half of subjects (Haahtela 1980).

Kilpeläinen et al. (2001) examined university students aged 18–25 years that consisted of altogether 150 students with a history of wheezing or asthma and 140 students without asthmatic symptoms. At least one prick test positivity was found in 68.7% of those with asthma symptoms and in 42.1% of those without symptoms. The high proportions may be due to the large allergen panel used as well as to the selection procedures.

A cross-sectional study on a random population sample of subjects aged 25–54 years was performed in eastern Finland; 34.2% of subjects had at least one positive prick test reaction to airborne allergens (Vartiainen et al. 2002).

2.2.4 Factors associated with allergic sensitization

Family history of atopy is a well-known risk factor for allergic sensitization. Other risk factors include many environmental conditions such as exposure to furred animals during childhood, type of living environment, dampness problems at home and domestic crowding. The role of breastfeeding has been controversial.

Urban living has been shown to increase the risk for allergic sensitization (Bråbäck et al. 1994). The cause for the urban-rural difference was initially thought to be pollution, but the prevalence of atopy was demonstrated to be higher in less polluted areas (Bråbäck et al. 1994, von Mutius et al. 1994, Nicolai et al. 1997). The focus was then turned to the farm environment and to pet ownership. Living on a farm during childhood was shown to protect against allergic sensitization in adulthood (Svanes et al. 1999, Kilpeläinen et al. 2000, Leynaert et al. 2001). Living in a community with more than 100 000 inhabitants was a risk factor for allergic sensitization in Germany (Nicolai et al. 1997). In Japan, allergic rhinoconjunctivitis due to Japanese cedar was more common among subjects living near inter-city roads than among those living in the city or in farming areas and in the mountains, which was explained by effects of air pollution and car exhaust fumes (Ishizaki T et al. 1987).

Cat ownership was inversely related to allergic sensitization to animals in Estonia, Poland and Sweden in subjects aged 10–12 years (Bråbäck et al. 1995). Having pets at home during childhood was also shown to be a protective factor for allergic sensitization (Roost et al. 1999). Further, a dose-response relationship was discovered: exposure to more than two cats or dogs in early life reduced the risk of allergic sensitization at the age of 6–7 years (Ownby et al. 2002), and persistent exposure during childhood yielded the most pronounced reduction in early teenage years (Rönmark et al. 2003). Allergic sensitization was inversely related to the number of older siblings in the UK (Strachan et al. 1997). Domestic crowding and larger family size decreased the risk of allergic sensitization in children in the Baltic area (Bråbäck et al. 1995) and in Latin America (Cooper et al. 2004).

Low socio-economic status protected against atopy in Latin America (Cooper et al. 2004), and higher socio-economic status was related to allergic sensitization in the UK (Strachan et al. 1997). A higher level of education also increased the risk for allergic sensitization in Germany (Nicolai et al. 1997). Low socio-economic status, by contrast, was a significant risk factor for cockroach sensitization in asthmatic children in the US (Sarpong et al. 1996). Cockroach sensitization together with sensitization to house dust mites were shown to be the main risk factors for asthma in inner city children in the US (Call et al. 1993).

Exposure to tobacco smoke (ETS) during infancy was a significant risk factor for allergic sensitization in Estonia, but not in Sweden or Poland (Bråbäck et al. 1995). A prospective study in the first three years of life in children with both parents atopic showed ETS exposure to be a risk factor for asthma, but it had little or no effect on allergic sensitization (Murray et al. 2004). Recently, parental smoking during childhood was found to be a significant risk factor for allergic sensitization in adults (Larsson ML et al. 2005). Serum IgE level is higher in smokers than in non-smokers (Zetterström et al. 1981). In rats, exposure to tobacco smoke was shown

to increase serum IgE levels and enhance sensitization to ovalbumin (Zetterström et al. 1985).

Higher levels of endotoxin exposure at home have been associated with decreased risk for allergic sensitization in adults, which may be related to a farm environment and pet ownership, as both of these result in higher exposure to endotoxins (Gehring et al. 2004). In the last few years, a growing body of evidence has emerged that suggests that higher endotoxin exposure is protective against allergic sensitization (Gereda et al. 2000, 2001, Braun-Fahrländer et al. 2002, Gehring et al. 2002). Endotoxin stimulates immunity towards non-allergic pathways rather than allergic ones.

Geographical position as well as factors related to climate and housing affect the profile of important allergens. In northern Sweden, house dust mite and cockroach allergens are generally unmeasurable (Perzanowski et al. 1999) and sensitization to dust mites and cockroaches is rare (Rönmark et al. 1998, Perzanowski et al. 1999), whereas the cockroach is the major allergen in Tallinn, Estonia (Raukas-Kivioja et al. 2003).

WHO (2002) recommendations for prevention of allergy and allergic asthma emphasize such measures in primary prevention as avoidance of smoking and exposure to environmental tobacco smoke, breast-feeding exclusively until 6 months, avoidance of damp housing conditions, reduction of indoor pollutants and elimination of sensitizing and highly irritating agents in occupational environments.

2.2.5 Multiple sensitization

There is growing interest in quantifying allergic sensitization. Besides assessing specific allergens to which a person is sensitized, quantifying the level of allergic sensitization to IgE-mediated specific allergens and to allergens overall would be useful. This can be done by summarizing the responses to positive prick test reactions or by summarizing specific IgE values.

In children, the prevalence rates of asthma and hay fever have been shown to increase with an increasing number of positive prick test responses (Sears et al. 1993). The probability of allergic disease rises with an increasing sum of allergen-specific IgE levels or an increasing number of positive IgE responses (Wickman 2004).

2.3 Epidemiology and diagnosis of chronic bronchitis

2.3.1 Diagnosing chronic bronchitis

The diagnosis of chronic bronchitis is based on symptoms and patient history. Chronic bronchitis is defined as the presence of cough and sputum production on most days for at least 3 months in two consecutive years when other causes have been excluded. This definition dates back to the 1950s and

it was approved by WHO (Ciba Guest Symposium 1959). In patients with these symptoms the disease may progress to chronic obstructive pulmonary disease (COPD), which can be diagnosed when airway obstruction is demonstrated. The GOLD (Global Initiative for Chronic obstructive Lung Disease) guidelines refer to chronic bronchitis without obstruction as stage 0; i.e. at risk for COPD. The GOLD criteria define COPD as FEV1/FVC<0.7. Subjects with chronic bronchitis or COPD may also have emphysema, which is a pathological term meaning permanent enlargement of the distal airways. Early diagnosis of chronic bronchitis is important to prevent progression to COPD (Lindberg et al. 2005). Further, chronic bronchitis was associated with increased mortality among the elderly in the Copenhagen City Heart Study (Lange et al. 2003).

2.3.2 Chronic bronchitis in Sweden

In the mid-1960s, the prevalence of chronic bronchitis was 2.1% among men and 1.8% among women aged 16–64 years in southern Sweden (Julin and Wilhelmsen 1967). In that study, 46% of men and 27% of women were smokers, but 90–91% of those with chronic bronchitis smoked. In the OLIN studies, an estimated prevalence of 9% was established, and a considerable under-reporting of symptoms was revealed among middle-aged and elderly smokers (Lundbäck et al. 1993). Further reports from the OLIN studies suggested an underdiagnosis of COPD since only one-third of the subjects fulfilling the BTS (British Thoracic Society) criteria for COPD (FEV1/VC<0.7 and FEV1<80%) had been diagnosed as having chronic bronchitis, emphysema or COPD (Lundbäck et al. 2003b). In a report from the FinEsS studies, chronic productive cough was reported by 7.0% in Norrbotten, northern Sweden, while the prevalence of physician-diagnosed chronic bronchitis was 3.8% (Lindström et al. 2001).

2.3.3 Chronic bronchitis in Estonia

In the 1970s, the prevalence of chronic bronchitis among subjects aged 35–54 years was around 7% in Tallinn and 8% in Saaremaa (Utkin et al. 1989). The same study showed an increasing trend in mortality rates due to chronic bronchitis, from 7.7 to 11.0 per 100 000 between 1980 and 1985. A recent FinEsS publication revealed a higher prevalence of physician-diagnosed chronic bronchitis in non-Estonians (mainly Russians), 13.5%, than in Estonians, 7.9%, living in Estonia (Jannus-Pruljan et al. 2004). This difference was explained by more extensive smoking habits and exposure to ETS in non-Estonians, as well as by socio-economic factors.

2.3.4 Chronic bronchitis in Finland

The prevalence of chronic bronchitis has been higher in Finland than in Sweden since the 1960s. Prevalence estimates of up to 27.0% among all men and 5.5% among all women in the age group 40–64 years were reported in

Finland, the corresponding proportions among non-smokers being 5.7% and 4.5%, respectively (Huhti 1965). In that study, 58.8% of men and 10.2% of women were smokers. A prevalence of 8% among Finnish farmers was found in the early 1980s (Terho et al. 1987). In a study on elderly Finns, chronic productive cough was reported by 12.5% of men and 6.5% of women (Isoaho et al. 1994). Furthermore, a considerable rate of underdiagnosis of COPD was revealed: a previous diagnosis of COPD had been assigned to 50% of men and 40% of women. In a nationally representative sample of subjects aged 30 years or over, an age-adjusted prevalence of chronic bronchitis was found in 19.3% of men and 6.5% of women, and a prevalence of clinically significant airways obstruction in 10.8% and 5.1%, respectively (von Hertzen et al. 2000). Half of the bronchitic women had never smoked.

In the FinEsS studies, a chronic productive cough rate of 11% of was observed in northern Finland, while only 3.1% reported physician-diagnosed chronic bronchitis (Lindström et al. 2001). Recently, an overall prevalence of COPD by BTS criteria was 5.4% and by GOLD criteria 9.4% in northern Finland (Kotaniemi et al. 2005).

2.3.5 Factors associated with chronic bronchitis and chronic obstructive pulmonary disease

Smoking

Smoking is the principal risk factor for chronic bronchitis and COPD (Siafakas et al. 1995, Lundbäck et al. 2003b, Mannino et al. 2003). It was previously held that 15–20% of smokers develop COPD, but the OLIN studies revealed that up to 50% of elderly smokers may develop COPD (Lundbäck et al. 2003b). Screening of smokers aged 40–55 years uncovered a high prevalence of COPD, 27%, in Sweden (Stratelis et al. 2004).

