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Asthma and Rhinitis among Adults in Sweden and China

Risk Factors in the Home Environment

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Abstract

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The main aim of this thesis was to evaluate associations between selected home environment factors and asthma, rhinitis and respiratory symptoms among adults from Sweden, China and northern Europe. Two studies were performed in Sweden, one in China, and one longitudinal cohort study was performed in northern Europe. Dampness/mould was common, and was a main risk factor in all studies. Other risk factors for asthma symptoms in Sweden included window pane condensation in winter, multi-family buildings constructed from 1961-1975, rented apartments, environment tobacco smoke (ETS), and living in a colder climate zone. Higher ventilation flow in Sweden was associated with less asthma symptoms. Risk factors for rhinitis in Sweden included window pane condensation, a higher moisture load, concrete slab foundation constructed before 1991, multi-family buildings constructed from 1976-1985, rented apartments and living in densely populated areas. Risk factors for rhinitis in China included window pane condensation, recent redecoration, new furniture, presence of cockroaches, pet keeping, ETS and living near a main road or highway. Frequently cleaning of the home and putting beddings to sunshine were protective factors for rhinitis in China. Other risk factors for respiratory infections in Sweden included houses with a brick façade, window pane condensation, a higher moisture load, multi-family buildings constructed from 1976-1985, rented apartments and living in densely populated areas. Furthermore, dampness and mould, and mould odour were risk factors for onset of asthma and rhinitis in northern Europe. In conclusion, indoor dampness and mould can be a risk factor for asthma and rhinitis in Sweden, China and northern Europe. Certain construction years (1961-1985), ETS, recent redecoration, new furniture, living in urban areas and exposure to traffic air pollution can be risk factors for asthma, rhinitis or respiratory infections. A high ventilation flow and daily cleaning at home can be protective.

Keywords: Rhinitis, Asthma, Home, Dampness, Mould, Ventilation

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If you’re walking down the right path,
and you’re willing to keep walking,
eventually you’ll make progress.

Barack Obama

To my family
致我亲爱的家人

List of Papers

This thesis is based on the following papers, which are referred to in the text by their Roman numerals.

I. Wang J, Li B, Yu W, Yang Q, Wang H, Huang D, Sundell J, Norbäck D. Rhinitis symptoms and asthma among parents of preschool children in relation to the home environment in Chongqing, China. PLoS One. 2014 Apr 14;9(4):e94731

II. Wang J, Engvall K, Smedje G, Norbäck D. Rhinitis, asthma and respiratory infections among adults in relation to the home environment in multi-family buildings in Sweden. PLoS One. 2014 Aug 19;9(8):e105125.

III. Wang J, Engvall K, Smedje G, Nilsson H, Norbäck D. Current wheeze, asthma, respiratory infections, and rhinitis among adults in relation to inspection data and indoor measurements in single-family houses in Sweden-The BETSI study. Indoor Air. 2017 Jul 27(4):725-736.

IV. Wang J, Pindus M, Janson C, Jogi R, Sigsgaard T, Kim JL, Holm M, Sommer J, Orru H, Gunnbjörnsdottir M, Gislason T, Johannessen A, Bertelsen RJ, Norbäck D. Adult onset and remission of respiratory symptoms, asthma and rhinitis in relation to dampness, mould and odour: the RHINE cohort. (submitted)

Contents

Abbreviations

ASHRAE	American Society of Heating, Refrigerating and Air-Conditioning Engineers
BETSI	Building Energy, Technical Status and Indoor Environment
BMI	Body mass index
CCHH	China, Children, Homes, Health
CI	Confidence interval
CO	Carbon monoxide
CO_2	Carbon dioxide
ETS	Environment tobacco smoke
ECRHS	The European Community Respiratory Health Survey
ISAAC	The International Study of Asthma and Allergies in Childhood
MVOC	Microbial volatile organic compounds
NO_x	Nitrogen oxide
NO_2	Nitrogen dioxide
OR	Odds ratio
O_3	Ozone
PM	Particulate matter
$PM_{2.5}$	Particulate matter<2.5 µm in diameter
PM_{10}	Particulate matter<10 µm in diameter
PVC	Polyvinyl chloride
RH	Relative air humidity
RHINE	Respiratory Health in Northern Europe
RRR	Relative risk ratio
SCB	Statistics Sweden
SES	Socio-economic status
SPT	Skin prick test
TRAP	Traffic-related air pollution

Introduction

Asthma and rhinitis

Asthma is a common chronic inflammatory airway disease. It is characterized by variable and recurring symptoms of wheezing, coughing, chest tightness, and shortness of breath, and by variable airflow limitation [1]. Rhinitis is a nasal disease linked to irritation and inflammation of the nasal mucosa. The main rhinitis symptoms are stuffy nose, runny nose and sneezing [2]. Asthma and rhinitis are often classified as of allergic or non-allergic nature. However, there can be a mixture of allergic and non-allergic rhinitis [3]. One study including 975 rhinitis patients, showed that allergic rhinitis, non-allergic rhinitis and mixed rhinitis accounted for 43%, 23%, and 34%, respectively [4].

There is a large variation of the asthma prevalence globally [1]. Epidemiological studies have reported that asthma affects 1-18% of the population in different countries [1]. The highest adult asthma prevalence (6.0%-12.0%) can be found in developed western countries [5]. Asthma continues to increase, especially in low and middle income countries [5, 6]. A Swedish study conducted in Stockholm in 2007 reported a prevalence of 9.3% asthma among adults [7]. In west Sweden, the prevalence of asthma for adults was 8.3% in 2008 [8]. A third Swedish study found that adult asthma had increased slightly from 6.0% in 1990 to 8.0% in 2008 among Swedish young adults [9]. A much lower prevalence of adult asthma were reported in Chinese studies: 1.5% of urban adults across China had mild asthma [10], 1.8% of adults from Shanghai had physician diagnosed asthma [11], and 0.67% of adults from rural Beijing had asthma symptoms [12]. Two national surveys in China reported that the asthma prevalence among children aged 0-14 years had increased from 0.91% in 1990 to 1.5% in 2000 and from 1.59% to 2.11% from 2000 to 2010 [13, 14]. A multi-centre study performed during 2010-2011 among preschool children found higher prevalence of doctor diagnosed asthma (3.5%-9.9%) [15, 16]. We found no previous studies on time trend of adult asthma in China, but since preschool children nowadays have a relatively high prevalence of asthma [15, 16], we can expect an increase of asthma among adults in the furture in China.

It has been estimated that 10%-20% of the population in USA and Europe has allergic rhinitis [17]. In Sweden, the prevalence of allergic rhinitis increased from 22% to 31% from 1990 to 2008 among adults [9]. Another Swedish study found an increase of adult allergic rhinitis from 12.4% in 1992 to 15% in 2000 [18]. A third Swedish cohort study reported that the prevalence of adult allergic rhinitis was unchanged (28%) from 1996 to 2006 [19]. Chinese studies have reported an increase of allergic rhinitis from 2004-2005 to 2008 in two cities: from 13.3% to 30.3% in Nanjing, and from 24.1% to 37.9% in Urumqi [20]. It has been estimated that non-allergic rhinitis among adolescent/adult population is at least 25% [21]. Little information is available on time trends of non-allergic rhinitis.

Asthma and allergic rhinitis commonly coexist. A Swedish population-based study found that 64% of those with asthma had allergic rhinitis and 20% of those with allergic rhinitis had asthma [22]. A cohort study found that asthma symptoms at baseline increased the incidence of allergic rhinitis and decreased the remission [18]. Moreover, allergic rhinitis is a risk factor for the development of asthma [23]. Impaired nasal function can affect the lower airways of asthmatic patients [24]. It has been proposed in the 'united airways' hypothesis that asthma and allergic rhinitis have common pathologic and physiologic origin [25] with similar involvement of airway epithelial cells [26].

Gender differences in adult asthma and rhinitis

Asthma is more common among males during childhood, but becomes more prevalent among females after puberty [27, 28]. Adult asthma is more common among females, it has been demonstrated in many population-based studies worldwide [29-31]. It was concluded in two recent reviews that the prevalence of allergic rhinitis is higher among males in childhood, but changed to a female predominance in adolescents [32, 33]. Those two reviews both concluded that there is no sex-specific prevalence difference for allergic rhinitis among adults [32, 33].

The role of own tobacco smoking for adult asthma and rhinitis

Active smoking is related to more common respiratory symptoms among adults [34-36], these symptoms could be due to the direct effect from smoking. Moreover, smoking can be associated with bronchial hyperresponsiveness, a marker of asthma [37]. Incident asthma was more common among current smokers in Sweden [38]. Male and female ex-smokers and female smokers had increased risk of asthma-onset in a retrospective population study in Sweden, which indicates a possible association between tobacco smoking and development of asthma [39]. One large cohort study from USA found that active smoking increased the risk of asthma onset in adulthood [40]. Based on eight studies among adults, a review conclude that smokers were 1.6 times more likely to develop asthma than non-smokers [41]. Moreover, there can be interaction between genes and active tobacco smoking in the development of asthma among adults [42]. One recent meta-analysis concluded that smoking may be causally related to increased risk of asthma, but slightly decreased the risk of hay fever [43]. Two other recent reviews concluded that tobacco smoking has no effect on allergic rhinitis [44, 45].

The role of environmental tobacco smoke (ETS) for adult asthma and rhinitis

The literature shows that ETS (passive smoking) is related to respiratory symptoms, asthma, impaired lung function and increased bronchial responsiveness [46]. Among non-smokers, passive smoking in the workplace was associated with respiratory symptoms, current asthma and bronchial hyperresponsiveness in a multi-centre cross-sectional study [47]. One large longitudinal population study found that passive smoking among non-smokers increased the risk of development of asthma in adulthood [40]. A systematic review concluded that passive smoking is a risk factor for allergic rhinitis among adults [45]. Another review including only prospective cohort or case-control studies found that the majority of the studies showed positive associations between passive smoking and adult allergic rhinitis [48].

Risk factors and protective factors

The increase of asthma, rhinitis and allergic disease seems to be linked to the economic development of the country [49, 50]. Nowadays, the increase of wheeze and allergic rhinoconjunctivitis is most pronounced among children in middle-income countries, especially in Asia [50, 51]. Since allergic sensitization is an important risk factor for the development of allergic asthma and rhinitis [52, 53], factors causing an increased risk of IgE mediated allergy in childhood will increase the prevalence of adult asthma and rhinitis when the children become adults.

The specific causes linked to the increase of asthma and rhinitis observed in many countries remains unclear. In principle, the increase can be linked to an increase of risk factors or a decrease of protective factors. It has been suggested that prenatal or early life exposure to chemicals [54, 55], lack of early life exposure to microbial compounds postulated to be protective ("the hygiene hypothesis") [56-58] or the change of diet in the modern society [59, 60] can explain the observed increase. Indoor [61, 62] and outdoor [49, 63] environmental exposure can contribute to the increase of asthma and rhinitis. Since we spend around two third of our time at home [64], the home environment is an important indoor environment. Risk factors at home include allergens, dampness and mould [65], insufficient ventilation [66], and chemical emissions from building materials [67].

Indoor allergens

House dust mites, cockroaches and animals are common allergen sources in the home environment [68]. Domestic allergens can aggravate asthma and allergic rhinitis among sensitized occupants [68, 69]. Der p 1, Der f 1 and Der p 2 are the major house dust mite allergens. Common cockroach allergens include Bla g 1, Per a 1, and Bla g 2. The main cat allergen is Fel d 1, and the main dog allergen is Can f 1. Moreover, allergen Mus m 1 from mouse and Rat n 1 from rat has been detected in the home environment [68].

Pollen from trees, grasses and weeds in the outdoor air can enter the indoor environment through ventilation, contaminated clothes or contaminated pets. Most indoor plants do not flower and are therefore not indoor pollen sources. Allergens in the leaves of *Ficus benjamina* (weeping fig) can cause allergic asthma and rhinitis [70].

Cladosporium sp., *Penicillium sp.*, *Aspergillus sp.*, and *Alternaria sp*. are the most commonly detected allergenic mould in homes. The main *Cladosporium* allergen are Cla h 8 and Cla h 6. The major allergens in *Penicillium sp*. include the serine proteases Pen ch 13 and Pen ch 18. The major allergen in *Aspergillus sp.* is Asp f 1, and the main *Alternaria* allergen is Alt a 1.