Other risk factors

Other risk factors include alpha-1-antitrypsin deficiency, genetic factors, occupational exposures, low socio-economic status and possibly dietary or childhood environmental factors (Antó et al. 2001). In China, the incidence of COPD decreased after household coal stoves were improved (Chapman et al. 2005). The Copenhagen City Heart Study revealed a considerable difference in FEV1 between the lowest and highest socio-economic group adjusted for smoking (Prescott et al. 1999). This difference was 400 ml for men and 259 ml for women. Further, those in the lowest socio-economic group had a threefold risk for hospital admission for COPD. Low socio-economic position was associated with an increased risk for chronic bronchitis in Sweden (Montnémery et al. 2001). A French study, by contrast, showed no difference in chronic bronchitis occurrence between socio-economic classes; however, classification to only three socio-economic classes was used, which may have yielded an insensitive rating (Huchon et al. 2002).

Occupational exposures have been recognized as a risk factor for COPD (Becklage 1989, Bakke et al. 1991). The attributable fraction of occupation on the development of COPD was 11% overall and more than 50% among non-smokers in a recent Swedish study on construction workers (Bergdahl et al. 2004). Low education level has also been associated with an increased risk for chronic bronchitis-related symptoms and obstructive lung disease (Bakke et al. 1995, Eagan et al. 2004). The FinEsS comparison of northern Sweden and northern Finland showed an additive effect of smoking and having a family history of obstructive airway disease on the risk for chronic bronchitis (Lindström et al. 2001).

2.3.6 Burden of chronic bronchitis and chronic obstructive pulmonary disease

According to the WHO, COPD is expected to be the third most common cause of death worldwide by 2020. Prevalence of COPD is 4–10% in most studies, and it is expected to increase in the future (Halbert et al. 2003, Lundbäck et al. 2003a). Comparison of prevalence rates internationally is difficult because different diagnostic criteria have been used (Halbert et al. 2003).

Already in 1997, the total costs of chronic bronchitis and COPD were estimated to be more than 800 million euros in Finland, and a rise in costs was anticipated (Laitinen and Koskela 1999). National Finnish guidelines of chronic bronchitis and COPD stress early detection and active treatment (Laitinen and Koskela 1999). Early detection is essential because of the irreversibility of the disease and the steeply rising costs with its progression. Further, the response to medication is limited in COPD. The most important treatment of chronic bronchitis and COPD is smoking cessation, which has been shown to relieve symptoms and to halt excessive lung function decline (Willemse et al. 2004). Public campaigns on the harms of smoking and measures to reduce exposure to tobacco smoke are valuable preventive means.

2.4 Respiratory symptoms in the general population

Respiratory symptoms are markers of lung disease, and assessment of symptoms is an essential part of diagnostics and follow-up. Further, respiratory symptoms in the elderly are strong predictor of mortality (Hewitt et al. 2005).

The prevalence of respiratory symptoms in the ECRHS varied substantially between countries and even within a country (ECRHS 1996). Highest prevalence estimates of symptoms were generally found in English-speaking countries, including the UK, US, New Zealand and Australia. The prevalence of wheezing ranged from 19.8% to 23.2% in Sweden, while the prevalence

in Tartu, Estonia, (26.8%) ranked among the highest (ECRHS 1996). The same question on wheezing was used in the FinEsS questionnaire, yielding prevalence estimates of 18.6% in northern Sweden, 18.9% in northern Finland and 21.7% in Estonia (Lindström et al. 2001, Meren et al. 2001).

The most common respiratory symptom in the different FinEsS centres was sputum production, with 19.1% reporting this in northern Sweden, 25.0% in northern Finland and 29.5% in Estonia (Lindström et al. 2001, Meren et al. 2001). Long-standing cough was another common symptom; in the FinEsS study, it was reported by 24.0% of subjects in Estonia and by 16.7% in northern Finland (Kotaniemi et al. 2001, Meren et al. 2001). In the OLIN studies, the prevalence of long-standing cough was lower, around 10%, while sputum production at 22% was similar to in the FinEsS studies (Lundbäck et al. 1991).

2.5 Reasons for conducting epidemiological studies

Peat et al. (2001) have summarized the goals and benefits of epidemiological studies as follows:

- To measure prevalence and to quantify the burden of illness
- To identify etiological factors and understand mechanisms in order to develop better preventive and treatment strategies
- To identify "at risk" groups in order to administer preventive pharmacological or environmental strategies efficiently
- To evaluate responses to new treatments or interventions

3 Aims of the study

1. To assess prevalence and risk factors for respiratory symptoms, asthma and chronic bronchitis in Helsinki

2. To compare prevalence of respiratory symptoms, asthma and chronic bronchitis between Helsinki, Stockholm and Tallinn

3. To compare risk factors, including socio-economic status, for respiratory conditions between Finland, Sweden and Estonia

4. To compare diagnostic practices of asthma and chronic bronchitis between Finland, Sweden and Estonia

5. To evaluate the prevalence and determinants of allergic sensitization in Helsinki

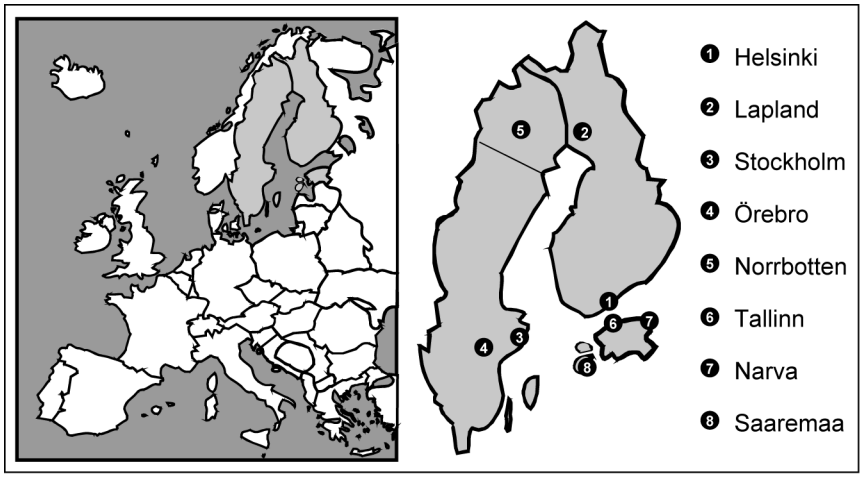
4 Materials and methods

4.1 Study areas

The FinEsS study was performed in altogether eight areas in three countries. The study centres in Finland were Helsinki and the southwestern and central parts of Lapland, including Kemi, Kemijärvi, Tornio and Rovaniemi. In Estonia, Tallinn, Saaremaa and Narva participated. In Sweden, the study areas were Stockholm, Örebro and the province of Norrbotten (Figure 1).

Studies I and V report results for Helsinki. Study II is a comparison between Helsinki, Stockholm and Tallinn for subjects aged 20–64 years. Studies III and IV are based on the pooled data of all centres for subjects aged 20–64 years.

Figure 1. Map of the study areas.



4.2 Study design

The first part of the FinEsS study consisted of a postal questionnaire, which was distributed in 1995–1996. The same questionnaire in each subject`s native language, i.e. in Swedish, Finnish, Estonian or Russian, was used (Appendix 1).

The second part of the FinEsS study consisted of a structured interview and clinical examinations. All subjects underwent a structured interview and spirometry. Skin-prick tests were performed on subjects under 61 years of age. A bronchial provocation test with histamine was performed and exhaled nitric oxide (NO) was conducted on half of the subjects, and lung

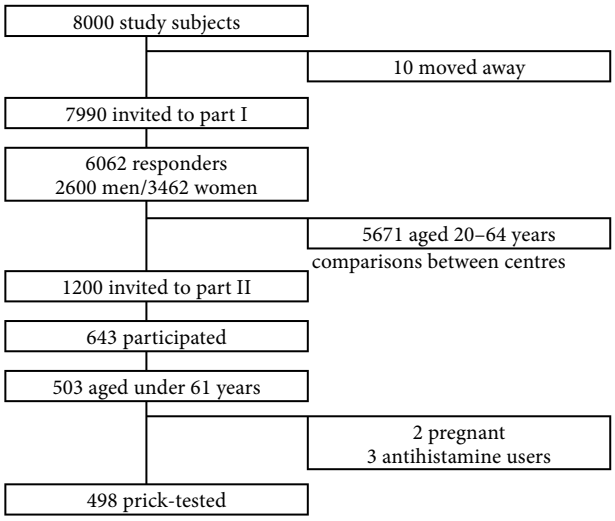
sounds were recorded in one-fourth. This thesis presents the results of the prick tests; results of the different lung function measurements are not reported here.

4.3 Study population

The study population consisted of randomly selected subjects obtained from population registers (Väestörekisterikeskus in Finland, Estonian State Computing Centre in Estonia, Swedish Population Register in Sweden) and designed to correspond to the general population with respect to age and gender. The study populations in Finland and Sweden comprised of subjects aged 20–69 years, and in Estonia 15–64 years.

In Helsinki, 8000 subjects were originally randomized for the study, but 10 subsequently moved away from Helsinki and were excluded. Of the 7990 invited, 4 were deceased, 3 did not answer personally, and a further 119 had moved away from Helsinki. A total of 6062 (76%) participated in the first part of the study. Of those who responded, a randomly selected sample of 1200 subjects was invited to the second part of the study; 643 (54%) participated. Of these, 503 were under 61 years of age and eligible for prick tests. Prick tests were not performed on five subjects: two were pregnant and three used regular antihistamine treatment. Thus, 498 prick tests were carried out. After exclusion of those showing no response to the positive control (4 subjects) and those reacting to the negative control (29 subjects), 465 valid prick tests remained for analysis.

Figure 2. Study population in Helsinki.



The study populations used in comparisons between the countries are shown

in Table 1. Study II compares the data of Helsinki, Stockholm and Tallinn for the age group of 20–64 years. Studies III and IV have pooled the data of all centres for this age group, thus including information for 44 483 (76%) participants out of the 58 661 invited.

Table 1. Study populations in comparisons between centers.