Associations with dampness and indoor mould for adult asthma and rhinitis

Building dampness can increase the occurrence of house dust mites [71], microbial agents [72], bacteria [72], microbial volatile organic compounds (MVOC) [72] and even chemical emissions due to degradation of building materials [67]. Signs of dampness and mould includes water leakage/damage, visible mould growth, mould odour and bubbles/discoloration of floor materials. Review articles have concluded that indoor dampness-related factors are consistently associated with current asthma and asthma-like symptoms including wheeze and cough [65, 73]. Moreover, dampness and mould in homes can be related to increased doctor diagnosed asthma [73] and increased asthma incidence [61]. A systematic review with meta-analysis concluded that indoor dampness and mould can increased the risk of rhinitis [62]. However, most of the studies cited in these review articles are on children. We found some studies among adults, mostly prevalence studies. A Swedish case-control study demonstrated associations between damp dwellings, especially dampness in the floor construction, and increased current asthma among young adults [74]. One study from Finland found that moisture in dwellings was associated with nocturnal dyspnoea among adults [75]. Another study from Finland showed that visible signs of moisture damage in dwellings were associated with wheeze among adults [76]. One study from Norway found that mould or water damage at home was associated with doctor diagnosed asthma and wheeze [77]. A longitudinal multi-centre study from Europe found that water damage and indoor mould were risk factors for new onset of adult asthma [78]. Moreover, dampness in dwellings in Sweden was found to be related to a higher prevalence of adult hay fever [79]. One study from Finland found that mould in homes was related to adult rhinitis [75]. Another study from Finland reported that home dampness and mould was associated with allergic rhinitis and rhinitis among adults [80].

Associations with mould odour for adult asthma and rhinitis

Indoor microbial growth can lead to mould odour. Mould odour can be produced by mould or bacteria, but also from the degradation of chlorophenols in wood preservatives to chloroanisoles [81]. One review on associations between building dampness and incidence of asthma concluded that mould odour at home had the strongest health association [61]. Another review concluded that among different dampness indicators mould odour had the strongest association with rhinitis [62]. However, most of the studies included in these reviews were on children. We found only three studies among adults. One study found that mould odour in Swedish homes was related to adult asthma symptoms [79]. Indoor mildew odour or musty smell was associated with an increase of asthma symptoms and rhinitis symptoms among American adults [82]. Moreover, mould odour at home was related to a higher prevalence of hay fever among Swedish adults [79, 83].

Associations with window pane condensation for adult asthma and rhinitis

Window pane condensation in winter can be a sign of insufficient ventilation or high air humidity in a cold climate. One study from Stockholm found that window pane condensation in winter was related to higher indoor relative air humidity and increased levels of house dust mite allergens [84]. A few studies have reported associations between window pane condensation and asthma/rhinitis symptoms in adults. One cohort study demonstrated that window pane condensation in winter at home was a risk factor for incidence of asthma symptoms among Swedish civil aviation pilots [85], and prevalence of wheeze symptoms among Japanese university students [86]. Moreover, window pane condensation in winter has been associated with a higher prevalence of asthma symptoms among Japanese schoolchildren [87]. Moreover, one Japanese study found that window pane condensation in homes was associated with adult nasal symptoms [88]. Another Japanese study among schoolchildren (12-15 y) reported a positive association between window pane condensation at home and the prevalence of pollen allergy [89].

Associations with ventilation, type of ventilation system, air exchange rate and adult asthma and rhinitis

Ventilation is an important indoor factor since it helps to remove indoor pollutants. Window opening or installation of a mechanical ventilation system are the main measures to increase ventilation. In workplace buildings, a higher ventilation flow has been shown to be associated with less asthma and asthma-related symptoms [66]. According to the ASHRAE standard, indoor CO_2 should not exceed 1000 ppm [90]. The Swedish national standard recommends that the air exchange rate in homes should not be less than 0.5 air changes per hour (h(-1)) [91]. There are few studies on associations between home ventilation flow and adult asthma or rhinitis. One Chinese study reported that frequent window opening at home was associated with less rhinitis symptoms among adults [92]. As compared with nature ventilation only, adults living in homes with a mechanical ventilation system had less nasal symptoms [93]. We found no studies on associations between measured air exchange rate in homes and adult asthma or rhinitis.

Associations with indoor painting, renovation, new furniture and adult asthma and rhinitis

Indoor painting [94], renovation, new materials or new furniture and plastic materials [95] can emit chemicals to the indoor environment [96]. One review concluded that new furniture, plastic materials, painting and renovation can be risk factors for respiratory or allergic health among infants/children [96]. However, few studies existed on associations between such chemical emissions in homes and adult asthma/rhinitis.

One review on respiratory health effects of emissions from domestic paints concluded that indoor painting was associated with wheeze among children, but could not draw any conclusions on adults [97]. Few studies exist on associations between indoor painting and adult asthma or rhinitis. Recent indoor painting in Swedish homes was associated with an increased prevalence of asthma symptoms among adults [94]. Another Swedish study showed that indoor painting in the dwelling was related to rhinitis symptoms among adults [98]. Moreover, recent indoor painting at home was associated with more asthma symptoms among Japanese schoolchildren (12-15 years) [87].

In China, indoor painting is usually combined with home renovation. One Chinese study including mainly adults found that home renovation was a risk factor for allergic rhinitis [99]. Another Chinese study among women only showed that home renovation was associated with a higher prevalence of allergic rhinitis [100]. New floor materials in Japanese homes were associated with night time attacks of breathlessness among schoolchildren aged 12-15 years [87]. Chinese studies have shown that new furniture can emit chemicals, including formaldehyde [101-103]. We have found no previous studies on emissions from new furniture and adult asthma/rhinitis. However, new furniture at home was associated with asthma among school children in Russia [104], wheeze and asthma among Chinese school children [103, 105].

We have found no previous studies on associations between type of floor materials and asthma/rhinitis in adults. A few studies exist among children. Polyvinyl chloride (PVC) flooring at home in Sweden was associated with increased asthma incidence in children [106, 107]. The presence of linoleum floors in Russian homes was related to an increased prevalence of wheeze and asthma among schoolchildren [104].

The role of urbanization and outdoor air pollution (especially traffic exhausts) for adult asthma and rhinitis

Urbanization is causing an increase of air pollution, especially from vehicle emissions. The most common air pollutants in urban areas are nitrogen dioxide (NO_2), ozone (O_3) and particulate matter (PM) [108], especially particulate matter<2.5 μm in diameter ($PM_{2.5}$) [109].

One recent review concluded that urbanization is associated with increased asthma prevalence in low or middle income countries [110]. There were few studies on associations between urbanization and adult asthma. One cross-sectional study from Macedonia demonstrated that urban population had higher prevalence of asthma as compared to the rural population [111]. A population-based study from Brazil reported that the prevalence of physician diagnosed asthma was higher among adults in urban centres as compared to rural areas nearby [112]. One multi-centre study from Northern European countries showed that adults growing up in the inner-city had higher prevalence of asthma as compared to those growing up on livestock farms, and revealed an urban-rural gradient in asthma among women [113]. A national study from Korea reported that increased urban land-use (degree of urbanization) was associated with asthma symptoms and asthma diagnosis among adults [114]. Increased level of urbanization was associated with allergic asthma and allergic rhinitis among Danish adults [115]. Moreover, higher degree of urbanization was associated with rhinitis symptoms and rhinoconjunctivitis among elderly in Korea [116].

One review concluded that the higher asthma prevalence in urban areas can be due to the higher levels of vehicle emissions [117]. A systematic review and meta-analysis concluded that traffic-related air pollution (TRAP), including black carbon, nitrogen dioxide (NO_2), nitrogen oxides (NO_X), particulate matter<2.5 μm in diameter ($PM_{2.5}$), and Particulate Matter<10 μm in diameter (PM_{10}) are associated with an increased risk of asthma incidence among children [118]. Another systematic review and meta-analysis included only birth cohort studies found that increased exposure to black carbon and $PM_{2.5}$ was associated with subsequent higher risk of developing asthma in childhood [119]. Few studies have investigated associations between traffic-related air pollution and adult asthma/rhinitis. One population based study in Italy found that self-reported traffic intensity was associated with adult asthma [120]. Living close to a highway along in Switzerland was associated with more common wheeze without a cold among adults [121]. One Swedish study found that living close to a road with intensive traffic was associated with allergic asthma and allergic rhinitis among adults [122]. Self-reported traffic-related indicators and measured traffic-related NO_2 concentrations were both related to rhinitis among Italian adults [120]. Locally generated road wear particles at residential addresses was associated with rhinitis symptoms and hay fever among adults in Sweden [123].

The indoor home environment and adult infections

Respiratory infections include infections in the lower and upper respiratory tract, and otitis media, and sinusitis sometimes are included [124]. Respiratory infections are caused by virus or bacteria, but indoor factors can influence the attack rate or the duration. Several reviews has concluded that indoor dampness in general is a risk factor for respiratory infections [65, 124-126]. One recent review with meta-analysis including studies in adults, children and infants concluded that residential dampness or mould are associated with an increased risk of respiratory infections and bronchitis [124]. Separate analysis showed that residential dampness or mould was associated with respiratory infections among both adults and children [124]. One study from Finland found that moisture at home was associated with acute bronchitis and sinusitis, and mould growth was associated with common cold among adults [75]. Another study from Finland showed that living in damp homes was associated with adult bronchitis and common cold [80]. Moreover, visible signs of moisture damage in dwellings were associated with adult sinusitis in Finland [76]. One Japanese study among female university students found that new floor materials at home was related to more respiratory infections [86]. One Swedish study reported that dampness at home was associated with adult chronic rhinosinusitis [127]. One multi-centre longitudinal study in Europe found that home traffic intensity and outdoor NO_2 were associated with new onset of chronic bronchitis among female adults [128].

Short description of the home environment in Sweden

Most of the houses in Sweden are older buildings, many houses are more than 40 years old. Different construction periods have different type of buildings. Brick or stone buildings were common among residential buildings built before 1960's. In the 1960's and 1970's, many high-rise buildings ("the million house program") were constructed to meet the demand of hosing linked to the ongoing urbanisation. These buildings were often poor quality buildings and usually had only exhaust ventilation. From the middle of the 1970's, new building technologies linked to demands to save energy started to influence residential buildings in Sweden. Dampness problems in the foundation or the floor construction caused chemical emissions. One example is the use of a self-level mortar containing casein, a protein from the dairy industry. Later, more energy saving demands were applied. Wall constructions became thicker, triple window glazing were introduced, and heat exchangers extracting heat from the exhaust ventilation system became common. Moreover, older buildings were renovated in order to save energy, by adding tight window frames, external insulation materials on the walls or mineral insulation in the attic.

Many different wall materials are used in modern residential buildings in Sweden. The floor materials usually consist of PVC, wood or linoleum. Nowadays, wall-to-wall carpets are uncommon. Wall paper or water-based paint are the most common internal surface material for the walls and the ceilings. A gypsum board layer, which is fire-resistance, is usually attached between the indoor surface material and the dampness barrier. A plastic film is usually used as a dampness barrier. The building itself is usually constructed by reinforced concrete. Outside the concrete wall is a thermal insulation layer made from mineral wool (stone wool or glass wool). Furthermore, there is usually an empty space between the thermal insulation layer and the façade material, which is often called wind barrier. The façade can be of different materials, such as brick, wood, stone materials, plaster and metal materials.

About half of the population in Sweden lives in single-family houses or attached houses, and another half lives in apartments. Normally, there is no air conditioning system in Swedish dwellings. Around two third of the multi-family buildings in Sweden have installed mechanical ventilation system [129], mostly exhaust ventilation systems only in the kitchen and in the bathrooms. Only 22% have a general mechanical ventilation system including bedrooms and living rooms [130, 131]. Almost all of the Swedish dwellings use an electric stoves for cooking or baking, and gas cooking is very uncommon. Pets, especially cats and dogs, are common in Swedish families. About one third of the families (36%) have a pet at home [130, 131]. One study reported that 26% of the families with school children had cats, 20% had dogs, and 8% had rodents as pets [132]. Around 8%-15% reported exposure to ETS at home [47, 131]. Swedish homes are regularly re-painted indoors. Recent indoor painting of the home (in the past 12 months) was reported by 25% of randomly selected adults in Sweden [130] and in the city of Uppsala [131]. A total of 30% of subject living in apartments in Stockholm had any type of redecoration of their apartment in the past 12 months, including painting and exchange of indoor materials [83]. In the past decades there has been a focus on reducing chemical emissions from building materials in Sweden. One example is the shift from solvent based indoor paints to water based paints [94]. Indoor levels of formaldehyde, an important indoor air pollutant, is low in Swedish dwellings. Median concentrations of formaldehyde in Swedish dwellings is 22-23 $\mu g/m^3$ [133] well below the WHO standard for formaldehyde (100 $\mu g/m^3$) [134]. Reports on dampness or indoor mould are common in Swedish homes. Signs of dampness or mould at home were reported by 24% of randomly selected adults in a national random population sample [130] and by 9.5% of randomly selected adults in the city of Uppsala [131]. Among randomly selected apartments in Stockholm, 15% had dampness or water leakage over the last five years as reported by the inhabitants [83]. Among different types of signs of dampness in Swedish homes, water damage was the most common sign and visible indoor mould was rare.

Short description of the home environment in China

The Chinese population has doubled in the past decades and the urbanization process is still ongoing. The migration to the cities has created a high demand for new residential buildings in urban areas. In China, most of the residential buildings are high-rise apartment buildings in the cities, often constructed after 1990. There are very few single-family houses in urban areas. China is divided into northern and southern China, with the Yangze River as the border. Residential buildings in northern China are better insulated and has an inbuilt heating system. Residential buildings in southern China has no heating system, but the outdoor temperature can reach zero degree during the coldest months. In winter, additional electric heaters are sometimes used. Air conditioning is common in south China due to hot summers. In winter, the air conditioners installed in the rooms can also be used as heaters. However, the cost of electricity limits the use of these additional heating sources.

In southern China, the wall construction in a modern apartment building consists of a frame of reinforced concrete with traditional bricks or concrete bricks as the wall material. This brick material is the main thermal insulation. Recently, additional mineral insulation on the outside part of the wall has started to be used. The wall has an inside layer and an outside layer of waterproof cement mortar, used as dampness barriers. The façade material is usually ceramic tiles. The interior surface can consist of putty, wall paper or emulsion paint. Ceramic material, stone and wood are common floor materials used in dwellings in China. In the past, bare concrete floors with no additional floor surface material was common. The majority of residential buildings do not have a general mechanical ventilation system, but an exhaust fan in the bathroom is common [135]. Dwellings in Shanghai seems to have good general ventilation especially in spring and autumn, however, over half of the measured children's bedrooms had insufficient ventilation during night, with CO_2 concentrations above 1000 ppm [136]. One study from Wuzhou in south China found that in winter, only 3% of the homes had a CO_2 level above 1000 ppm in winter [137]. Gas stoves are common in China and only few homes use electric stoves. Few Chinese families are pet owners. According to one multi-centre Chinese study, 2% of the families had cats and 5% had dogs [138]. However, studies have demonstrated that house dust mite allergens and cockroach allergens are common indoor allergens in Chinese dwellings [139]. ETS exposure at home is common, since around half of the males are smokers in China [16]. An even higher prevalence of ETS exposure has been reported in another older study. In this study, 80% had ETS at home, and 36% had daily exposure to ETS [103]. Renovation and new furniture are common in residential buildings in China. In a multi-centre study across China, 17.6% reported that their current dwelling had been renovated in the past years and 36.3% reported that they had new furniture at home [140]. Renovation and new building materials and furniture are the main sources of formaldehyde emissions in Chinese homes [101]. It was estimated that more than 60-80% of newly renovated homes (in the past year) in urban China had a median formaldehyde concentration above the national standard (the standard is 100 $\mu g/m^3$) [101]. Moreover, dampness and indoor mould are commonly found in Chinese homes. In the recent multi-centre study across China, it was reported that 12% had indoor mould or damp stains and 13% had water damage in their current home [138].

Background to this thesis

A large number of epidemiological studies have been published on associations between different environment risk factors in the home environment and respiratory health. Most of these studies are prevalence studies on respiratory symptoms or allergic symptoms among children. The most investigated risk factor is dampness at home and indoor mould growth. Few studies exist on associations between risk factors in the home environment and asthma, respiratory symptoms and rhinitis among adults. Moreover, few longitudinal studies among adults have been published, especially longitudinal studies on incidence and remission of rhinitis in relation to the home environment are rare. Most studies on respiratory risk factors in the home environment are from industrialised western countries in Europe or North America. Since more than half of the global population lives in Asia [141], it is important to study the role of domestic risk factors for respiratory illnesses in Asia. China is the largest country in Asia and is currently in a rapid development process that may influence risk factors for asthma, rhinitis and allergy, both in the indoor and outdoor environment. This thesis was performed to add new knowledge on domestic risk factors for adult respiratory health in Sweden and China.

Aims of the investigation

1. To estimate cumulative incidence of allergic asthma and allergic rhinitis, and prevalence of current rhinitis among adults with young children in Chongqing, China.

2. To identify selected domestic environmental factors (including dampness and mould, floor materials, new furniture, indoor characteristics and life-style factors) associated with allergic asthma, allergic rhinitis and current rhinitis among adults in Chongqing.

3. To investigate the prevalence of asthma, rhinitis and respiratory infections among adults living in multi-family buildings in Sweden.

4. To study home environment factors in relation to asthma, rhinitis and respiratory infections among adults living in multi-family buildings in Sweden.

5. To study the differences of these health associations in relation to age (≤65 y vs. >65 y) of the participants living in multi-family buildings in Sweden.

6. To study associations between inspection and indoor measurement data (focus on dampness and mould, ventilation flow and degree of insulation of the buildings) from homes and current wheeze, current asthma symptoms, respiratory infections and current rhinitis (without respiratory infection) among adults in single-family houses in Sweden.

7. To study associations between onset and remission of respiratory symptoms, asthma and rhinitis among adults and indoor dampness, mould and mould odour at home and in the workplace buildings in a multi-centre longitudinal study in Northern Europe.

Material and methods

Ethics statement

Study I and the consent procedure were approved by the Medical Research Ethics Committee of School of Public Health, Fudan University, Sweden. Study II, study III and the consent procedure were approved by the Regional Ethical Committee in Uppsala, Sweden. Ethics approval for study IV was obtained for each centre from their ethical committees. All participants in the studies gave informed consent.

Study design and study population

Paper I

This study is a cross-sectional survey performed from December 2010 to April 2011 in the city of Chongqing, China. It is part of a multi-centre study on asthma and allergies among children and the home environment in China (China, Children, Homes, Health, CCHH) [15, 142, 143]. All children (1-8 y) from 54 random selected kindergartens were invited to participate (N=7117). Completed questionnaires were gathered by teachers in respective kindergartens one week later. Participants in this study were restricted to parents with children aged 3-6 y (N=4530).

Paper II and III

The Building Energy, Technical Status and Indoor Environment (BETSI) study is a national study aiming to investigate energy performance, technical status and indoor environment in the Swedish building stock. Study II and III were based on two separate samples selected by a multi-stage sampling procedure performed by Statistics Sweden (SCB) [144]: study II includes multi-family buildings and Study III single-family houses. There were totally 690 multi-family buildings (totally 8841 apartments) and 605 single-family houses selected from 30 out of a total of 290 municipalities in Sweden. Adult occupants (≥18 y) from the selected multi-family buildings and single-family houses answered a medical questionnaire with questions on personal factors, respiratory symptoms, asthma and allergy. Moreover, each home received an indoor environment questionnaire. SCB distributed the questionnaires in spring 2008. Two reminders were sent to non-responders. Trained inspectors investigated a subsample of the single-family houses and measured the indoor environment from October 2007 to April 2008, before the questionnaire survey.

Totally 5775 adults (46%) answered the medical questionnaire in study II, and 4369 indoor environment questionnaires (49%) for apartments from the multi-family buildings were returned. A total of 1160 adults from 605 single-family houses took part in study III. In study III, inspection and measurements were done in a total of 605 (74%) single-family houses. The response rate for self-administered medical questionnaire in single-family houses was 50%.

Paper IV

The Respiratory Health in Northern Europe (RHINE II) study is a follow up study of the European Community Respiratory Health Survey stage I (ECRHS I). The ECRHS I study was carried out during 1989-1992. Around 3000-4000 subjects (aged 20-44 y) randomly selected from the population in each centre, received a postal questionnaire. The RHINE II study included all subjects from seven centres in northern Europe; Reykjavik (Iceland), Bergen (Norway), Umeå, Uppsala and Göteborg (Sweden), Aarhus (Denmark) and Tartu (Estonia). A total of 21,659 subjects (response rate 86%) from these seven centres in Nordic countries answered a postal questionnaire in ECRHS I. These participants received a postal questionnaire ten years later (RHINE II, 1999-2000), and 16,106 of them responded (response rate 75%). The questionnaire used in RHINE II included questions on respiratory health and indoor environment at home and at work. A second follow up (RHINE III) was performed in 2010-2012 for the RHINE II participants, use a postal questionnaire with identical questions on respiratory health as in RHINE II. Totally 12,013 of those who participated in RHINE II study took part in the RHINE III study (response rate 75%). We defined RHINE II and III study as the baseline and follow up study, respectively.

Assessment of personal factors

Information on gender, age, smoking habits were collected from the self-administered questionnaire in study I, II and III. Age was calculated from gestation age plus children age for women only in study I (no data for men). In study IV, information on gender, age, height, weight and smoking habits were obtained from the baseline questionnaire, while data on education level was available only in the follow up questionnaire. Body mass index (BMI) was calculated as weight (kg)/height (m^2). Education level had three alternatives: primary school, high school and university education.

Assessment of asthma

There was one question in study I on a history of allergic asthma. In study II and III, questions related to asthma or asthma symptoms included: ever had doctor diagnosed asthma; current wheeze, current day time attacks of breathlessness at rest, current day time attacks of breathlessness at rest after exercise, current night time attacks of breathlessness; current asthma attack (current means in the last 12 months) and current asthma medication.

Totally six questions on asthma or asthma symptoms were included in study IV: ever doctor diagnosed asthma, wheeze, and nocturnal attacks of breathlessness, nocturnal cough and productive cough in the last 12 months and current asthma medication. Current asthma in study IV was defined as having either asthma attack in the last 12 months or current asthma medication, or both [38].

Assessment of rhinitis

In study I, there was one question on a history of allergic rhinitis. There was one question on current rhinitis which was included in study I, II and III. Current rhinitis was from the Örebro questionnaire [145] and the Northern Swedish Office Illness study [146]. The question asked "During the last three months, have you had irritating, stuffy or runny nose?" There were three alternatives in the question: often (weekly); sometimes; never. In study IV, there were two questions on rhinitis. They are "Do you have hay fever or any other type of allergic nose symptoms currently (allergic rhinitis)?" and "Have you ever had nose symptoms such as stuffy nose, runny nose and/or sneezing when not having a cold (ever rhinitis symptoms)?"

Current rhinitis in study II was categorized into four types: no rhinitis, infection rhinitis, allergic rhinitis and non-allergic rhinitis. Infection rhinitis was defined as having both current rhinitis and any respiratory infections in the last three months. Allergic rhinitis was defined as having current rhinitis and pollen or furry pet allergy, but no respiratory infections. Non-allergic rhinitis was defined as having current rhinitis, but no pollen or furry pet allergy and no respiratory infections.

Current rhinitis (without report of respiratory infection) in study III was defined as subjects with current rhinitis but without any respiratory infection in the last three months.

Assessment of respiratory infections and allergies

In study II and III, there was one question on respiratory infections: number of respiratory infections in the last three months. Another question related to respiratory infections asked about use of antibiotic medication for respiratory infections in the last 12 months, which was only included in study II. Questionnaire data on pollen allergy and furry pet allergy were obtained in study II and III.

Assessment of onset and remission of asthma and rhinitis

Onset and remission of a particular aspect of respiratory health were calculated in study IV.

Participants with doctor diagnosed asthma at baseline were excluded from the calculation of onset of respiratory symptoms. Onset of a particular respiratory symptom (wheeze, nocturnal breathlessness, nocturnal cough, productive cough or current asthma) among those without doctor diagnosed asthma at baseline was defined as not reporting the particular symptom at baseline but reporting the particular symptom at follow up [147]. Remission of a particular respiratory symptom (wheeze, nocturnal breathlessness, nocturnal cough, productive cough or current asthma) was defined as reporting the particular symptom at baseline but not at follow up. Onset of doctor diagnosed asthma, allergic rhinitis and rhinitis symptoms was defined as not reporting at baseline but reporting at follow up. Remission of allergic rhinitis was defined as reporting allergic rhinitis at baseline but not at follow up.

Assessment of self-reported home environment

Data on building characteristics, home exposures and lifestyle factors in study I were obtained through a self-administered questionnaire. Information regarding building characteristics included house site, living near a main road or highway, construction year, residence area, wall materials and floor materials. Factors related to indoor exposure included recent redecoration, new furniture, mould spots, damp stains, water damage, window pane condensation in winter, presence of cockroaches, rats, mosquitoes/flies, pet-keeping, using of mosquito-repellent incense and incense at home. Lifestyle factors included frequency of cleaning child's bedroom, putting child's bedding to sunshine and frequency of opening windows in child's bedroom. Based on the indoor factors mentioned above, four scores were created; one indoor environment risk factors score (Continuous Score, range from 0-13), one categorized indoor environment risk factors score (Categorized Score, range from 0-4), one indoor dampness score (Continuous Dampness Score, range from 0-4) and one categorized indoor dampness score (Categorized Score, range from 0-2).

The indoor environment questionnaire used in study II included questions on: number of persons living at home, ownership, type of ventilation, pet-keeping, contact with horses, environmental tobacco smoke (ETS) at home, new indoor painting, new floor materials, window pane condensation in winter, water leakage, floor dampness, visible mould, mould odour and other odour in the last 12 months, damp spot, visible mould or water leakage in the last five years, consultant investigation for home dampness. A dampness index was created based on questions on dampness related exposures in the last 12 months and in the last five years (range from 0-2). A window-opening index was created based on two questions about window opening habit (range from 0-5). A higher window-opening index indicates longer window opening time. Furthermore, data on construction year of the buildings (from National Building Register), population and area of each municipality [148] and temperature zone (from Swedish government report [149]) were collected. Data on self-reported indoor environment was available for study III, but not analysed in this thesis.