		Age group 20–64 years			
		Male	Female	Total	
Sweden	*Stockholm*	3721	3732	7453	
	participants	2484	2851	5335	72%
	Norrbotten	4025	3628	7653	
	participants	3349	3162	6511	85%
	Örebro	3349	3360	6709	
	participants	2660	2823	5483	82%
Finland	*Helsinki*	3564	3964	7528	
	participants	2429	3242	5671	75%
	Lapland	3781	3603	7384	
	participants	2971	3126	6097	83%
Estonia	*Tallinn*	5170	6146	11 316	
	participants	3099	4320	7419	66%
	Narva	2511	2949	5460	
	participants	1670	2145	3815	70%
	Saaremaa	2608	2550	5158	
	participants	1975	2177	4152	80%

4.4 Methods

4.4.1 Questionnaires

The postal questionnaire contained 20 questions. It was developed from the OLIN studies questionnaire (Lundbäck et al. 1991, 1993), which in turn was based on a revised version of the British Medical Research Council questionnaire (MRC 1960). The questionnaire included modifications from the ATS (American Thoracic Society) (Ferris 1978) and Tucson (Lebowitz et al. 1975) questionnaires, also containing questions from the IUATLD (International Union Against Tuberculosis and Lung Disease) (Burney et al. 1989). Two reminders were sent for those who did not respond to earlier letters.

The screening question for asthma, questions 10 (any wheezing during the last 12 months), 10a (with breathlessness) and 10b (without colds), was identical to ECRHS (Burney et al. 1994) questions 1, 1.1 and 1.2. Question number 10 (ECHRS 1) was originally in the British Medical Research Council`s questionnaire in 1986 and in the IUATLD questionnaire of the same year. The question on chronic productive cough refers to the largely used definition of chronic bronchitis, the CIBA definition (CIBA Guest Symposium 1959). Questions 1–10, 13 and 14 were the same as in the OLIN studies. Questions 11, 12 and 17–20 were not included in the OLIN questionnaire. The FinEsS questionnaire is presented in Finnish and English in Appendices 1 and 2.

The interview in the second part of FinEsS consisted of 162 questions asked by physicians involved in the study. Study V is based on answers to this interview questionnaire. Questions about physician-diagnosed asthma, long-standing cough and any wheezing were identical to the postal questions 3, 7 and 10. The three additional questions are described in the definitions section. The interview questionnaire was not included in this thesis as an appendix because results are mainly based on the postal questionnaire.

4.4.2 Skin-prick tests

Skin-prick tests were performed to 15 common allergens using commercial extracts and validated methods. The tests were performed according to the recommendations in the EAACI position paper, except as single tests on one forearm (Dreborg 1989). The allergens consisted of cat (10 HEP), dog (10 HEP), cow (1:100 w/v), horse (10 HEP), birch (10 HEP), timothy (10 HEP), mugwort (10 HEP), *Alternaria alternata* (100 bu/ml), *Cladosporium herbarum* (1:20 w/v), *Dermatophagoides pteronyssinus* (10 HEP), *Dermatophagoides farinae* (10 HEP), *Acarus siro* (1:100 w/v), *Lepidoglyphus destructor* (100 bu/ml), *Blatella germanica* (cockroach)(1:100 w/v) and latex (100 IR/ml) extracts. Histamine 10 mg/ml was used as a positive control, and the solvent (glycerin) as a negative control. All allergen extracts were provided by ALK, Denmark, except for latex, which was provided by Stallergenes, France. After 15 min, the wheal size was measured in millimetres in two perpendicular directions starting from the longest diameter, and their mean was recorded as the response. A response of at least 3 mm was regarded as positive. Those who did not react to the positive control and those who reacted to the negative control were excluded from the analyses.

4.5 Definitions

Asthma and chronic bronchitis were classified in two ways: Those who answered ”yes” to the question ”Have you been diagnosed as having asthma by a doctor?” or ”Have you been diagnosed as having chronic bronchitis

or emphysema by a doctor?" were classified as having *physician-diagnosed asthma* or *physician-diagnosed chronic bronchitis.* Those who answered "yes" to "Have you ever had asthma?" or "Have you ever had chronic bronchitis or emphysema?" were labelled as *ever-asthma* or *ever-chronic bronchitis.*

Definitions of term used are as follows:

Any wheeze: "Have you had wheezing or whistling in your chest at any time in the last 12 months?"

Wheezing with shortness of breath apart from colds: "yes" to the question about any wheeze, and "yes" to the following two questions "Have you been at all breathless when the wheezing noise was present?" and "Have you had this wheezing or whistling when you did not have a cold?"

Recurrent wheeze: "Have you had wheezing, whistling, or a noisy sound in your chest when breathing?"

Attacks of shortness of breath: " Have you now or have you had asthma symptoms in the last 12 months (intermittent breathlessness or attacks of breathlessness). The symptoms may exist simultaneously with or without cough or wheezing."

Current asthma: *Physician-diagnosed asthma* and *use of asthma medication or attacks of either shortness of breath during the previous 12 months or wheezing.*

Sputum production: "Do you usually have phlegm when coughing, or do you have phlegm which is difficult to bring up?"

Long-standing cough: "Have you had long-standing cough during the last years?"

Chronic productive cough: Sputum production when coughing on most days during periods of at least 3 months in 2 successive years.

In Study V, the answers are based on an interview. Definitions of physician-diagnosed asthma, long-standing cough and any wheeze are the same as above. Two new questions were introduced: allergic rhinoconjunctivitis and attacks of shortness of breath in the last 12 months, as described below:

Allergic rhinoconjunctivitis: " Do you have or have you had hay fever or allergic rhinitis or conjunctivitis?"

Attacks of shortness of breath in the last 12 months: " Have you had any attacks of breathlessness or attacks of shortness of breath in the last 12 months?"

Allergic sensitization was defined as at least one positive skin-prick test reaction.

Multisensitization refers to at least four positive reactions in the prick tests.

4.6 Socio-economic classification

The socio-economic classification used in Studies I and III is based on occupation according to the socio-economic classification system elaborated by Statistics Sweden (Appendix 3). The classification was developed by Statistics Sweden to also be used for research purposes and has been used in many studies in Sweden, including the OLIN studies. This classification is primarily based on occupation and in its most aggregated form consists of six groups formed by merging the 18 basic categories of the economically active population: 1) unskilled and semi-skilled workers, 2) skilled workers, 3) assistant non-manual employees, 4) intermediate non-manual employees, 5) employed and self-employed professionals, higher civil servants and executives, and 6) self-employed (other than professionals).

Low socio-economic status and "manual workers" refer to both manual workers in industry and manual workers in service (groups 1 and 2). In our study, we have combined groups 4 and 5 since no significant differences were found between them. Results for housewives, students and those with unknown occupation have been presented separately.

4.7 Statistical methods

Chi-square and Fisher´s exact tests were used to analyse differences between groups. A p-value of less than 0.05 was considered significant. One-way analysis of variance (ANOVA) was used for testing trends when analysing differences between age groups or smoking categories. The Mantel-Haenszel test was used to calculate prevalence rates standardized by age and smoking in study II. Multiple logistic regression analysis was applied to calculate odds ratios (ORs) when taking several independent

variables into account. Most statistical analyses were performed with Statistical Package for Social Sciences (SPSS, Chicago, USA), version 11.0.

5 Results

5.1 Helsinki (Studies I and V)

5.1.1 Respiratory symptoms and smoking

The prevalence of respiratory symptoms was high in the adult population in Helsinki (Study I: Figure 1). When analysed in 10-year age groups, the highest prevalence figures for different symptoms were usually found in the elderly (60–69 years) in both genders. This was true for long-standing cough, sputum production, chronic productive cough and recurrent wheezing. Tightness in the chest when waking up and any wheezing were the most common in the youngest age group of 20–29 years. Prevalences of chronic productive cough and recurrent wheezing were two- or threefold among the elderly compared with the youngest age group, while differences in other symptoms were smaller between age groups. Attacks of shortness of breath, tightness in the chest upon awakening and long-standing cough were significantly more common among women than men, while the opposite was true for any wheezing. No gender difference was seen for sputum production or chronic productive cough.

Smoking was common among those aged less than 40 years; more than 40% of men and 34% of women smoked. Of the elderly, 26% of men and 19% of women were smokers. Respiratory symptoms were significantly associated with smoking (Study I: Figures 1–3). "Any wheezing" during the last year was reported by 31% of smokers and 13% of non-smokers ($p<0.001$). Prevalence of recurrent wheezing was 12% in smokers and 4% in non-smokers ($p<0.001$). Similarly, shortness of breath during the last year was present in 16% of smokers and 10% of non-smokers ($p<0.001$), with the corresponding proportions for long-standing cough being 25% and 17% ($p<0.001$).

5.1.2 Asthma

There were 398 subjects (6.6%) with physician-diagnosed asthma: 145 men (5.6%) and 253 women (7.3%) ($p=0.007$). Ever-asthma was reported by 159 men and 278 women. Among the elderly (60–69 years), physician-diagnosed asthma was reported by 10.6% of men and 12.1% of women, and asthma medication was used by 9.5% and 11.2%, respectively. Attacks of shortness of breath and wheezing during the last year were reported by 71–84% of those with asthma. Men reported significantly more wheezing than women (Table 2). Table 2 below presents the prevalences of different respiratory symptoms in subjects with physician-diagnosed asthma according to smoking habits.

Because the smoking status of four asthmatics was unknown, they are not included in this table. Clearly, asthmatics who smoke are more symptomatic than non-smoking ones, but the use of asthma medication is less frequent among them. Assessing the proportion of asthma diagnosis among subjects with asthma-related symptoms revealed a greater proportion in women than in men; 26.2% of women and 20.4% of men reporting any wheezing had physician-diagnosed asthma. Similarly, 16.0% of women and 11.3% of men with long-standing cough had asthma diagnosed by a physician. No gender difference was seen in subjects with attacks of shortness of breath, 38–39% of them being diagnosed as having asthma.

Seven women and 25 men reported physician-diagnosed asthma among the 465 subjects with prick test results. Altogether 18 of those reporting asthma (56%) were atopic: 3 women (43%) and 15 men (60%) were atopic. One woman and one man reporting physician-diagnosed asthma were excluded because of dermographism. Of the 643 participants in the clinical part of the study, 70 reported having had asthma at some point in their lives. Onset of asthma symptoms was reported by 58 of these subjects. The median age of onset was 33 years (range 4–63 years).