Home and workplace exposures were obtained through a self-reported questionnaire in study IV. Questions on dampness, mould, and mould odour at home at baseline included water damage, floor dampness, visible mould, mould odour in the last 12 months. In the follow up questionnaire there were two additional questions on dampness or mould exposures in the past 10 years, one about the home environment and one about the indoor environment in the workplace buildings.

Building inspections

Building inspections were performed in the Swedish single-family houses by trained inspectors (trained and evaluated through a standard protocol). Inspection data used in study III focused mainly on risk of dampness and mould growth:

(1) Construction year of the building;

(2) Indoor building volume (m^3) (The heated volume was measured and calculated from the heated area and mean room height);
(3) Type of ventilation (natural ventilation/supply air ventilation/supply and exhaust air ventilation);
(4) Type of foundation (basement/concrete slab/crawlspace);
(5) Any risk of moisture or microbial growth in the foundation (damp foundation): (see Table 1)
(6) Signs of indoor window pane condensation (window pane condensation) (yes/no);
(7) Mould odour or musty odour indoors perceived by the inspectors (mould odour) (yes/no);
(8) Mould in the attic (defined as visible mould in the cold attic or mould odour or other musty odour in the attic) (yes/no)
(9) Brick façade located in such way that it could be exposed to rain/wind driven rain (brick façade) (yes/no).

Table 1. Classification of the risk of moisture or microbial growth for different types of foundation.

Foundation type	Any risk of moisture of microbial growth in the foundation	Indication of a risk
Concrete slab	Working drainage (yes/no)	No
	Wooden joist floor on the concrete slab (yes/no)	Yes
Basement	Working drainage (yes/no)	No
	Internally insulated wood frame on the basement wall (yes/no)	Yes
Crawl space	Working drainage (yes/no)	No
	Moisture sensitive building materials (yes/no)	Yes
	Free water in the crawl space (yes/no)	Yes
	Elevated moisture content in the crawl space wood (yes/no, yes means the measured moisture content was >14%)	Yes
	Visible mould (yes/no)	Yes
	Mould or other musty odour (yes/no)	Yes

Damp foundation for each type of foundation (concrete slab/basement/crawl space) was defined as having at least one of the risk factors listed above.

Buildings with a concrete slab foundation were further categorized into two groups based on construction year: old concrete slabs (buildings built before 1991) and new concrete slabs (built after 1990). It was assumed that buildings constructed before 1991 had mainly overlying thermal insulation, and buildings constructed after 1990 had underlying thermal insulation. Furthermore, a U value for each inspected building was calculated by the inspectors. The U value is the overall heat transfer coefficient for the building construction. A high U value (expressed in watts per meter squared kelvin W/m^2K) indicates a high level of thermal transmittance (poor thermal insulation).

Indoor measurements

Temperature, relative air humidity and air exchange rate were measured in the Swedish single-family houses by trained inspectors during the heating season (October-April). Equipment was placed inside in a central position of the house 1.6 to 1.8 meters above the floor.

(1) Indoor air temperature (°C) and relative air humidity (RH, %):
Indoor air temperature and relative air humidity were measured during 14-15 days. Temperature and RH were logged by a data logger (Mitec Instrument, Säffle, Sweden). The measurement range was 10-95% RH and -40 to +80 °C. The uncertainty for temperature readings was ±0.3 °C and for humidity readings ±3 RH%.
(2) Moisture load (g/m^3):
Data on outdoor temperature and outdoor relative air humidity were obtained from the Swedish Meteorological and Hydrological Institute (SMHI). Moisture load was defined as the difference in absolute air humidity between the indoor and the outdoor environment.
(3) Air exchange rate (per h):
The air exchange rate was measured by a passive tracer gas technique [150]. Perfluorocarbon tracer gases were used and different tracer gas sources were positioned in different rooms of the house, following the instructions from the laboratory. The tracer gases were collected passively in charcoal tubes during 14-15 days, and analysed by Pentiaq AB, Gävle, Sweden. The average air exchange rate in the home was calculated.
(4) Moisture content in cold attic's underlayment wood and in crawl space wood (%):
Moisture content in the wood was measured with a Protimeter Surveymaster® moisture meter (General Electric Company, Connecticut, USA). This is a non-invasive pin instrument for moisture measurements in building materials, based on conductivity measurement. The instrument is calibrated for moisture content in wood (range 7-99%). The critical RH value for mould growth in wood is estimated to be 75-80% which corresponds to a moisture content of 15-18% in the wood [151]. We have chosen a moisture content above 14% to indicate a possible risk of mould growth.

Statistical methods

Paper I, II and III

In paper I, factor analysis was used to identify patterns of all exposure indicators and building characteristics, using principal component analysis and rotated component matrix (varimax rotation with Kaiser normalization). In paper III, correlations between continuous indoor exposure variables were analysed by Kendal-tau-b test.

Multiple logistic regression were applied to study associations between exposure variables and health outcomes (paper I, II and III). Ordinal regression models were applied for associations between exposure variables and ordinal health outcome variables (paper II and III). Multi-nominal regression models were applied when analysing associations between exposures and a nominal outcome variable (paper II and III). For ordinal regression models, the test of parallel lines was applied (paper III). If the test of parallel lines showed a significant value, indicating that the ordinal regression was not valid, we used a nominal regression model instead.

Paper IV

Two level (centre, individual) logistic regression models were used in paper IV to estimate associations between dampness indicators at baseline or during follow up and onset of respiratory symptoms, doctor diagnosed asthma, allergic rhinitis and rhinitis symptoms. Similar two level logistic regression models were used to study associations between dampness indicators and remission of respiratory symptoms and allergic rhinitis.

Potential confounders included both in paper I and II were gender and current smoking. Age was a third confounder included in paper II. Potential confounders in paper III included gender, age, current smoking and outdoor temperature. Potential confounders in paper IV included gender, age, smoking habits at baseline, BMI at baseline and education level at follow up. Associations were expressed as ORs with a 95% confidence interval (CI) for logistic regression and ordinal regression models. Odds Ratios (ORs) were expressed for one step on the scale of the dependent variable for ordinal regression models. For multi-nominal regression models, associations were expressed as relative risk ratio (RRR) with a 95% (CI) for multi-nominal regression models. All statistical tests were two-tailed, using a 5% level of significance. The statistics were performed by SPSS (v.17.0 for paper I, and v.21.0 for paper III), and STATA (v.11.0 for paper II, and v.13.0 for paper IV).

Results

Paper I

Totally 5299 questionnaires were returned (response rate 75%). A total of 769 questionnaires answered by children' grandparents or other persons were excluded from the analyses. Thus, the analysis was based on a total of 4530 questionnaires answered by children' parents. The mean age of the female participants were 31 years (range 19-41 y). The prevalence of history of allergic asthma, history of allergic rhinitis and current rhinitis were 1.6%, 2.7% and 47.1%, respectively (Table 2). A total of 16.4% were current smokers (50.8% men and 2.4% women). Women had more often allergic rhinitis. Men were more often current smokers.

Table 2. The prevalence of history of allergic asthma, history of allergic rhinitis, current rhinitis and current smokers among participating parents (%) (n=4530).

Demographic information	Subcategory	Total	Male	Female	p
		100	29.6	70.4	
History of allergic asthma		1.6	1.6	1.6	0.934 [a]
History of allergic rhinitis		2.7	1.6	3.2	0.005 [a]
Current rhinitis	Weekly	3.1	2.9	3.2	
	Less common	44.0	43.0	44.5	
	Never	52.9	54.1	52.3	0.533 [b]
Current smoker [c]		16.4	50.8	2.4	<0.001 [a]

[a] p value Chi-square test for 2×2 contingency table.
[b] p value Chi-square test for 2×3 contingency table.
[c] Subjects who are current smokers.

The prevalence of home environment characteristics is given in Table 3. Totally 71.3% of the homes were in urban areas and 44.2% were located less than 200 meters from a main road or highway. Redecoration and new furniture were common. Around two third (67.6%) of the dwellings had single-glass windows. Descriptive data on other home environment characteristics, including construction year, home area, wall and floor materials, damp stains, rats, mosquito/flies, mosquito-repellent incense and incense can be found in the published article.

Table 3. Home environmental characteristics of participating parents (n=4530).

Home environment	Subcategory	Total (%)
House site	Urban	71.3
	Suburban	18.6
	Rural	10.1
Living near a main road or highway [a]		44.2
Redecoration [b]		34.1
New furniture [c]		57.4
Mould spots		5.4
Water damage		9.2
Window pane condensation		33.5
Cockroaches [d]		76.1
Current pets		20.8
Cleaning every day		41.1
Frequently put bedding to sunshine		40.6
Frequently open window in winter		35.7

[a] Subject's home located within a distance of 200 meters of a main road or highway.
[b] Subject's home has been redecorated/renovated since one year before pregnancy.
[c] Subject's home has acquired new furniture since one year before pregnancy.
[d] Subject has seen cockroaches/rats/mosquitoes/flies in home.

Smokers reported less allergic asthma (OR(95%CI):0.39(0.15,0.99), p=0.047) in logistic regression models with adjustment for gender. Non-smoking women exposed to ETS from their husbands had more current rhinitis (OR(95%CI): 1.17(1.004,1.36), p=0.044).

Factor analysis was performed to identify patterns of environment characteristics. Three factors were identified among variables reported in Table 3: (1) redecoration and new furniture; (2) window pane condensation and frequently open window in winter (negative association); (3) cleaning every day and frequently put bedding to sunshine. Eight other factors were identified from other environment characteristic variables and can be found in the published article. Four variables were not included in any factor: living near a main road or highway, water damage, current pets and use of incense.

Initially, exposure logistic regression models were applied with adjustment for gender and smoking. Risk factors identified for current rhinitis included living near a main road or highway, new furniture, pet keeping, dampness indicators, cockroaches, rats, mosquitoes/flies, current pets, using mosquito-repellent incense and incense. Frequently put bedding to sunshine was a protective factor for current rhinitis. Risk factors for a history of allergic rhinitis included living near a main road or highway, redecoration, new furniture, mould spots, window pane condensation and current pets. Cleaning every day was a protective factor for a history of allergic rhinitis.

As a next step, stepwise logistic regression was applied to reduce the models. Significant factors in reduced models for current rhinitis included house site, living near a main road or highway, new furniture, water damage, cockroaches, current pets and frequent window opening in winter. All the significant factors from stepwise regression in relation to current rhinitis were reanalysed by multiple logistic regression models, always including gender and current smoking. The data is shown in Table 4. Reduced multi-nominal models for current rhinitis including the same factors as for multiple logistic regression models above found similar associations for less common current rhinitis (data given in published article). Significant factors identified in stepwise regression models for history of allergic rhinitis included living near a main road or highway, redecoration, mould spots, window pane condensation, cleaning every day and frequently open window in winter. Reduced multiple logistic regression models were analysed for history of allergic rhinitis, with data showing in Table 4.

The only risk factor for a history of allergic asthma was water damage. Water damage was related to a history of allergic asthma (OR(95%CI): 2.56(1.34,4.86), p=0.004) when adjusting for gender and current smoking in reduced multiple models.

Table 4. Significant variables identified in reduced multiple models for current rhinitis and history of allergic rhinitis.

Health	Factors	OR(95%CI) [a]	p
Current rhinitis	Male gender	0.92(0.75,1.12)	0.400
	Current smoker	1.05(0.83,1.34)	0.675
	House site		
	Urban	1.00	
	Suburban	1.13(0.93,1.37)	0.221
	Rural	1.43(1.10,1.85)	0.007
	Living near a main road or highway	1.31(1.13,1.52)	<0.001
	New furniture	1.28(1.11,1.49)	0.001
	Water damage	1.68(1.29,2.18)	<0.001
	Cockroaches	1.46(1.23,1.73)	<0.001
	Current pets	1.24(1.04,1.49)	0.020
	Frequently put bedding to sunshine	0.79(0.68,0.92)	0.002
History of allergic rhinitis	Male gender	0.66(0.33,1.31)	0.235
	Current smoker	0.19(0.04,0.84)	0.029
	Living near a main road or highway	2.44(1.48,4.03)	<0.001
	Redecoration	2.14(1.34,3.41)	0.001
	Mould spots	2.23(1.06,4.68)	0.035
	Window pane condensation	2.04(1.28,3.26)	0.003
	Cleaning every day	0.40(0.22,0.71)	0.002
	Frequently open window in winter	0.84(0.52,1.37)	0.488

[a] Gender, current smoking and factors significant in stepwise regression (enter model p value level is p<0.10).

Paper II

A total of 5775 personal (response rate 46%) and 4369 indoor environment questionnaires (response rate 49%) were included in this study. A total of 36.5% were older than 65 years.

Table 5 shows the prevalence of smoking, allergy, rhinitis, asthma symptoms and respiratory infections. Totally 56.5% were female, 12.0% were current smokers, and 11.5% had doctor diagnosed asthma. The elderly were less often smokers, and had less pollen allergy, furry pet allergy, current rhinitis, asthma attacks and respiratory infections. However, the elderly had more often wheeze, day time attacks of breathlessness and night time attacks of breathlessness.

Table 5. Data on gender, smoking, allergy, rhinitis, asthma and respiratory infections.

Health	Subcategory	≤65 y n=3637 [b] (%)	>65 y n=2089 [b] (%)	p [c]	Total n=5775 (%)
Female		54.2	60.4	<0.001	56.5
Current smoking		14.8	7.2	<0.001	12.0
Pollen allergy		28.3	15.7	<0.001	23.8
Furry pet allergy		15.5	5.4	<0.001	11.9
Pollen or furry pet allergy		32.7	17.6	<0.001	27.3
Rhinitis in the last three months	Never	47.4	52.1	0.007	49.0
	Sometimes	40.3	36.7		39.1
	Weekly	12.3	11.2		11.9
Type of rhinitis	Never	47.6	52.4	<0.001	49.2
	Infection rhinitis	34.9	23.5		31.1
	Allergic rhinitis	8.3	6.5		7.7
	Non-allergic rhinitis	9.2	17.6		12.0
Wheeze in the last 12 months		16.4	19.9	0.001	17.7
Day time attacks of breathlessness in the last 12 months		10.3	14.0	<0.001	11.7
Night time attacks of breathlessness in the last 12 months		5.9	6.1	0.727	6.0
Doctor diagnosed asthma		12.0	10.3	0.056	11.5
Current asthma [a]		7.5	7.8	0.728	7.7
	Asthma attack	3.9	2.7	0.016	3.5
	Asthma medication	6.9	7.6	0.339	7.2
Respiratory infections in the last three months	No infection	48.0	63.1	<0.001	53.6
	One time	38.4	29.6		35.1
	Two or more times	13.6	7.3		11.3
Used antibiotic medication for respiratory infections in the last 12 months		11.2	12.9	0.058	11.9

[a] Subjects who have had asthma attacks or have taken asthma medicine during the last 12 months.
[b] Subjects with missing data on age (n=49) were excluded.
[c] p value by Chi-square test.

Table 6 shows descriptive data on indoor environment factors. 50.7% of the participants lived in rented apartments. Window pane condensation in winter (19.0%), dampness problems in the last 12 months (14.7%) and in the last five years (19.3%) were common. The elderly (>65 y) had less contact with cats and horses, and reported less exposure to ETS, new indoor painting, new floor materials, dampness, mould and odours.

Table 6. Data on home building characteristics and indoor environment factors.

Home environment	≤65 y n=3637 [e] (%)	>65 y n=2089 [e] (%)	p [f]	Total n=5775 (%)
Temperature zone [a]				
1	2.5	2.8	0.016	2.6
2	10.1	12.6		11.0
3	53.2	50.4		52.1
4	34.2	34.1		34.3
Construction year				
-1960	13.6	10.5	<0.001	12.5
1961-1975	34.0	31.0		33.0
1976-1985	17.0	19.1		17.9
1986-1995	15.1	17.5		16.0
1996-2005	20.2	21.9		20.7
Living alone	36.6	48.4	<0.001	40.9
Rented apartments	52.7	47.0	<0.001	50.7
Natural ventilation only	46.5	43.6	0.063	45.4
Have dog	8.1	6.9	0.112	7.7
Have cat	9.7	6.7	<0.001	8.7
Horse contact	4.4	1.8	<0.001	3.5
ETS	13.1	10.2	0.003	12.1
New indoor painting in the last 12 months	19.1	13.6	<0.001	17.1
New floor materials in the last 12 months	10.8	7.4	<0.001	9.5
Window pane condensation	21.3	15.2	<0.001	19.0
Water leakage in the last 12 months	7.4	5.4	0.004	6.7
Floor dampness in the last 12 months	7.6	5.1	<0.001	6.8
Visible moulds in the last 12 months	4.5	2.4	<0.001	3.8
Mouldy odour in the last 12 months	3.2	1.5	<0.001	2.7
Other odour in the last 12 months	9.2	7.2	0.026	8.5
Any dampness in the last 12 months [b]	16.4	11.4	<0.001	14.7
Any dampness in the last five years	21.3	15.3	<0.001	19.3
Consultant investigation for home dampness	15.8	12.4	0.003	14.5
Dampness index [c]				
0	72.3	79.5	<0.001	74.7
1	17.1	13.7		15.9
2	10.6	6.9		9.3
Window-opening index [d]				
0	2.2	1.4	<0.001	1.9
1	3.1	2.0		2.7
2	24.2	21.8		23.2
3	11.9	9.3		11.0

4	34.6	41.0	37.1
5	23.9	24.5	24.2

[a] Higher number stands for warmer climate.
[b] Subjects have reported one of the following dampness problems: water leakage, floor dampness, visible moulds or mouldy odour in the last 12 months.
[c] Dampness index, number of "yes" answers to "any dampness in the last 12 months" and "any dampness in the last five year": 0, answers were both "no"; 1, only one answer was "yes"; 2, answers were "yes" to both questions.
[d] Higher number stands for more window opening.
[e] Subjects with missing data on age (n=49) were excluded.
[f] p value by Chi-square test.

Participants living in buildings constructed from 1976-1985, living in densely populated areas, living alone and living in rented apartments had a higher risk of current rhinitis (Table 7, mutually adjusted models).

Table 7. Associations between current rhinitis and building characteristics and indoor environment factors analysed by ordinal regression models.

Home environment	All subjects, n=5775, Mutual adj. OR(95% CI) [c]	≤65 y n=3637 [f], Mutual adj. OR(95% CI) [d]	>65 y n=2089 [f], Mutual adj. OR(95% CI) [e]
Construction year			
-1960	1.00	1.00	1.00
1961-1975	1.12(0.90,1.41)	1.17(0.90,1.52)	1.12(0.73,1.72)
1976-1985	1.43(1.12,1.84)**	1.45(1.07,1.96)*	1.54(0.97,2.46)
1986-1995	1.27(0.99,1.63)	1.30(0.96,1.74)	1.32(0.83,2.11)
1996-2005	1.15(0.91,1.46)	1.24(0.93,1.64)	1.12(0.71,1.76)
Population density/10000 [a]	1.61(1.13,2.29)**	1.74(1.14,2.64)*	1.81(0.90,3.64)
Living alone	1.25(1.09,1.43)**	1.54(1.30,1.82)***	0.88(0.69,1.11)
Rented apartments	1.23(1.07,1.40)**	1.25(1.06,1.48)**	1.21(0.95,1.54)
Window pane condensation	1.16(0.98,1.38)	1.15(0.94,1.41)	1.22(0.88,1.68)
Odour, other than mouldy odour in the last 12 months	1.25(0.98,1.60)	1.30(0.97,1.73)	1.03(0.63,1.67)
Dampness index [b]			
0	1.00	1.00	1.00
1	1.07(0.88,1.29)	1.32(1.05,1.67)*	0.67(0.46,0.98)*
2	1.19(0.88,1.60)	1.46(1.03,2.06)*	0.64(0.34,1.21)

[a] The ORs were expressed per 10000 increase of the population density (number of persons per km^2).
[b] Dampness index, number of "yes" answers to "any dampness in the last 12 months" and "any dampness in the last five year": 0, answers were both "no"; 1, only one answer was "yes"; 2, answers were "yes" to both questions.
[c] Mutual adjustment models including gender, age and smoking for all subjects (inclusion criteria is p<0.1 in total sample).
[d] Mutual adjustment models including gender, age and smoking for younger and middle aged subjects (≤65 y) (inclusion criteria is p<0.1 in total sample).
[e] Mutual adjustment models including gender, age and smoking for elderly (>65 y) (inclusion criteria is p<0.1 in total sample).
[f] Subjects with missing data on age (n=49) were excluded.
*** p<0.001, ** p<0.01, * p<0.05.

Wheeze was associated with colder climate zones, rented apartments and dampness problems (dampness index). Day time attacks of breathlessness were more common among those living in buildings constructed from 1961-1975, in rented apartments, in homes with dampness problems and in homes with more window opening time (high window-opening index). Night time attacks of breathlessness was more common in colder climate zones and in homes with more window opening time (Table 8, mutually adjusted models).

Table 8. Associations between wheeze, day time attacks breathlessness, night time attacks of breathlessness, building characteristics and indoor environment factors (by logistic regression models).

Health	Home environment	All subjects n=5775, mutual adj. OR(95% CI) [d]	≤65 y n=3637 [g], mutual adj. OR(95% CI) [e]	>65 y n=2089 [g], mutual adj. OR(95% CI) [f]
Wheeze	Temperature zone [a]	0.89(0.80,0.99)*	0.87(0.75,1.00)*	0.90(0.76,1.06)
	Rented apartments	1.20(1.02,1.41)*	1.10(0.89,1.35)	1.37(1.06,1.77)*
	Window pane condensation	1.15(0.95,1.41)	1.13(0.89,1.44)	1.17(0.83,1.65)
	Dampness index [b]			
	0	1.00	1.00	1.00
	1	1.06(0.85,1.33)	1.27(0.96,1.67)	0.77(0.52,1.15)
	2	1.42(1.08,1.86)*	1.90(1.38,2.62)***	0.69(0.38,1.22)
Day time attacks of breathlessness	Construction year			
	-1960	1.00	1.00	1.00
	1961-1975	1.53(1.03,2.29)*	1.47(0.93,2.33)	2.13(0.91,4.99)
	1976-1985	1.28(0.82,2.01)	1.11(0.65,1.91)	2.20(0.89,5.45)
	1986-1995	1.39(0.89,2.18)	1.38(0.81,2.36)	1.94(0.78,4.81)
	1996-2005	1.12(0.71,1.76)	0.95(0.55,1.63)	1.92(0.78,4.71)
	Rented apartments	1.31(1.04,1.66)*	1.25(0.93,1.69)	1.45(0.99,2.12)
	Natural ventilation only	1.13(0.90,1.42)	1.04(0.77,1.39)	1.47(1.01,2.14)*
	ETS	1.15(0.83,1.57)	1.03(0.70,1.54)	1.41(0.82,2.41)
	New indoor painting in the last 12 months	0.71(0.50,1.01)	0.70(0.45,1.07)	0.76(0.39,1.47)
	New floor materials in the last 12 months	0.62(0.38,1.00)	0.61(0.35,1.08)	0.62(0.24,1.55)
	Dampness index [b]			
	0	1.00	1.00	1.00
	1	1.35(1.00,1.81)*	1.44(1.00,2.07)	1.26(0.76,2.10)
	2	1.57(1.09,2.27)*	2.18(1.44,3.31)***	0.48(0.19,1.25)
	Window-opening index [c]	1.10(1.01,1.20)*	1.06(0.95,1.19)	1.20(1.02,1.40)*
Night time attacks of breathlessness	Temperature zone [a]	0.74(0.61,0.90)**	0.76(0.59,0.97)*	0.69(0.50,0.97)*
	Construction year			
	-1960	1.00	1.00	1.00

1961-1975	1.19(0.70,2.01)	1.39(0.76,2.57)	0.93(0.32,2.67)
1976-1985	1.23(0.69,2.18)	1.18(0.59,2.35)	1.54(0.51,4.64)
1986-1995	1.04(0.57,1.89)	0.95(0.45,1.99)	1.39(0.47,4.15)
1996-2005	0.55(0.29,1.05)	0.53(0.24,1.17)	0.63(0.19,2.06)
Rented apartments	1.34(0.98,1.84)	1.27(0.85,1.89)	1.51(0.87,2.62)
Natural ventilation only	0.99(0.72,1.35)	1.02(0.69,1.50)	0.99(0.56,1.73)
New indoor painting in the last 12 months	0.64(0.40,1.01)	0.53(0.31,0.92)*	0.95(0.42,2.19)
Window pane condensation	1.10(0.76,1.59)	1.01(0.65,1.58)	1.28(0.64,2.55)
Dampness index [b]			
0	1.00	1.00	1.00
1	1.10(0.72,1.68)	1.27(0.77,2.09)	0.87(0.39,1.92)
2	1.60(0.96,2.64)	2.63(1.46,4.36)**	-
Window-opening index [c]	1.18(1.04,1.34)*	1.13(0.97,1.32)	1.26(0.99,1.61)

[a] The ORs were expressed per one unit increase for temperature zone.
[b] Dampness index, number of "yes" answers to "any dampness in the last 12 months" and "any dampness in the last five year": 0, answers were both "no"; 1, only one answer was "yes"; 2, answers were "yes" to both questions.
[c] The ORs were expressed per one unit increase for window-opening index.
[d] Mutual adjustment models including gender, age and smoking for all subjects (inclusion criteria is p<0.1 in total sample).
[e] Mutual adjustment models including gender, age and smoking for subjects ≤65 years old (inclusion criteria is p<0.1 in total sample).
[f] Mutual adjustment models including gender, age and smoking for subjects >65 years old (inclusion criteria is p<0.1 in total sample).
[g] Subjects with missing data on age (n=49) were excluded.
*** p<0.001, ** p<0.01, * p<0.05.