Table 2. Respiratory symptoms and use of asthma medication by smoking status among subjects with physician-diagnosed asthma. Difference (*p*-value) compared with non-smokers.

	Non-smoker n=187	Ex-smoker n=85	p-value	Smoker n=122	p-value
	%	%		%	
Asthma medication	71.7	76.5	ns	65.6	ns
Attacks of shortness of breath	72.2	84.7	<0.025	75.4	ns
Long-standing cough	38.5	48.2	ns	47.5	ns
Chronic productive cough	24.6	35.3	ns	40.2	<0.01
Any wheeze	63.1	81.2	<0.01	80.3	<0.01

5.1.3 Chronic bronchitis

Physician-diagnosed chronic bronchitis or emphysema was reported by 226 subjects (3.7%): 106 men (4.1%) and 120 women (3.5%). The prevalence increased with age: 11.5% of men and 8.0% of women aged 60–69 years reported physician-diagnosed chronic bronchitis or emphysema. Subjects with this condition were highly symptomatic (Table 3). Men significantly

more often reported wheezing than women. Smoking was strongly associated with chronic bronchitis ($p<0.001$). Of non-smokers, 7.9% reported chronic productive cough and 2.1% physician-diagnosed chronic bronchitis. Of elderly subjects (60–69 years) reporting chronic productive cough, 61% of women and 23% of men were non-smokers. Men reporting bronchitic symptoms were more often diagnosed as having chronic bronchitis; 15.3% of men and 10.1% of women with long-standing cough had physician-diagnosed chronic bronchitis. Similarly, 12.8% of men with sputum production versus 10.0% of women had a diagnosis of chronic bronchitis. This difference was not seen in those reporting chronic productive cough, 19% of whom had been diagnosed as chronic bronchitis by a physician.

Table 3. Prevalence (%) of respiratory symptoms among subjects with physician-diagnosed asthma or chronic bronchitis by gender in Helsinki.

	Men	Women	p-value
Any wheeze			
in asthma	83.1	71.4	0.011
in chronic bronchitis	77.2	60.2	0.010
Recurrent wheeze			
in asthma	48.6	34.0	0.005
in chronic bronchitis	65.7	45.8	0.003
Attacks of shortness of breath			
in asthma	78.4	83.8	ns
in chronic bronchitis	63.7	63.8	ns
Long-standing cough			
in asthma	37.9	47.2	ns
in chronic bronchitis	69.2	63.8	ns
Sputum production			
in asthma	55.9	53.7	ns
in chronic bronchitis	82.5	80.5	ns
Chronic productive cough			
in asthma	53.2	46.3	ns
in chronic bronchitis	70.5	76.5	ns

5.1.4 Risk factors

In the study population of Helsinki, significant risk factors for physician-diagnosed asthma were having a family history of asthma and female gender. Smoking was not a significant risk factor for asthma, but was the main risk for chronic productive cough. Having a family history of obstructive airway disease (asthma or chronic bronchitis) and belonging to the older age group were also significant risk factors for chronic productive cough. Belonging to the socio-economic group of manual workers was a significant risk for wheezing during the previous year as well as for chronic productive cough.

5.1.5 Allergic sensitization

A positive response in skin-prick tests was common, seen in 46.9% of all subjects. Subjects aged 26–39 years were most often sensitized, with a prevalence of 56.8%. The most common sensitizing allergen was a dog. The prevalence of being sensitized differed significantly between the three age groups of 26–39, 40–49 and 50–60 years ($p<0.001$). Men were more often sensitized in all age groups, but this gender difference was not significant. In the youngest age group, 58.9% of men and 55.2% of women had at least one positive prick response, while the respective proportions were 56.9% and 42.2% at 40–49 years, and 36.2% and 35.2% at 50–60 years.

Sensitization to any furred animal was most common among the youngest in both genders. In the age group 40–49 years, men were significantly more often sensitized than women to animals (41.4% vs. 21.9%, $p=0.02$). Among the elderly, sensitization to animals was more common in women. Sensitization to pollens predominated in women in the youngest age group, and in men in the group 40–49 years. This difference between genders was significant among those aged 40–49 years, with 44.8% of men and 23.4% of women being sensitized ($p=0.012$). Sensitization to any of the home dust mites or storage mites prevailed among the younger subjects in both genders. The gender difference was significant among the elderly, with 18.8% of men and 4.8% of women being sensitized ($p=0.003$).

Being sensitized to at least four allergens was common among the youngest participants, with 23.7% of the sensitized reacting to multiple allergens. In the age group 40–49 years, 19.0% of men and 7.8% of women were multisensitized, but this difference was not statistically significant ($p=0.068$). Elderly men and women were equally multisensitized, with altogether 15.7% having multiple responses. Belonging to the youngest age group was the strongest risk factor for allergic sensitization (OR 2.15 [1.35–3.43]), followed by a family history of allergic rhinitis or conjunctivitis (OR 1.59 [1.07–2.37]). The age group 26–39 years also yielded an increased risk for multiple sensitization (OR 4.29 [2.00–9.20]).

5.2 Comparison of Helsinki, Stockholm and Tallinn (Study II)

The comparison between Helsinki, Stockholm and Tallinn included subjects aged 20–64 years; subjects aged 65–69 years were excluded from these analyses because the upper age limit in the study in Estonia was 64.

5.2.1 Respiratory symptoms and smoking

Asthma-related symptoms, attacks of shortness of breath and wheezing during the last year were most common in Tallinn (Study II: Table 2). The prevalence of attacks of shortness of breath during the last year among those

aged 20–29 years was similar in the capitals: 11.7% in Stockholm, 12.6% in Helsinki and 11.8% in Tallinn. In the same age group, wheezing during the last year was reported by 17.2% in Stockholm, 22.3% in Helsinki and 20.1% in Tallinn.

Long-standing cough and sputum production were most common in Tallinn, while chronic productive cough was most prevalent in Helsinki (Study II: Table 2). Again, with regard to the youngest participants, long-standing cough was reported by 15.1% in Stockholm, by 18.2% in Helsinki and by 22.5% in Tallinn. In the same age group, the prevalence of those reporting sputum production was 18.3% in Stockholm, 25.3% in Helsinki and 27.4% in Tallinn, and chronic productive cough was reported by 4.8% in Stockholm, 8.0% in Helsinki and 6.4% in Tallinn.

Respiratory symptoms (attacks of shortness of breath, wheezing, cough) in selected circumstances are presented in Table 4. Dusty environment and tobacco smoke were frequent respiratory irritants in all capitals, whereas subjects in Helsinki and Stockholm more often reported symptoms from pollens or animals than in Tallinn.

Table 4. Proportion of subjects (%) reporting respiratory symptoms provoked by different factors according to area and gender.

	Helsinki			Stockholm			Tallinn			Difference between
	Men	Women	Total	Men	Women	Total	Men	Women	Total	areas (p-value)
Cold weather	9.6	14.1	**12.2**	9.2	13.4	**11.4**	11.7	16.1	**14.2**	p<0.001
Physical exercise	16.1	18.6	**17.5**	16.2	20.0	**18.3**	12.0	12.0	**12.0**	p<0.001
Dusty environment	28.4	35.8	**32.6**	16.5	20.2	**18.5**	22.1	26.4	**24.6**	p<0.001
Tobacco smoke	16.7	26.6	**22.3**	16.0	21.9	**19.2**	22.0	27.3	**25.1**	p<0.001
Car exhaust fumes	15.2	22.7	**19.5**	8.2	12.8	**10.7**	15.4	21.1	**18.7**	p<0.001
Strong smelling scents	14.6	26.0	**21.1**	11.1	17.8	**14.7**	12.1	20.2	**16.8**	p<0.001
Pollen	13.7	18.5	**16.4**	10.6	12.9	**11.9**	3.2	5.4	**4.5**	p<0.001
Animals	9.5	12.3	**11.1**	9.6	10.1	**9.9**	2.1	3.7	**3.1**	p<0.001

Smoking habits were similar among women, with around 30% being current smokers in all capitals. Heavy smoking (≥15 cigarettes daily) in women was more common in Helsinki and Stockholm, 10% each, while the prevalence was only 5% in Tallinn. Among men, 32% were smokers in Stockholm, 38%

in Helsinki and 57% in Tallinn. Heavy smoking in men was reported by 14% in Stockholm, 19% in Helsinki and 26% in Tallinn. All respiratory symptoms increased in prevalence with increasing smoking habits in each capital.

5.2.2 Asthma

Physician-diagnosed asthma was most common in Stockholm and least common in Tallinn (Study II: Table 2). The same differences were seen in the youngest age group, 20–29 years: physician-diagnosed asthma was reported by 5.6% of men and 9.8% of women in Stockholm, 6.1% of men and 6.4% of women in Helsinki and 3.7% of men and 2.0% of women in Tallinn.

Among those with physician-diagnosed asthma, attacks of shortness of breath during the last year were reported by 75.6% in Helsinki, 71.4% in Stockholm and 67.4% in Tallinn. Prevalence of recurrent wheezing in the same subjects was 37.6%, 45.4% and 52.6%, respectively. Asthma medication was used by 69.7% of these subjects in Helsinki, 75.5% in Stockholm and 52.0% in Tallinn.

In multiple logistic regression analysis, after adjusting for gender, smoking, family history of asthma and area of domicile, the strongest risk factor for physician-diagnosed asthma was family history of asthma (OR 3.43 [2.96–3.96]). Living in Stockholm yielded an OR of 3.08 (2.55–3.72), and in Helsinki an OR of 2.54 (2.11–3.07) for physician-diagnosed asthma as compared with Tallinn. Having a family history of asthma as a risk factor for physician-diagnosed asthma differed somewhat when calculating risk factors separately for the capitals: OR in Stockholm was 3.72 (2.97–4.66), in Helsinki 3.41 (2.72–4.28) and in Tallinn 2.69 (1.86–3.88).