Doctor diagnosed asthma was more common among those living in homes with odour, other than mouldy odour. Current asthma was associated with ETS and odour, other than mouldy odour. Respiratory infections were more common among those living in buildings constructed from 1976-1985, in densely populated areas and in rented apartments. Antibiotic medication for respiratory infections was associated with window pane condensation only (Table 9, mutually adjusted models).

As a next step, we analysed associations among elderly only. Current rhinitis was negatively related to dampness problems. Wheeze was more common among those living in rented apartments. Day time attacks of breathlessness was more common in homes without mechanical ventilation and in homes with high window-opening index. Night time attacks of breathlessness was more common among those living in colder climate zones. Doctor diagnosed asthma was more common among those living in rented apartments. Respiratory infections were more common among those living in buildings constructed during 1976-1985 and 1996-2005, and was associated with living in less populated areas. For these associations, ORs were higher among elderly as compared to the other younger subjects (≤65 y) (Table 7, 8 and 9).

Table 9. Associations between doctor diagnosed asthma (logistic regression), current asthma (logistic regression), respiratory infections (ordinal regression), antibiotic medication for respiratory infections (logistic regression) and building characteristics and indoor environment factors.

Health	Home environment	All subjects n=5775, mutual adj. OR(95% CI) [f]	≤65 y n=3637 [i], mutual adj. OR(95% CI) [g]	>65 y n=2089 [i], mutual adj. OR(95% CI) [h]
Doctor diagnosed asthma	Temperature zone [b]	0.95(0.83,1.08)	0.86(0.74,1.01)	1.16(0.90,1.50)
	Rented apartments	1.13(0.93,1.38)	0.97(0.76,1.23)	1.69(1.15,2.46)**
	Odour, other than mouldy odour in the last 12 months	1.49(1.08,2.06)*	1.66(1.15,2.39)**	1.04(0.50,2.16)
	Dampness index [c]			
	0	1.00	1.00	1.00
	1	1.14(0.87,1.49)	1.32(0.98,1.80)	0.67(0.36,1.25)
	2	1.20(0.79,1.81)	1.48(0.95,2.33)	0.50(0.15,1.66)
Current asthma [a]	Temperature zone [b]	0.90(0.75,1.06)	0.78(0.64,0.95)*	1.25(0.90,1.74)
	Construction year			
	-1960	1.00	1.00	1.00
	1961-1975	1.08(0.72,1.63)	0.99(0.62,1.58)	1.32(0.53,3.27)
	1976-1985	1.02(0.64,1.62)	0.96(0.56,1.64)	1.26(0.47,3.35)
	1986-1995	0.88(0.55,1.42)	0.73(0.42,1.28)	1.29(0.49,3.40)
	1996-2005	0.70(0.43,1.13)	0.75(0.44,1.30)	0.60(2.12,1.72)
	Rented apartment	1.05(0.81,1.36)	0.95(0.69,1.29)	1.45(0.90,2.32)
	ETS	1.53(1.09,2.16)*	1.43(0.94,2.17)	1.79(0.97,3.34)
	New indoor painting in the last 12 months	0.69(0.47,0.99)*	0.69(0.45,1.04)	0.61(0.27,1.37)
	Odour, other than mouldy odour in the last 12 months	1.52(1.03,2.24)*	1.71(1.10,2.65)*	1.05(0.43,2.52)
	Dampness index [c]			
	0	1.00	1.00	1.00
	1	1.29(0.93,1.79)	1.57(1.07,2.29)*	0.76(0.37,1.58)
	2	1.14(0.68,1.92)	1.62(0.93,2.82)	0.22(0.03,1.63)
Respiratory infections in the last three months	Construction year			
	-1960	1.00	1.00	1.00
	1961-1975	1.07(0.90,1.28)	1.07(0.87,1.31)	1.11(0.79,1.56)
	1976-1985	1.46(1.21,1.78)***	1.33(1.06,1.68)*	1.87(1.30,2.69)**
	1986-1995	1.08(0.88,1.31)	1.03(0.81,1.31)	1.25(0.86,1.80)
	1996-2005	1.12(0.93,1.35)	0.97(0.78,1.21)	1.56(1.09,2.22)*
	Population density [d]	1.72(1.30,2.29)***	1.68(1.20,2.34)**	2.21(1.27,3.87)**
	Rented apartments	1.13(1.01,1.26)*	1.13(0.99,1.29)	1.14(0.94,1.37)

Antibiotic medication for respiratory infections in the last 12 months	Population density [d]	1.63(0.94,2.85)	1.96(0.99,3.90)	1.53(0.58,4.09)
	Rented apartments	1.13(0.91,1.40)	1.46(1.10,1.92)**	0.84(0.59,1.20)
	Window pane condensation	1.41(1.10,1.82)**	1.49(1.09,2.03)*	1.23(0.78,1.94)
	Odour, other than mouldy odour in the last 12 months	1.23(0.85,1.80)	1.20(0.75,1.91)	1.22(0.64,2.35)
	Dampness index [c]			
	0	1.00	1.00	1.00
	1	1.08(0.80,1.47)	1.29(0.90,1.86)	0.77(0.42,1.39)
	2	1.40(0.92,2.12)	1.84(1.14,2.97)*	0.63(0.24,1.64)
	Window-opening index [e]	1.09(1.00,1.18)	1.05(0.95,1.17)	1.13(0.97,1.31)

[a] Subjects who have had asthma attacks or have taken asthma medicine during the last 12 months.
[b] The ORs were expressed per one unit increase for temperature zone.
[c] Dampness index, number of "yes" answers to "any dampness in the last 12 months" and "any dampness in the last five year": 0, answers were both "no"; 1, only one answer was "yes"; 2, answers were "yes" to both questions.
[d] The ORs were expressed per 10000 increase of the population density (number of persons per km^2).
[e] The ORs were expressed per one unit increase for window-opening index.
[f] Mutual adjustment models including gender, age and smoking for all subjects (inclusion criteria is p<0.1 in total sample).
[g] Mutual adjustment models including gender, age and smoking for subjects ≤65 years old (inclusion criteria is p<0.1 in total sample).
[h] Mutual adjustment models including gender, age and smoking for subjects >65 years old (inclusion criteria is p<0.1 in total sample).
[i] Subjects with missing data on age (n=49) were excluded.
*** p<0.001, ** p<0.01, * p<0.05.

Age interaction was studied comparing associations among elderly with associations among younger subjects (≤65 y). There was an age interaction for the associations between dampness index and current rhinitis (for interaction, p=0.001), wheeze (p=0.001), day time attacks of breathlessness (p=0.002), night time attacks of breathlessness (p=0.004), doctor diagnosed asthma (p=0.024), current asthma (p=0.021) and antibiotic medication for respiratory infections (p=0.015). Furthermore, an age interaction was found for the association between ownership and antibiotic medication for respiratory infections (p=0.015). In all cases, the associations were stronger among younger subjects (≤65 y).

Paper III

Totally 48.9% of the participants were females and 7.3% were current smokers. The prevalence of doctor diagnosed asthma, pollen or furry pet allergy and current rhinitis was 8.7%, 26.3% and 38.9%, respectively. The prevalence of current wheeze, current asthma symptoms; and current rhinitis (without respiratory infections) is shown in Table 10. Women reported more wheeze and respiratory infections than men.

Table 10. Data on smoking, asthma, allergy, rhinitis and respiratory infections, stratified by gender.

Health	Male n=591 [a] (%)	Female n=565 [a] (%)	p [b]	Total n=1160 (%)
Wheeze in the last 12 months	9.3	13.3	0.033	11.2
Current asthma symptoms [c]	8.1	11.0	0.099	9.5
Respiratory infections in the last three months				
No infection	53.7	45.6	0.022	49.7
One time	37.9	43.5		40.6
Two/more times	8.5	10.9		9.6
Current rhinitis (without report of respiratory infection) in the last three months [d]				
Never	75.9	72.3	0.36	74.0
Sometimes	20.6	21.8		21.5
Weekly	3.4	5.9		4.5

[a] Subjects with missing data on gender (n=4) were excluded.
[b] p value in Chi-square test.
[c] Subjects with any of the following symptoms: day time attacks of breathlessness, breathlessness during exercise, night time attacks of breathlessness, asthma attacks during the last 12 months or using asthma medication currently.
[d] Subjects with any respiratory infections in the last three months were excluded.

The buildings were between 3 to 408 years old (median age 35 y), and 74.5% were constructed before 1991. Inspected indoor environmental data is shown in Table 11. Natural ventilation was common (45.7%). Mould odour was detected in 9.6% of the buildings by the inspectors, and 29.6% had a brick façade. Homes with a damp foundation had more mould odour indoors as compared to those without a damp foundation (14.9% vs 4.4%, p<0.001).

Table 11. Inspection data on indoor environment factors in the 605 houses.

Home environment	Subcategory	Total (%)	Missing data (n)
Type of ventilation	Natural ventilation only	45.7	5
	Exhaust air ventilation	37.0	
	Supply and exhaust air ventilation	17.3	
Type of foundation	Basement	26.3	0
	New concrete slab (1991-2005)	17.2	
	Old concrete slab (-1990)	26.9	
	Crawlspace with moisture [a]	22.6	
	Crawlspace without moisture [a]	6.9	

Damp foundation	50.7	0
Window pane condensation	11.1	38
Mouldy odour	9.6	14
Observed mould in the attic	23.6	135 [b]
Brick façade	29.6	0

[a] Crawlspace with moisture included the presence of any of the following risk factors: moisture sensitive building materials; free water in the crawl space; elevated moisture content in the crawl space wood (>14%); visible mould; mould or other musty odour. A crawlspace without moisture had none of the risk factors mentioned above.
[b] The building had no attic or the attic could not be inspected.

Totally 50.7% of the buildings had a damp foundation. Buildings with a crawl space (76.5%) or a basement (61.0%) were most likely to have a damp foundation. The prevalence of a damp foundation was 40.5% for concrete slab buildings constructed before 1991 (risk constructions due to the overlying thermal insulation), but only 6.7% among concrete slab buildings constructed after 1990 (with the thermal insulation under the slab).

Measured indoor and outdoor environment factors are shown in Table 12. The mean indoor temperature and outdoor temperature was 21.4 °C and 2.6 °C, respectively. The mean indoor relative air humidity (RH) was 34.2%. The mean moisture load was 1.70 g/m^3. Moisture load exceeded 3 g/m^3 in 8.3% of the buildings. The mean air exchange rate was 0.36 per h. The mean moisture content in the attic wood and in the crawl space was 12.9%, 13.2%, respectively. A total of 27.6% of the buildings with a crawlspace had measured moisture content in wood exceeding 14%.

Table 12. Outdoor and indoor environment factors (n=605).

Environment factors	Unit	Mean	SD	Missing data (n)
Indoor building volume per person	m^3/person	157.8	95.8	18
Room temperature	°C	21.4	1.47	53
Outdoor temperature	°C	2.6	2.71	0
Relative air humidity	%	34.2	6.21	86
Moisture load [a]	g/m^3	1.70	0.879	88
Air exchange rate	ac/h	0.36	0.180	23
Moisture in the attic wood [b]	%	12.9	2.78	146
Mean U value including cold bridges	W/m^{2}K	0.491	0.208	0

[a] Moisture load was calculated based on mean RH and temperature indoors and outdoors. The difference between outdoor and indoor humidity levels constitutes the indoor vapour contribution.
[b] Measured moisture content in attic's underlayment (wood) (%).

Health associations were analysed by logistic regression, adjusting for age, smoking and outdoor temperature. Wheeze was positively associated with a damp foundation (OR=1.50, 95%CI 1.02-2.20; p=0.039) and negatively associated with living in a house with a crawlspace (OR=0.55, 95%CI 0.32-0.93;

p=0.025). Current asthma symptoms was negatively associated with air exchange rate (OR=0.86, 95%CI 0.75-0.98; p=0.022) and positively associated with mould odour indoors (OR=1.84, 95%CI 1.02-3.32; p=0.044).

Associations for respiratory infections and current rhinitis (without respiratory infection) were analysed by ordinal logistic regression, adjusting for gender, age, smoking and outdoor temperature. Both respiratory infections (OR=1.21, 95%CI 1.04-1.40; p=0.011) and current rhinitis (OR=1.42, 95%CI 1.07-1.88; p=0.015) were more common among those living in buildings with a higher moisture load (as a continuous variable). Moreover, respiratory infections (OR=2.18, 95%CI 1.42-3.34; p<0.001) were more common among those living in buildings with moisture load higher than 3 g/m^3. Current rhinitis (without respiratory infection) was more common among those living in buildings with concrete slab foundations built before 1991 (OR=1.81, 95%CI 1.09-3.02; p=0.022) and in buildings with brick façades (OR=1.80, 95%CI 1.19-2.72; p=0.005). There were no associations between wheeze, current asthma symptoms, respiratory infections, current rhinitis and building age or indoor volume per person. Test of parallel lines were applied for the ordinary logistic regression models. A non-significant p value means that the ordinal regression model is valid. Only one significant p value was detected from the test, which is for the relationship between current rhinitis (without respiratory infection) and mouldy odour (p=0.022). For this association, we run a nominal regression model. Mouldy odour was a risk factor for weekly current rhinitis in this nominal regression model.

Finally, associations were analysed in mutual adjustment models including factors with a p value less than 0.1 (Table 13). Wheeze was more common among those living in buildings with damp foundations and less common among those living in buildings with a crawlspace. A higher air exchange rate was the only significant factor that associated with a lower risk of having current asthma symptoms (p=0.03). Current asthma was not related to mouldy odour in the mutually adjusted model. Moisture load was calculated based on relative air humidity, thus these two variables could not be included in the mutually adjusted model at the same time. Respiratory infections were related to moisture load in the final model. Current rhinitis (without respiratory infection) was associated with living in homes with old concrete slab and homes with brick façades.

Table 13. Mutually adjusted models, controlling for gender, age and smoking (n=1160).

Health	Home environment	OR(95%CI)	p
Current wheeze [a]	Foundation type, basement	1.00	
	Foundation type, new concrete slab (1991-2005)	0.90(0.46,1.74)	0.74
	Foundation type, old concrete slab (-1990)	1.08(0.66,1.74)	0.77
	Foundation type, crawlspace	0.49(0.29,0.84)	0.010
	Damp foundation	1.79(1.16,2.78)	0.009
Current asthma symptoms [a]	Relative air humidity/10 [d]	1.16(0.78,1.72)	0.47
	Air exchange rate/0.1 [e]	0.85(0.73,0.99)	0.030
	Mouldy odour	1.41(0.69,2.88)	0.35
Respiratory infections [b]	Moisture load [f]	1.21(1.04,1.40)	0.011
Current rhinitis (without report of respiratory infection) [b, c]	Foundation type, basement	1.00	
	Foundation type, new concrete slab (1991-2005)	1.27(0.62,2.61)	0.51
	Foundation type, old concrete slab (-1990)	2.21(1.24,3.92)	0.007
	Foundation type, crawlspace	1.21(0.65,2.25)	0.55
	Moisture load [f]	1.36(1.02,1.83)	0.038
	Brick façade	1.71(1.07,2.73)	0.025

[a] Logistic regression models (OR (95%CI)), adjusting for gender, age, smoking and outdoor temperature.
[b] Ordinal logistic regression models (OR(95%CI)), adjusting for gender, age, smoking and outdoor temperature.
[c] All subjects with respiratory infections (n=580) in the last three months were excluded.
[d] The ORs were expressed per 10% increase for relative air humidity.
[e] The ORs were expressed per 0.1 ac/h increase for air exchange rate.
[f] The ORs were expressed per 1 g/m^3 increase for moisture load.

Paper IV

A total of 12,013 subjects participated in the follow up (53.1% females). The prevalence of ever smokers (ex-smokers/current smokers) at baseline was 54.3%. Mean age was 40 years (SD=7.3) at baseline.

The onset rate for wheeze, productive cough and allergic rhinitis during the 10 year follow up time was 9.9%, 9.3% and 9.5%, respectively. The onset rate for rhinitis symptoms (25.9%) was the highest. The onset rate for doctor diagnosed asthma was 4.3%. The remission rate for wheeze (47.5%), nocturnal cough (48.2%) and productive cough (54.8%) were similar. Remission of nocturnal breathlessness (65.8%) was most common (Table 14).

Table 14. Onset and remission over the 10 year follow up period of respiratory symptoms, asthma, allergic rhinitis and rhinitis symptoms (%).

Category	Subcategory	Total (%)
Onset	Wheeze	9.9
	Nocturnal attacks of breathlessness	3.7
	Nocturnal cough	17.0
	Productive cough	9.3
	Current asthma [a]	4.1
	Doctor diagnosed asthma	4.3
	Allergic rhinitis	9.5
	Rhinitis symptoms	25.9
Remission	Wheeze	47.5
	Nocturnal attacks of breathlessness	65.8
	Nocturnal cough	48.2
	Productive cough	54.8
	Current asthma	38.9
	Allergic rhinitis	24.7

[a] Current asthma was defined as either asthma attack in the last 12 months, current asthma medication or both.

Water damage (13.4%) and visible mould (6.7%) were the most common dampness signs at baseline (Table 15). Dampness or mould were common at home (25.7%) and at the workplace (19.1%) during follow up period.

Table 15. Prevalence of signs of indoor dampness and mould at home and in the workplace building in seven centres (%).

Category	Subcategory	Total (%)
Baseline (at home)	Water damage	13.4
	Floor dampness	3.8
	Visible moulds	6.7
	Mould odour	3.6
	Other odour than mouldy odour	6.5
	Any dampness [a]	17.9
Follow up	Dampness or mould at home during follow up	25.7
	Dampness or mould in the workplace building during follow up	19.1

[a] Any dampness was defined as water damage, floor dampness or visible mould in the last 12 months at baseline.

Dampness at baseline was positively associated with onset of wheeze, nocturnal breathlessness, nocturnal cough, productive cough, current asthma and doctor diagnosed asthma (Table 16). Mould odour at baseline was a risk factor for onset of wheeze, nocturnal breathlessness, current asthma and doctor diagnosed asthma (Table 16). Remission of nocturnal breathlessness, nocturnal cough and productive cough at follow up were less common among those living in homes with water damage, visible mould or dampness problems at baseline (Table 17).

Dampness or mould at home during the follow up period was associated with onset of wheeze, nocturnal breathlessness, nocturnal cough, productive cough, doctor diagnosed asthma, allergic rhinitis and rhinitis symptoms (Table 16). Dampness or mould at home during the follow up period was associated with less remission of nocturnal cough and allergic rhinitis (Table 17).

Dampness or mould at work during the follow up period was a risk factor for onset of wheeze, nocturnal breathlessness, nocturnal cough, productive cough, doctor diagnosed asthma and rhinitis symptoms (Table 16). Dampness or mould at work during the follow up period was associated with less remission of wheeze (Table 17).

Table 16. Adjusted odds ratio (OR) with 95% confidence intervals (CI) for onset of respiratory symptoms, doctor diagnosed asthma, and rhinitis.

Health	Water Damage	Floor dampness	Visible mould	Mould odour	Any dampness [a]	Dampness or mould at home during follow up	Dampness or mould in the workplace building during follow up
Wheeze	1.54(1.26,1.87)***	2.17(1.57,2.99)***	1.46(1.11,1.91)**	1.47(1.01,2.13)*	1.56(1.30,1.87)***	1.39(1.18,1.64)***	1.45(1.22,1.73)***
Nocturnal breathlessness	1.27(0.95,1.70)	1.97(1.24,3.14)**	1.38(0.95,2.01)	1.98(1.26,3.10)**	1.44(1.11,1.86)**	1.35(1.06,1.71)*	1.39(1.08,1.80)*
Nocturnal cough	1.21(1.01,1.46)*	1.52(1.10,2.09)*	1.28(1.00,1.65)	1.36(0.97,1.91)	1.31(1.11,1.54)**	1.23(1.07,1.42)**	1.43(1.23,1.66)***
Productive cough	1.17(0.95,1.45)	1.42(0.99,2.04)	1.47(1.11,1.93)**	1.35(0.92,1.97)	1.34(1.11,1.61)**	1.53(1.29,1.80)***	1.37(1.14,1.63)**
Current asthma	1.33(1.01,1.75)*	1.48(0.94,2.35)	1.37(0.95,1.99)	1.67(1.05,2.64)*	1.41(1.10,1.80)**	1.12(0.89,1.41)	1.25(0.97,1.59)
Doctor diagnosed asthma	1.34(1.03,1.75)*	1.99(1.33,2.97)**	1.35(0.94,1.93)	2.17(1.45,3.27)***	1.43(1.13,1.82)**	1.30(1.04,1.61)*	1.40(1.11,1.77)**
Allergic rhinitis	1.13(0.91,1.39)	0.99(0.67,1.49)	1.05(0.78,1.41)	0.92(0.60,1.42)	1.10(0.90,1.33)	1.26(1.07,1.49)**	1.19(0.98,1.43)
Rhinitis symptoms	1.01(0.84,1.21)	1.07(0.74,1.55)	1.03(0.79,1.34)	1.24(0.86,1.79)	1.08(0.91,1.27)	1.37(1.19,1.58)***	1.30(1.11,1.52)**

Two level logistic regression models (centre, individual), adjusted for age (baseline), gender (baseline), smoking (baseline), BMI (baseline) and education (follow up).

[a] Any dampness was defined water damage, floor dampness or visible mould in the last 12 months at baseline.

*** $p<0.001$, ** $p<0.01$, * $p<0.05$.

Table 17. Adjusted odds ratio (OR) with 95% confidence intervals (CI) for remission of respiratory symptoms and allergic rhinitis.

Health	Water Damage	Floor dampness	Visible mould	Mould odour	Any dampness [a]	Dampness or mould at home during follow up	Dampness or mould in the workplace building during follow up
Wheeze	0.90(0.71,1.14)	0.97(0.66,1.41)	1.13(0.83,1.53)	1.09(0.74,1.59)	0.92(0.74,1.13)	0.87(0.72,1.05)	0.74(0.60,0.91)**
Nocturnal breathlessness	0.63(0.40,0.99)*	0.58(0.29,1.14)	0.51(0.29,0.90)*	0.73(0.37,1.44)	0.58(0.38,0.88)*	0.86(0.57,1.29)	0.75(0.48,1.17)
Nocturnal cough	0.78(0.64,0.95)*	0.83(0.60,1.15)	0.81(0.62,1.05)	0.99(0.70,1.39)	0.83(0.70,0.99)*	0.85(0.72,0.998)*	0.91(0.76,1.09)
Productive cough	0.77(0.60,0.99)*	0.83(0.55,1.25)	0.74(0.53,1.03)	0.92(0.60,1.43)	0.75(0.59,0.94)*	1.07(0.87,1.32)	0.93(0.74,1.18)
Current asthma	1.37(0.88,2.14)	0.99(0.52,1.87)	0.98(0.57,1.68)	1.05(0.51,2.16)	1.00(0.68,1.46)	1.20(0.83,1.72)	1.06(0.72,1.55)
Allergic rhinitis	1.05(0.81,1.37)	1.19(0.76,1.85)	1.13(0.81,1.57)	1.38(0.92,2.05)	1.10(0.87,1.39)	0.77(0.62,0.96)*	0.96(0.76,1.21)

Two level logistic regression models (centre, individual), adjusted for age (baseline), gender (baseline), smoking (baseline), BMI (baseline) and education (follow up).

[a] Any dampness was defined as water damage, floor dampness or visible mould in the last 12 months at baseline.

*** $p<0.001$, ** $p<0.01$, * $p<0.05$

General discussion

Risk factors for asthma and rhinitis in the home environment were identified in Sweden, northern Europe and in the central-south part of China. The questionnaires on the home environment used in the different studies were from different standardized questionnaires, adapted to local conditions, thus, the questions were somewhat different in the different studies. Signs of building dampness, such as water leakage and indoor mould growth, were consistent risk factors for asthma and rhinitis in Sweden, northern Europe and China. Window pane condensation in wintertime, an indicator of poor ventilation flow and high air humidity, was a consistent risk factor in Sweden as well as in China. Home visits and inspections by professional building inspectors in single-family homes in Sweden revealed that many homes (50.7%) had signs of dampness in the floor construction and observed dampness was a risk factor for wheeze. Moreover, measured excess of water vapour in indoor air (moisture load) was a risk factor for rhinitis and respiratory infections.

In Sweden, the building technology have changed over time, and living in multi-family buildings constructed from 1961-1975 and from 1976-1985 were risk factors for rhinitis, day time attacks of breathlessness and respiratory infections. Buildings constructed in 1961-1975 in Sweden are often of poor quality (the "million program" houses). Buildings constructed from 1976-1985 in Sweden were influenced by energy saving demands, with many changes in construction techniques. New building materials were tested, including a self-level mortar containing the protein casein. This floor material causes chemical emissions in combination with dampness. Moreover, we found that subjects living in buildings with a brick façade had more respiratory infections. Brick facades can get dampness problems when there is a combination of wind and heavy rain. In China, most buildings (64%) were new multi-family buildings (constructed 2000-2010) and construction year was not a significant risk factor for asthma or rhinitis. The typical façade material in modern buildings in China consists of ceramic tiles which are not sensitive to rain.