5.2.3 Chronic bronchitis

Physician-diagnosed chronic bronchitis was most prevalent in Tallinn and least common in Stockholm (Study II: Table 2). The prevalence among the youngest subjects, aged 20–29 years, differed largely between the capitals; physician-diagnosed chronic bronchitis was reported by 1.2% of men and 1.5% of women in Stockholm, by 0.8% of men and 1.7% of women in Helsinki and by 9.4% for men and 6.0% for women in Tallinn. Among those with physician-diagnosed chronic bronchitis, long-standing cough was reported by 66.0% in Helsinki, 47.2% in Stockholm and 59.5% in Tallinn. The respective proportions for sputum production were 83.5%, 55.8% and 64.8%. Chronic productive cough was reported by 62.4% of these subjects in Helsinki, 31.3% in Stockholm and 28.6% in Tallinn.

Smoking was a significant risk factor, with OR for heavy smokers being 2.49 (2.06–3.01) compared with non-smokers. The risk increased with age, with OR 3.33 (2.63–4.22) for those aged 60–64 years compared with the youngest subjects aged 20–29 years. Living in Tallinn yielded an increased risk, OR 3.29 (2.72–3.97) compared with Stockholm, but living in Helsinki was not a significant risk factor.

5.3 All centers (Studies III and IV)

Comparisons of all centers were made for subjects aged 20–64 years, which comprised 44 483 of the 58 661 persons (76%) invited. Comparison of respiratory symptoms between Finland, Estonia and Tallinn revealed a pattern similar to that yield in comparing the capitals; respiratory symptoms were most common in Estonia, except for chronic productive cough, which was most prevalent in Finland (Study IV: Table 3).

In the whole sample of 44 483 subjects, physician-diagnosed asthma was more common among women than men: 5.5% versus 5.0% (p=0.013). Physician-diagnosed asthma was reported by 5.8% of those aged 20–34 years, 4.6% of those aged 35–49 years and 5.6% of those aged 50–64 years. In each of these age groups, asthma was more common among women than men. Also physician-diagnosed chronic bronchitis was more prevalent among women (6.4%) than men (5.0%) (p<0.001). Women reported more physician-diagnosed chronic bronchitis (1517 subjects) than asthma (1322 subjects). Among men, 1022 reported physician-diagnosed chronic bronchitis and 1039 asthma. Prevalences of physician-diagnosed asthma and chronic bronchitis by age, gender and country are presented in Table 5. Prevalence estimates for both conditions in Finland and Sweden were similar, while chronic bronchitis was more common and asthma less common in Estonia.

Table 5. Prevalence of physician-diagnosed asthma and physician-diagnosed chronic bronchitis by age, gender and country.

		20–34 years		35–49 years		50–64 years		
		Men	Women	Men	Women	Men	Women	Total*
		%	%	%	%	%	%	%
Sweden	asthma	8.4	9.5	7.0	7.7	6.8	7.3	7.8
	chronic bronchitis	1.3	2.0	2.6	3.5	4.2	5.5	3.1
Finland	asthma	5.7	5.9	4.1	5.8	6.6	7.9	5.9
	chronic bronchitis	1.2	1.6	2.6	2.7	5.7	4.7	2.9
Estonia	asthma	2.0	1.7	1.6	1.5	1.9	3.4	2.0
	chronic bronchitis	8.7	7.6	8.2	10.8	11.7	16.7	10.7

***** The prevalence of asthma (p<0.001) and of chronic bronchitis (p<0.001) differed significantly between countries calculated by chi square test.

Although diagnosed asthma was more common among women, recurrent wheezing and any wheezing were significantly more common among men. Any wheezing was reported by 19.8% of men and 18.8% of women, and the respective rates for recurrent wheezing were 11.0% and 9.8%. On the other hand, attacks of shortness of breath were more common in women, 13.1%, than in men, 11.3% (p<0.001), as was long-standing cough. No difference in sputum production was seen, but chronic productive cough was more common in men, 9.2%, than in women, 8.0% (p<0.001). All of

these symptoms were most prevalent in the age group of 50–64 years than in the two younger age groups in both genders.

Comparing symptom levels among women in different countries showed that the prevalence of attacks of shortness of breath was similar, around 13%. Wheezing was most common among Estonian women, with 12.4% reporting recurrent wheezing and 20.3% any wheezing. Long-standing cough, 25.9%, and sputum production, 29.6%, also predominated among Estonian women, while chronic productive cough was most common in Finnish women, 10.7%. Among men, asthma-related symptoms, attacks of shortness of breath and wheezing were most common in Estonia, as were sputum production and long-standing cough. Chronic productive cough was most common in Finnish men.

Analyses in the whole study population revealed a high prevalence of chronic respiratory symptoms in the socio-economic groups of manual workers in industry and in service in each country (Study III: Table 3). There were significantly more manual workers in industry and fewer in service in both genders in Estonia than in Finland or Sweden. In particular, women working as manual workers in industry had high rates of respiratory symptoms; long-standing cough was reported by 26.0% of women and 18.5% of men ($p<0.001$). Sputum production was found in 32.2% of women and 27.4% of men ($p<0.001$). Recurrent wheezing was also more common in women, 16.3%, than in men, 14.5%, working in industry ($p=0.0138$), as was any wheezing. Long-standing cough was most frequent in Estonian manual workers in industry, 25.5%, while the rates were 18.9% in Finland and 11.9% in Sweden. Recurrent wheezing was also most common in Estonia in the same socio-economic group, 18.3%, while the rates were 9.4% in Finland and 12.3% in Sweden. Prevalences of different respiratory symptoms reported by subjects with physician-diagnosed asthma and chronic bronchitis are presented in Table 6.

Table 6. Prevalence (%) of respiratory symptoms among subjects having physician-diagnosed asthma and physician-diagnosed chronic bronchitis in Finland, Sweden, and Estonia by gender.

	Finland		Sweden		Estonia	
	Men	Women	Men	Women	Men	Women
Wheezing						
in asthma	74.6	69.6	66.6	69.8	65.0	73.9
in chronic bronchitis	72.7*	58.2*	55.3	56.2	61.4*	52.5*
Attacks of shortness of breath						
in asthma	73.9	78.4	67.9*	75.8*	62.6	72.9
in chronic bronchitis	55.3	55.5	53.5	53.9	42.2	40.0
Sputum production						
in asthma	56.1	57.6	45.9	45.6	63.4	62.8
in chronic bronchitis	83.9	77.5	64.2	59.9	67.6	64.9
Chronic productive cough						
in asthma	32.4	29.9	21.8	20.0	31.7	29.8
in chronic bronchitis	57.1	56.0	35.8	33.8	35.7**	27.3**

Gender differences by chi-square test. Significant difference in p-value: *=$p<0.01$; **=$p<0.001$.

6 Discussion

6.1 Discussion of methodology

The FinEsS postal questionnaire is based on the OLIN questionnaire (Lundbäck 1991, 1993), which was developed from international questionnaires, including the ATS (Ferris 1978), the revised British Medical Research Council questionnaire (MRC 1960), the IUATLD (Burney et al. 1989) and the Tucson studies questionnaires (Lebowitz et al. 1995). The original questionnaires have been validated in many studies and also reviewed (Burney et al. 1989, Torén et al. 1993). Apart from its use in the OLIN studies, the OLIN questionnaire has been used in other Swedish studies throughout the country (Larsson L et al. 1993, Montnémery et al. 1998, 2001, Hasselgren et al. 2001).

The study sample was obtained from population registers in a random manner in each of the countries. This procedure controls the risk of selection bias. The total sample in the postal questionnaire in Helsinki was 8000, exceeding the populations used in the ECRHS, which varied from 3000 to 6734 (ECRHS 1996). The ECRHS protocol recommends inviting at least 3000 subjects for their questionnaire study and at least 600 subjects for the clinical component (Burney et al. 1994). All FinEsS centres had large study populations and exceeded the ECRHS recommendations. The sample size for the clinical component in Helsinki was limited to 1200 due to restricted resources. Despite this limitation, analysis of data from single centres are useful when estimating prevalence of, for instance allergic sensitization, BHR, and COPD, although comparisons of prevalence levels between centres are limited.

Good response rates were obtained in the postal survey, the total participation rate in Helsinki being 76% of the original study sample, which is similar to the median participation rate in the ECRHS (ECRHS 1996). Young men were least likely to participate. The satisfactory response rate reduces the risk of non-response bias. A non-responder analysis was also carried out in northern Finland in the FinEsS; typical non-responders were young male smokers. The reasons for not responding were lack of interest and forgetting to mail back the response. In conclusion, only the rate of current smoking was slightly biased by non-responders (Kotaniemi et al. 2001). Similarly, in a non-responder analysis from the OLIN studies, young male smokers were most likely not to participate (Rönmark et al. 1999b). Their report concluded that the prevalence of respiratory symptoms and diseases might even be slightly underestimated due to non-responders.

Comparison of diagnostic differences based on questionnaire data is not definitive, but it does large samples to be compared. Definitive comparison would require a careful examination of subjects, multiple lung function measurements, allergy testing, examination of earlier medical records and finally a physician`s conclusion of the diagnosis. This would be impossible in large-scale studies. The lack of a gold standard for asthma also makes comparisons difficult. BHR has often been used as a marker of asthma, but it has been shown to have a lower sensitivity than assessment based on symptoms in relation to clinical examination by a physician or a previous diagnosis of asthma (Pekkanen and Pearce, 1999). A recent review by the GINA Committee stated that the ECHRS question on wheezing during the last year, which was included in our questionnaire as well, is useful for detecting the prevalence of "clinical asthma" (Masoli et al. 2004). Pekkanen et al. (2005) agreed that wheezing in the last 12 months yielded the best combination of sensitivity and specificity when assessing prevalence of asthma with different questions and combinations of questions. The question on physician-diagnosed asthma had the highest positive predictive value, 0.82, in validation of different questions in relation to confirmed asthma by a chest physician interview with data on BHR and spirometry (Kilpeläinen et al. 2001). The specificity was high, 99%, but the sensitivity remained low, 36%.

The same problems are faced when diagnosing chronic bronchitis and COPD. A recent review on the prevalence of COPD worldwide concluded that comparison of prevalence rates was difficult due to variable diagnostic criteria, including different guidelines for diagnosis, and potential diagnostic bias (Halbert et al. 2003). Many studies assessed in that review, including our study, used criteria for chronic bronchitis compatible with that of the British Medical Research Council, i.e. productive cough on most days of the week for at least 3 months of the years in 2 successive years, with other causes excluded (MRC 1965). This corresponds to stage 0 in the GOLD criteria. In addition to being a disturbing symptom, chronic productive cough is associated with a faster decline in lung function, and thus, should be recognized as early as possible (Vestbo et al. 1996). A primary care study from the Netherlands revealed that chronic cough was a good predictor of airflow obstruction compared with other symptoms, and half of smokers aged over 60 years with cough had airway obstruction (van Schayck et al. 2002).

Questions on the main and current occupation were posed to assess socio-economic status. Socio-economic classification can be made based on occupation, education or income. In the Nordic countries, the level of education is usually high and differences between income levels low compared with the situation internationally. Occupation-based classification is subject to healthy worker bias. The classification used in our study is based on the main occupation in addition to the present one, which reduces the possibility of this bias.

Skin-prick tests are a practical method to assess atopy and are applied in routine practice. Total IgE has been used in some studies, but the ECRHS concluded that variations in prevalence of atopy and the level of IgE are independent of each other (Burney et al. 1997). Here, prick tests were performed by trained and experienced nurses. The skin test methods and allergens were the same in all centres.

6.2 Discussion of main results

6.2.1 Diagnostic labelling of obstructive airway diseases

Numerous studies have been performed on prevalence of asthma and differences in prevalence in various parts of the world. In the ECRHS, wide variation in occurrence of respiratory symptoms and physician-diagnosed asthma was noted between countries and even within countries (ECRHS 1996, Janson et al. 1997). The highest prevalences were generally found in the English-speaking countries; however, the prevalence for current asthma symptoms was among the highest in Estonia, even higher than in New Zealand and England (Masoli et al. 2004). An example of wide variation within a country is Spain, where the prevalence of wheezing during the previous year varied from 16% to 29% (ECRHS 1996). Comparison of adults from former West and East Germany, including questionnaire data, lung function and allergy testing, showed a higher prevalence of lung function impairment, BHR and atopy in the West, with rates of respiratory symptoms also being higher (Nowak et al. 1996). Comparison of adults in Sweden and in Estonia as part of the ECRHS showed wheezing, waking with chest tightness, waking with attacks of shortness of breath and waking with attacks of cough to be significantly more common in Tartu, Estonia, than in Uppsala, Sweden. Of the symptoms, only breathlessness while wheezing was significantly more common in Uppsala, and no significant difference was found for wheezing without cold, but still the authors concluded that the prevalence of symptoms suggesting current asthma was higher in Uppsala based on these two questions (Jõgi et al. 1996). Further, it was later shown that BHR to methacoline was more common in Tartu than in Uppsala (Jõgi et al. 2004).

The question regarding wheezing during the previous year from the ECRHS was included in the FinEsS questionnaire and referred to as "any wheeze". As in the ECRHS, any wheeze was more common in Estonia than in Sweden in our study, but the prevalence was somewhat lower. In the ECRHS, the prevalence of most symptoms in Tartu was higher than the median, while the rates for diagnosed asthma or asthma attack were lower than the median, which was consistent with our results. Our findings on symptom levels are also in agreement; often the highest prevalence of respiratory symptoms was found in Estonia rather than in Finland or Sweden. Our

conclusions are that asthma-related symptoms are highest in Estonia, but a significantly smaller proportion of subjects with the same symptoms have been diagnosed as having asthma compared with Finland and Sweden. Even young subjects (aged 20–30 years) with common asthma symptoms were diagnosed as chronic bronchitis in Estonia. High prevalence of smoking in Estonian men may contribute to these differences, but smoking is equally common among women in the three countries, and heavy smoking is the least common among Estonian women. Moreover, respiratory symptoms in Eastern Europe may easily be interpreted as bronchitic symptoms (von Mutius et al. 1992,1994). On the other hand, one-third of non-smoking Estonian women were exposed to environmental tobacco smoke (ETS) at home, and half of the men outside of the home (Larsson ML et al. 2003). Women were more troubled by ETS, but exposure at home was not related to increased risk for respiratory symptoms. ETS exposure of more than five hours daily outside the home environment yielded an increased risk for wheezing and physician-diagnosed asthma.

Diagnostic labelling of obstructive airway diseases in Estonia has been influenced by the former Soviet Union traditions; asthma used to be defined as an allergic disease, and subjects with asthma faced restrictions in their lives including traveling abroad, which could have made the diagnosis unpopular (Meren et al. 2001, Jannus-Pruljan et al. 2004). However, when defining asthma using symptom combinations together with BHR, the prevalence of asthma in Estonia would be around 5–8% (Meren et al. 2005). A diagnostic difference in asthma was suspected among children between Poland and Sweden already more than 10 years ago; asthma-related symptoms and diurnal peak expiratory flow (PEF) variability were more common, while asthma diagnosed by a doctor was much less common in Poland than in Sweden (Bråbäck et al. 1994). In this work, however, attention was directed to the large differences in atopy between counties, and less to results concerning asthma. The same pattern was found in our study in adults, suggesting a diagnostic difference of obstructive airway diseases. These differences are hardly surprising in view of the lack of a gold standard in diagnostics of these diseases. The latest ECRHS II results indicate increased prevalence rates of asthma attacks and diagnosed asthma, but no change in asthma-related symptoms (Chinn et al. 2004). An increased labelling of mild asthma or increased use of asthma medication was suspected. Attention should be focused on implementing uniform guidelines, at least within the European Community level.

Large differences in smoking habits were found between Finnish, Swedish and Estonian men. Only a small proportion of subjects reporting chronic productive cough in Sweden, Finland and Estonia, reported having physician-diagnosed chronic bronchitis, suggesting a considerable underdiagnosis of chronic bronchitis (Study IV: Figure 3). The OLIN studies have earlier showed similar results; only 23–25% of those with chronic

bronchitis had been diagnosed as having chronic bronchitis, emphysema or COPD prior to the study (Lindström et al. 2001). Similarly, in a French study, 24% of subjects with chronic bronchitis were diagnosed as having chronic bronchitis, and only 7.2% had a follow-up scheduled (Huchon et al. 2002). Data from Spain and the US were also consistent with the theory of considerable underdiagnosis of these conditions (Mannino et al. 2000, Peña et al. 2000). Thus, while chronic bronchitis can be detected with simple questioning on cough and smoking, its symptoms appear to receive inadequate attention from physicians, with most affected subjects remaining unidentified and without treatment (van Schayck et al. 2002). An interesting feature is that the levels of underdiagnosis in Sweden, Finland, France and the US are similar.

The high level of respiratory symptoms in each of the countries was worrisome and raised the question of whether sufficient resources are given to basic health care to take care of patients with these symptoms, and whether general practitioners are well-trained to identify asthma and chronic bronchitis. In a study on identifying these diseases in patients with persistent cough in the Netherlands, nearly half of the subjects with cough received a diagnosis of asthma or chronic bronchitis when properly assessed. The authors mentioned that 10% of visits to a general practitioner are made because of cough, and in most cases the diagnosis given is acute bronchitis or upper respiratory tract infection, while the diagnoses of asthma and chronic bronchitis are rarely considered (Thiadens et al. 1998).

Comparisons between countries are often based on questions about diagnosed asthma. This procedure is biased by diagnostic practices and public awareness. Repeated questioning of symptoms and earlier lung function measurement have been thought to increase awareness and reporting of respiratory symptoms, although this was not confirmed in a survey comparing a longitudinal and a cross-sectional study (Sears et al. 1997). BHR has also been used in comparisons, but it should be borne in mind that while it is specific it is not sensitive, even when combined with questions on asthma-like symptoms (de Marco et al. 1998). In this Italian component of the ECRHS, only one-third of subjects with obvious asthma were aware of it based on judgement of specialists (de Marco et al. 1998). However, practically no studies assessing diagnostic practices in adults exist although it has been stated that: " The prevalence of asthma is difficult to follow over time owing to changes in diagnostic practice" (Magnus and Jaakkola 1997). The GINA Committee decided to assess differences in asthma prevalence worldwide based on wheezing during the last year instead of by comparing physician-diagnosed asthma, asthma medication, or asthma attacks because of "the marked variation in the recognition and presentation to a doctor by an individual with recurrent wheezing episodes" (Masoli et al. 2004).

6.2.2 Risk factors for respiratory conditions and allergic sensitization

Family history of asthma was a strong risk factor for asthma in Helsinki, OR 3.32, which is consistent with results of the OLIN studies from Sweden, with a similar slightly increased risk for women as compared with men (Rönmark et al. 1997). Smoking was a greater risk factor for asthma in the OLIN studies than in our study, although smoking habits were assessed with the same questions. The strongest risk factor for chronic productive cough in Finland, Sweden and Estonia was heavy smoking. In Finland, women had a slightly higher risk for sputum production and chronic productive cough than men. Women have been shown to be more vulnerable to tobacco smoke and more susceptible to respiratory symptoms than men, although the reasons underlying this gender difference remain obscure (Langhammer et al. 2003). Family history of obstructive airway diseases doubled the risk for chronic productive cough in all three countries (Study III: Table 5). Recently, in a Swedish study, a family history of chronic bronchitis was found to be a significant risk factor for chronic bronchitis or COPD, with an OR of 2.80 (Nihlén et al. 2003). Besides genetic factors, this increased risk may be due to shared environmental and socio-economic factors, perhaps also to exposure to environmental tobacco smoke in families with members that have chronic obstructive lung disease.

Socio-economic risk factors associated with the main occupation revealed low socio-economic status to be a significant risk factor for respiratory symptoms in all three countries. This low socio-economic group comprises manual workers in industry and in service, including many occupations, such as cleaners, with a well-known risk for asthma (Kogevinas et al. 1999, Karjalainen et al. 2001, Zock et al. 2002). Our findings confirmed that being a manual worker was associated with an increased risk for the respiratory symptoms common in asthma and chronic bronchitis independently of smoking habits. A similar increased risk for bronchitic symptoms among manual workers has been found in northern Sweden (Lundbäck et al. 2001). Occupational exposures are often underestimated in asthma and frequently remain undetected in chronic bronchitis. Socio-economic status also includes factors other than occupation, such as housing, diet, economic position, educational level and environmental factors. In low socio-economic groups, housing conditions may be poorer and the home environment may be situated in more polluted areas than in higher socio-economic groups. Further, smoking is more common in low socio-economic groups, and exposure to environmental tobacco smoke is therefore also more likely. Many risk factors are thus clustered in low socio-economic groups, and their effects may be additive.

Recently, in a large study from Sweden, a reduced risk for allergic rhinitis was found for those conscripts who were raised on a farm or in a rural environment (Bråbäck et al. 2004). In our study, childhood environment

was assessed by asking whether the subject had resided in the countryside, in a suburban environment or in town during the first five years of life. Thus, living on a farm was not specifically enquired about. In risk factor analysis, urban living yielded an increased risk for sensitization to pollens, but not to animals. A clearer difference between the groups might have been emerged had we enquired about farm living, but otherwise our findings are consistent with earlier results.

6.2.3 Asthma, chronic bronchitis and respiratory symptoms in relation to earlier studies

Respiratory symptoms in Sweden were somewhat more common than previously reported (Lundbäck et al. 1991, Larsson et al. 1993). The prevalence of physician-diagnosed asthma in Sweden, 7.8%, was similar, and physician-diagnosed chronic bronchitis, 3.1%, lower than in the OLIN studies (Lundbäck et al. 1993, Rönmark et al. 1997). In Finland, the prevalence of asthma was higher than in earlier studies (Alanko 1970, Heinonen et al. 1987, Haahtela et al. 1990, Varjonen et al. 1992, Isoaho et al. 1994, Hedman et al. 1999). In the study by Hedman et al. (1999) based on 3102 responses to a mailed questionnaire from subjects aged 18–65 years, physician-diagnosed asthma was reported by 5.3%. The prevalence of physician-diagnosed chronic bronchitis in their study was exactly the same, 3.7%, as our result from Helsinki, but clearly lower than in the study by von Hertzen et al. (2000) and in earlier studies from the 1960s (Huhti 1965). In Finland, chronic bronchitis was more common than asthma some decades ago. Since then, however, asthma has become more prevalent; some of the conditions that may earlier have been diagnosed as chronic bronchitis may today be diagnosed as asthma. In Estonia, the prevalence of asthma was similar to that in the ECRHS, but the prevalence of chronic bronchitis was higher than in the 1980s (Utkin et al. 1989, ECRHS 1996).

Respiratory symptoms in Helsinki were surprisingly common; nearly one-third of subjects had sputum production, one-quarter had tightness in the chest awakening and one-fifth wheezing. An alarming prevalence of symptoms was also found in subjects with diagnosed obstructive airway diseases. The goals of asthma management were not achieved with more than 70% of asthmatics suffering from attacks of shortness of breath and wheezing during the previous year in Helsinki (Dahl and Bjermer 2000, Haahtela et al. 2001). Similarly, a comparison of asthma management across Europe revealed that asthma control was suboptimal in each of the seven countries evaluated, including Sweden (Vermeire et al. 2002). Our comparison of symptom levels in subjects reporting asthma showed no differences in levels of wheezing or attacks of shortness of breath between countries, but symptom levels overall were very high, suggesting undertreatment in all three countries (Table 6).

Bronchitic symptoms were also common in the age group 20–64 years; chronic productive cough was reported by 11.0% in Finland, 9.4% in Estonia and 6.2% in Sweden. Levels of sputum production and chronic productive cough were higher among those who reported having chronic bronchitis in Finland than in Sweden and Estonia, which also suggests undertreatment (Table 6). Bronchitic symptoms have been even more common in Finland in earlier studies (Huhti 1965, von Hertzen et al. 2000). In both of these studies, the prevalence of chronic bronchitis in men was more than 20% and in women 5.5–7%. The high prevalence in men during the 1960s was influenced by the high prevalence of smoking at that time and smoking being even more common before the 1960s. The high prevalence in the study by von Hertzen et al. (2000) was probably due to the inclusion of older subjects than ours; the prevalences of chronic bronchitis and COPD rise steeply with older age (Lundbäck et al. 2003b).

Respiratory symptoms were associated with smoking and increasing age. Recently, a study from Norway showed beneficial effects of smoking cessation on several asthma- and chronic bronchitis-related respiratory symptoms (Eagan et al. 2004). In the same study, increasing age, heavier smoking history and prior exposure to fumes or dusts predicted lower alleviation of symptoms. The most common irritant factor causing respiratory symptoms in Helsinki was dust, as also reported in an earlier study in Finland (Heinonen et al. 1987). Dust and tobacco smoke were the most common irritants in each capital, while symptoms associated with exposure to pollens or animals were reported less frequently in Tallinn than in Helsinki or Stockholm. This could be explained by sensitization to pollen and furred animals being less common in Tallinn (Raukas-Kivioja et al. 2003).

6.2.4 Allergic sensitization in Helsinki

Allergic sensitization was common in our study, 47%, with men more often being sensitized than women. The majority of young adults aged 26–39 years were sensitized to at least one allergen, with 42% of sensitized individuals responding to multiple allergens. Similarly in the ECRHS, IgE levels decreased with age and were higher in men (Burney et al. 1997). In an earlier study on skin-prick test reactivity, a relationship between reactivity and age was apparent, with the peak prevalence of reactivity (more than 40%) occurring during the third decade (Barbee et al. 1976). The FinEsS study results from Tallinn also showed the youngest subjects most often being sensitized (Raukas-Kivioja et al. 2003). Sensitization to multiple allergens was strongly associated with physician-diagnosed asthma, wheezing and allergic rhinoconjunctivitis, which was a very interesting feature and in concordance with clinical experiences. Multiple sensitization has earlier been associated with BHR in adults (Kerkhof et al. 2003). The prevalence of asthma rose with an increasing number of positive skin-prick test responses, a finding previously demonstrated in children (Sears et al. 1993). The prevalence of

allergic rhinoconjunctivitis also rose with an increasing number of positive skin-prick test responses, which has been shown in children as well (Sears et al. 1993). Urban living during childhood yielded an increased risk for allergic sensitization, concordant to earlier results of a childhood farm environment being protective against allergic sensitization in adulthood (Kilpeläinen et al. 2000, Leynaert et al. 2001).

The distribution of responses to different allergens was similar to earlier studies in Finland, with dogs, cats, birch and timothy being the most common sensitizers (Vartiainen et al. 2002). Surprisingly, 10% of subjects were sensitized to cockroaches, although these are not found in homes in Helsinki. Similarly, in an earlier study from eastern Finland 7.2% of participants had positive responses to cockroaches in skin-prick tests (Vartiainen et al. 2002). The cockroach was also found to be the most common sensitizer in Estonia, and sensitization to the cockroach was significantly associated with respiratory symptoms common in asthma (Raukas-Kivioja et al. 2003). Reactions to cockroaches could be the result of cross-reactivity to house dust mites or storage mites (Sidenius et al. 2001). Possibly, some of the sensitization to storage mites and cockroaches could have happened abroad, for example, in Spain, which is a popular travel destination. Storage mites are common sensitizers in Spain, as are house dust mites (Vidal et al. 2004). In our study, often subjects with positive responses to cockroaches had vacationed in Spain. Similarly, in a recent report on subjects with sensitization to house dust mites in Reykjavik, no significant exposure in subjects` homes could be verified, and the authors suspected exposure abroad or an unidentified exposure in an environment other than the home (Hallas et al. 2004).

7 Conclusions

1. Respiratory symptoms were common in the adult population of Helsinki. Compared with earlier Finnish studies, a higher prevalence of physician-diagnosed asthma, 6.6%, and a lower prevalence of physician-diagnosed chronic bronchitis, 3.7%, were found in Helsinki. Family history of asthma was the strongest risk factor for physician-diagnosed asthma (OR 3.3). Female gender also yielded an increased risk for asthma (OR 1.3). A considerable underdiagnosis of chronic bronchitis was noted; only 19% of those reporting chronic productive cough had physician-diagnosed chronic bronchitis. The risk factors for chronic productive cough were smoking, family history of obstructive airway disease, age >44 years and being a manual worker.

2. The comparison between Helsinki, Stockholm and Tallinn in subjects aged 20–64 years revealed physician-diagnosed asthma to be most common in Stockholm, 7.6%, while the prevalence in Helsinki was 6.2% and in Tallinn 2.3%. Asthma-related symptoms were, however, most common in Tallinn. Physician-diagnosed chronic bronchitis showed an inverse pattern, with prevalences of 10.6% in Tallinn, 3.4% in Helsinki and 3.0% in Stockholm. Chronic productive cough was most common in Helsinki. Subjects with symptoms commonly occurring in asthma were more likely to have a diagnosis of asthma in Helsinki and Stockholm than in Tallinn; the diagnosis of chronic bronchitis was favoured in Tallinn.

3. Comparison of all data on subjects aged 20–64 years in Finland, Sweden and Estonia revealed that belonging to the socio-economic group of manual workers was associated with an increased risk for chronic respiratory symptoms independently of smoking habits in each country. Comparison of risk factor profiles for respiratory symptoms between the countries showed a similar pattern, except that Estonian women were at higher risk than the others.

4. Comparison of diagnostic practices revealed a higher likelihood of asthma diagnosis and a lower likelihood of chronic bronchitis diagnosis in relation to respiratory symptoms in Finland and Sweden than in Estonia, suggesting a difference in diagnostic labelling between Estonia and the two other countries. The results indicate that asthma was considerably underdiagnosed in Estonia.

5. The prevalence of allergic sensitization in Helsinki was high, with 47% of subjects aged 26–60 years and 57% of subjects aged 26–39 years being sensitized to at least one allergen. Multiple sensitization was surprisingly common among the youngest age group (26–39 years), with 42% of the sensitized having at least four responses in skin-prick tests, while only 16% of those aged 50–60 years were multisensitized. Multiple sensitization was strongly associated with asthma, wheezing and allergic rhinoconjunctivitis.

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Appendix 1

FinEsS-questionnaire in Finnish

	Kyllä	Ei / En tiedä
1. Onko jollakin **vanhemmistasi** tai **sisaruksistasi** ?		
a) astmaa	☐	☐
b) allergista nuhaa (esim. heinänuhaa) tai allergista silmävaivaa	☐	☐
c) kroonista keuhkoputkentulehdusta tai keuhkonlaajentumaa	☐	☐
2. Onko **Sinulla** nyt tai onko Sinulla ollut aiemmin ?		
a) astmaa	☐	☐
b) allergista nuhaa (esim. heinänuhaa) tai allergista silmävaivaa	☐	☐
c) kroonista keuhkoputkentulehdusta tai keuhkonlaajentumaa	☐	☐
d) muu keuhko- tai hengityselinsairaus, mikä ? kirjoita vastaus tähän:		
3. Onko lääkäri todennut **Sinulla** olevan astmaa ?	☐	☐
4. Onko lääkäri todennut Sinulla olevan kroonista (pitkäaikaista) kroonista keuhkoputkentulehdusta tai keuhkonlaajentumaa ?	☐	☐
5. Käytätkö astmalääkkeitä ? Mitä lääkettä:	☐	☐
6. Onko Sinulla ollut astmaoireita nykyisin tai viimeisen 10 vuoden aikana ? (ajoittain hengenahdistusta tai hengenahdistuskohtauksia, samanaikaisesti voi olla yskää tai hengityksen vinkumista)	☐	☐
Jos vastasit kyllä:		
a) Onko sinulla ollut astmaoireita viimeisten 12 kuukauden aikana ?	☐	☐
7. Onko Sinulla ollut viime vuosina pitkäaikaista yskää ?	☐	☐
8. Nouseeko yskiessä keuhkoistasi yleensä limaa tai onko keuhkoissa limaa, jota on vaikea saada irtoamaan ?	☐	☐
Jos vastasit kyllä:		
a) onko limaa noussut useimpina päivinä vähintään kolmen peräkkäisen kuukauden aikana?	☐	☐
b) onko tällaisia vähintään kolmen kuukauden limannousujaksoja ollut vähintään kahtena peräkkäisenä vuonna?	☐	☐
9. Onko tavallista, että keuhkoissa hengityksesi rahisee äänekkäästi tai vinkuu?	☐	☐
10. Onko sinulla ollut hengityksen vinkunaa kertaakaan viimeisen 12 kuukauden aikana ?	☐	☐
Jos vastasit kyllä:		
a) oliko Sinulla ollenkaan hengenahdistusta vinkunan yhteydessä ?	☐	☐
b) oliko Sinulla hengityksen vinkunaa vaikka et ollut flunssassa ?	☐	☐

	Kyllä	Ei / En tiedä
11. Oletko viimeisten 12 kuukauden aikana herätessäsi kertaakaan kokenut hengityksesi olevan tukossa (keuhkoissa)?	☐	☐
12. Hengästytkö tai joudutko hengästymisen vuoksi kävelemään hitaammin kuin muut, kun kävelet ikäistesi henkilöiden kanssa tasamaalla normaalivauhdilla?	☐	☐
13. Saatko hengenahdistusta, hengityksen vinkunaa tai vaikeita yskänpuuskia?		
a) rasituksessa	☐	☐
b) kylmässä	☐	☐
c) pakkasessa rasituksen yhteydessä	☐	☐
d) pölyisissä olosuhteissa	☐	☐
e) tupakansavusta	☐	☐
f) autojen pakokaasuista	☐	☐
g) voimakkaista tuoksuista (esim. deodorantit, mausteet, painomuste, puhdistusaineet, kukkien tuoksut tms.)	☐	☐
h) kasvien tai puiden siitepölyistä	☐	☐
i) ollessasi tekemisissä eläinten kanssa	☐	☐
14. Tupakoitko tai poltatko piippua tai sikareita?	☐	☐
(vastaa **kyllä** vaikka olisitkin lopettanut viimeisten 12 kuukauden aikana)		
Jos vastasit kyllä:		
a) Kuinka monta savukellista, sätkää, sikaria tai piipullista olet polttanut ***keskimäärin vuorokaudessa***? a) vähemmän kuin 5 kpl	☐	☐
b) 5-14 kpl	☐	☐
c) 15 kpl tai enemmän	☐	☐
Jos vastasit ei:		
b) Oletko aiemmin ollut tupakoitsija, mutta lopetit yli vuosi sitten?	☐	☐
15. Missä ammatissa olet **pääasiassa** toiminut?		
kirjoita vastaus tähän:		
a) montako vuotta olet yhteensä ollut tässä työssä: vuotta		
16. Onko Sinulla nykyisin muu työ tai tehtävä (muu ammatti, opiskelu, työtön, kotityö, eläke, sairauseläke tms.)?		
jos on niin mikä?, kirjoita vastaus tähän:		
a) montako vuotta olet yhteensä ollut tässä työssä, eläkkeellä, tms.: vuotta		
17. Onko nykyinen työsi pääasiassa a) ulkotyötä?	☐	☐
b) sisätyötä?	☐	☐
18. Kuinka monta vuotta ***yhteensä*** olet ollut pääasiassa ulkotyössä? vuotta		
19. Oliko a) äitisi tupakoitsija lapsuutesi aikana?	☐	☐
b) isäsi tupakoitsija lapsuutesi aikana?	☐	☐
20. Oletko tai oletko ollut kilpahiihtäjä tai säännöllinen kuntohiihtäjä?	☐	☐

VASTAA TARKASTI - KIITOKSET AVUSTASI!

päiväys: puhelinnumerosi:

Allekirjoitus:

Appendix 2

FinEsS-questionnaire in English

	Yes	No / I don't know
1. Have any of your parents, brothers or sisters ?		
a) asthma	☐	☐
b) allergic eye-/nose catarrh (hay fever)	☐	☐
c) chronic bronchitis or emphysema	☐	☐
2. Have you now or have you had any of the following diseases ?		
a) asthma	☐	☐
b) allergic eye-/nose catarrh (hay fever)	☐	☐
c) chronic bronchitis or emphysema	☐	☐
d) any other lung or airways diseases - if "yes", which ?	☐	☐
3. Have you been diagnosed by a doctor as having asthma ?	☐	☐
4. Have you been diagnosed as having chronic bronchitis or emphysema by a doctor?	☐	☐
5. Do you currently use asthma medicines (permanently or as needed)?:	☐	☐
6. Have you now or have you had asthma symptoms during the last 10 years (intermittent breathlessness) or attacks of breathlessness? The symptoms may exist simultaneously with or without cough or wheezing.	☐	☐
If "yes":		
a) Have you had these symptoms during the last year (the last 12 months) ?	☐	☐
7. Have you had longstanding cough during the last years?	☐	☐
8. Do you usually have phlegm when coughing, or do you have phlegm which is difficult to bring up?	☐	☐
If "yes":		
a) do you bring up phlegm on most days during periods of at least successive three months?	☐	☐
b) Have you had such periods during at least two successive years?	☐	☐
9. Have you had wheezing, whistling, or a noisy sound in your chest when breathing?	☐	☐
10. Have you had wheezing or whistling in your chest at any time in the last 12 months?	☐	☐
If "yes":		
a) Have you been at all breathless when the wheezing noise was present ?	☐	☐
b) Have you had this wheezing or whistling when you did not have a cold ?	☐	☐
11. Have you awakened with a feeling of tightness in your chest at any time in the last 12 months?	☐	☐
12. Do you have to walk slower than other people of your age on the level because of breathlessness?	☐	☐

	Yes	No / I don't know
13. Do you usually have breathlessness, wheeze, or severe cough:		
a) on effort	☐	☐
b) in cold weather	☐	☐
c) on effort in cold weather during winter	☐	☐
d) in dusty places	☐	☐
e) from cigarette or tobacco smoke	☐	☐
f) from car exhaust fumes	☐	☐
g) from strong smelling scents (perfumes, spices, printing ink, cleaner,strong smelling flowers)	☐	☐
h) from pollens	☐	☐
i) from animal with fur (cat, dog, horse,cow)	☐	☐
14. Do you smoke? (Smokers also include those who smoke a few cigarettes or pipe fills a week, and those who have stopped smoking during the last 12 months)	☐	☐
If "yes":		
a) How many cigarettes do you smoke per day?		
a) less than 5	☐	☐
b) 5-14	☐	☐
c) 15 or more	☐	☐
If "no":		
b) Have you been a smoker, but have stopped smoking more than a year ago?	☐	☐

15. What has been your main work/occupation?
Please, write your answer here:
a) How many years have you been working in this occupation?: years

16. Have you now another work/occupation (other work/profession, studies, unemployed, house-wife, retired, sickness pension etc.)?
Please, write your answer here:
a) if you have another work etc., since how many years?

In addition, questions about working outdoors or indoors, being exposed to environmental tobacco smoke during childhood, and skiing habits were asked in the Finnish version of the FinEsS questionnaire.

Appendix 3

Brief description of socio-economic classification by Statistics Sweden

1 (11-12) Unskilled and semi-skilled workers
2 (21-22) Skilled workers
2 (33-36) Assistant non-manual employees
3 (44-46) Intermediate non-manual employees
4 (54-60) Employed and self-employed professionals, higher civil servants and executives
5 (76-87) Self-employed (other than professionals)

11-22 MANUAL WORKERS

11 *Unskilled employees in goods production*: occupations involving the production of goods and normally requiring less than two years of post-comprehensive school education
12 *Unskilled employees in service production*: occupations involving service production and normally requiring less than two years of post-comprehensive school education
21 *Skilled employees in goods production*: occupations involving the production of goods and normally requiring two years or more of post-comprehensive school education
22 *Skilled employees in service production*: occupations involving service production and normally requiring two years or more of post-comprehensive school education

33-57 NON-MANUAL EMPLOYEES

33 *Assistant non-manual employees, lower level*: occupations normally requiring less than two years of post-comprehensive school education
34-35 *Assistant non-manual employees, higher level*: occupations normally requiring two, but not three, years of post-comprehensive school education
44-45 *Intermediate non-manual employees*: occupations normally requiring three, but not six, years of post-comprehensive school education
54-55 *Professionals and other higher non-manual employees*: occupations normally requiring at least six years of post-comprehensive school education
57 *Upper-level executives*: Upper-level executives in private enterprises or organisations with at least 100 employees or upper-level executives in public service

60-87 SELF-EMPLOYED (including farmers)

101-687 OTHERS: students, housewives, pensioners, unemployed, conscripts