A number of lifestyle-related home environment factors were evaluated, especially in China. The role of ETS was evaluated in both Sweden and China. In Sweden, ETS exposure (defined as having a smoker in the home) was a risk factor for current asthma. In China, ETS exposure among females was a risk factor for rhinitis. In China, redecoration, new furniture, presence of cockroaches and keeping furry pets (mainly dogs) were risk factors for rhinitis. Hygiene measures, such as frequently cleaning of the home and putting beddings to sunshine (a traditional method to remove humidity in bed clothing), were protective factors for rhinitis in China.

Ventilation is an important measure to remove indoor air pollution but can increase the exposure to outdoor air pollution in polluted areas (e.g. in China). Most (80%) of the inspected single-family houses in Sweden did not fulfill the current Swedish ventilation standard for homes (0.5 air exchange/hour) and there was an inverse relationship between measured ventilation flow and current asthma symptoms (a protective effect of ventilation). The role of urbanization, linked to traffic-related air pollution, was evaluated in both countries. Allergic rhinitis in China was more common among those living near a main road or highway. In Sweden, living in densely populated areas (with higher urbanization) was a risk factor for rhinitis and respiratory infections. Finally, in Sweden, living in a colder climate zone was a risk factor for wheeze and night time attacks of breathlessness. Since the Chinese study was performed in one city only (Chongqing), we could not evaluate the role of the climate zone in China.

Comments on selection bias

Selection bias can exist in epidemiological studies. The Chinese study was based on parents of children attending randomly selected day care centres in one city in China (one parent per family). In whole China, 80.3% of all Chinese children aged 3-5 years attended a day care centre [138] and the participation rates is most likely even higher in the cities. More females than males participated which could have caused a gender-based selection bias. However, this study had a relatively high participation rate (74.5%).

In the Swedish questionnaire study, all adults (≥18 y) living in randomly selected apartments in randomly selected multi-family buildings in whole Sweden were included. The buildings were selected from 30 Swedish representative municipalities but there was an over-sampling of new buildings in order to get equal number of houses in different age classes of buildings (stratified random sampling). The participation rate was relatively low (46%). Statistics in Sweden, who did the sampling, have analysed differences between participants and non-participants. Elderly persons and married persons from multi-family buildings were more likely to answer the questionnaire, while lower participation rates occurred for subjects from larger cities, suburban municipalities and subjects living in older multi-family buildings. Nevertheless, most of the differences regarding participation rate were small. No major difference in participation rate was found between different municipalities, between Sweden-born and foreign-born persons, or between those with or without Swedish citizenships.

The original response rate for the self-administered medical questionnaire in single-family houses was 50%. Inspection and measurements were performed in a total of 605 (74%) single-family houses. The analysis of the differences between participants and non-participants performed by SCB also considered the study in single-family houses (similar differences).

The initial participation rate was high (86%) in the longitudinal study in Northern Europe. Differences between participants and non-participants have been analysed previously. As compared to the baseline population, long-term participants had less wheeze and more rhinitis [152]. However, associations between age, gender and smoking and respiratory outcomes were similar between long-term participants and baseline participants [152]. An overall conclusion is that it is unlikely that the observed associations been environmental factors and respiratory health in this thesis were seriously influenced by selection bias.

Internal validity of questionnaire studies

Information bias is another potential problem when questions about respiratory outcomes and environmental exposures are included in the same self-administered questionnaires. We used standardized questionnaires from previous studies, based on questions from the ECRHS study [153], the Dampness in Buildings and Health (DBH) study [154] and the Örebro questionnaire [145]. Recall bias can occur when reporting events (medical symptoms or exposure) happening in the past. We used three months or 12 months recall period for medical symptoms, as in previous studies [153, 154]. The question on doctor diagnosed asthma has high specificity but lower sensitivity [155]. Reporting bias can lead to an over-reporting of medical symptoms in exposed subjects or an over-reporting of environmental factors among subjects with medical symptoms. The two cross-sectional questionnaire studies could have been affected by reporting bias, but such bias would have been expected to be similar for all types of exposure and all types of symptoms. However, we found specific associations between certain home environment factors and certain respiratory symptoms Thus, it is unlikely that our observed associations in the cross-sectional questionnaires studies were seriously affected by information bias.

Respiratory symptoms can have seasonal variation. In the two Swedish studies, the questionnaires were answered during spring, the pollen season in Sweden (especially birch pollen). This could have influenced those subjects with birch pollen allergy. In the Chinese study, the questionnaire was answered in winter and early spring (from December to April), a season when the outdoor pollution levels are high and the window opening is limited. In the longitudinal study in northern Europe, data collection was spread over the year, but during a similar period at baseline and follow up.

The participants from the single-family houses had no information on inspections and measurements of their home when they answered the medical questionnaire, reducing the risk of reporting bias. In the longitudinal study, most analysis were based exposure data at baseline, which reduced reporting bias. Moreover, we found certain associations between specific environmental risk factors and specific health outcomes, rather than a general increase of associations between exposures variables and dependent variables. Moreover, similar results were obtained both in the crude analysis and in the final logistic regression models with adjustment of potential confounders. Hence, we don't believe that information bias played an important role in the studies included in this thesis. However, conclusions on causality are limited in cross-sectional studies.

Comments on methodological aspects of inspections and measurements

Inspections and measurements were conducted by trained inspectors in randomly selected single-family houses from whole Sweden, following a standardized protocol. The inspectors had no access to participants' health status, and the inspections and measurements were performed a few months before the medical questionnaire was sent out. The inspectors were professional building inspectors trained at a common workshop to standardize the inspections and the measurements. The same type of calibrated instruments were used in the indoor measurements. The measurement period for indoor climate and air exchange rate was reasonably long (two weeks). All diffusion samplers used to determine the air exchange rate were analysed at the same laboratory (Pentiaq AB, Gävle, Sweden). However, there were also some limitations. Information on how the thermal insulation was placed on concrete slab foundation was not included in the inspection data and we used the construction year to draw conclusions on this issue. Houses built before 1991 were mainly expected to have thermal insulation over the concrete foundation, which is classified as a risk construction. Indoor inspections and measurements were made only during heating season (October 2007 to April 2008). Nevertheless, the possible season effect was considered by including outdoor temperature as a confounder in the statistical analysis. Thus, we believe that our data on inspections and measurements has a reasonable validity.

Comments on external validity

The two Swedish studies were based on stratified random samples of buildings in whole Sweden and adults of all ages were included. These studies should have a good external validity concerning domestic environmental risk factors in Sweden, and other countries with similar climate and building technology (e.g. northern Europe). The longitudinal study was based on a random sample of younger adults living in seven cities in northern Europe, and should have good external validity for the north European climate zones. However, the focus on urban population may limit the possibility to draw conclusions on respiratory health risks of building dampness in rural areas. The Chinese study was based on parents of pre-school children attending a random sample of day care centres in one Chinese city. The mean age of the Chinese female participants were 31 years, ranged from 19-41 years. We have no information on age of the Chinese male participants, but they are expected to be mostly in the same age range as the female participants. This limits the possibility to draw conclusions on other age groups and home environment risk factors in other cities in China with a different climate. However, it is likely the results from the study can be valid for the central-south part of China. The study in Chongqing is a part of a larger multi-centre study (the CCHH study), including different parts of China. Publications from ongoing merged data analysis will reveal to what extent domestic risk factors for asthma and rhinitis differs between different parts of China.

Comments on descriptive data on asthma

Our studies showed that the prevalence of doctor diagnosed asthma in Sweden was 8.7% in 2008 among adults in single-family houses and 11.5% in multi-family buildings. The results were similar as in two other Swedish studies. One study from Stockholm reported that the prevalence of adult asthma was 9.3% in 2007 [7]. Another study from western Sweden found a prevalence of 8.3% of asthma among adults in 2008 [8]. In conclusion, the prevalence of asthma found in our studies were similar as in other Swedish studies from the same period.

In the North Europe study we found that the onset rate of doctor diagnosed asthma was 4.3% over the 10 year follow up period, which corresponds to 4.3 cases per 1000 person-years. This is higher than the incidence rate of asthma reported from RHINE II study (2.2 cases per 1000 person-years) [156]. The high rate of asthma incidence found in our study could be due to different definition of asthma onset as compared with the RHINE II study [156]. In conclusion, we found a higher incidence of asthma than in the previous RHINE study. The reasons could be different restrictions of symptoms at baseline, or difference in age.

Our Chinese study found that the prevalence of allergic asthma (1.6%) was low. Similar results have been reported in other studies from China. One recent study from 2010-2013 found that 1.5% of urban adults across China had mild asthma [10]. Another Chinese study from Shanghai from 2007-2010 found that 1.8% adults had physician-diagnosed asthma [11]. Moreover, one study from rural Beijing in China from 1996-1997 reported a prevalence of asthma symptoms of 0.67% among adults [12]. In conclusion, similar adult asthma prevalence as our study have been found in other Chinese studies.

In the two Swedish studies we found that the prevalence of current wheeze (in the last 12 months) was 11.2% among adults in single-family houses, and 17.7% in multi-family buildings. One Swedish study found a similar prevalence of wheeze (16.6%) in 2008 [8]. A slightly higher prevalence of wheeze was found in the RHINE II study (18.4%) conducted in 1999-2000 [147] and in the RHINE III (19.2%) study conducted in 2010-2012 in North Europe [157]. In conclusion, other Swedish population studies reported similar prevalence of wheeze as we found in Swedish multi-family buildings. However, the prevalence of wheeze in Swedish single-family houses was lower than in other Swedish studies.

Comments on descriptive data on rhinitis

In the two Swedish studies and the Chinese study, we had one question on rhinitis in the past three months [145]. Current rhinitis (weekly or sometimes) was common both in Sweden and China, 38.9% in single-family houses 51.0% in multi-family buildings and 47.1% in China. The prevalence of weekly rhinitis symptoms was 5.3% in single-family houses, 11.9% in multi-family buildings and 3.1% in China. Two other Swedish studies [129, 158] reported higher prevalence of weekly rhinitis symptoms among adults from Stockholm (13% in 1993, and 17% in 2005). Our prevalence of weekly rhinitis symptoms in China was similar as in another Chinese study, which reported a prevalence of 2.2% of weekly symptoms from central south China (Changsha) [92]. In conclusion, prevalence of rhinitis can be influenced by the type of questions that been used in studies. The most common used rhinitis questions is the rhinitis question asked in ISAAC questionnaire [51]. Our rhinitis question is not compatible with that question.

Totally 2.7% of the Chinese adults reported allergic rhinitis in our study, which is less than in other Chinese studies. A cross-sectional study from 2005 including 11 major cities in China reported that the prevalence of adult allergic rhinitis ranged from 8.7% to 24.1% [159]. Another Chinese cross-sectional study performed in 2011 reported that the prevalence of adult allergic rhinitis ranged from 9.6% to 23.9% in 18 major cities [160]. Different definitions of allergic rhinitis applied in questionnaire surveys can influence the prevalence. Our Chinese study asked if the subjects had a history of allergic rhinitis. The other two Chinese studies [159, 160] defined allergic rhinitis as subjects with rhinitis symptoms (sneezing, runny, blocked or itchy nose) in the last 12 months when not having a cold, which is from the ISAAC definition [51].

Associations between personal factors, asthma, rhinitis and respiratory infections

Gender, age and smoking habits were considered as potential confounders in the statistical analysis on home environment in relation to self-reported respiratory health. Comments on health associations regarding gender and smoking habits are given below.

Comments on gender

There were more females than males among the participants in our Chinese study (70.4% vs 29.6%), but a similar proportion of males and females in the other studies. Our studies found that females were more likely to have asthma in Sweden and China. Females from single-family houses had more doctor diagnosed asthma and wheeze. Females from multi-family buildings had more doctor diagnosed asthma and current asthma medication. A similar gender difference for adult asthma has been reported in review articles [29-31].

We found that females were more likely to have rhinitis both in Sweden and China. Females from single-family houses had more current rhinitis. Women reported more often a history of allergic rhinitis than men in our Chinese study. Moreover, females were more likely to affect by respiratory infections in Sweden. In contrast to previous review articles [32, 33] which found no gender difference, we found that women had more rhinitis than men.

Comments on smoking

Around half of the male participants (50.8%) from China were smokers, but very few females (2.4%) were smokers. A similar gender difference in smoking habits was found in another Chinese study [92]. In Sweden, totally 7.3%

of the adults in single-family houses and 12.0% in multi-family buildings were smokers. No difference was found for smoking habits between males and females in Sweden. We found that current smoking was associated with less history of allergic asthma in China (adjusted for gender). Negative associations on allergic sensitization and smoking has been shown in two other studies [161, 162]. The awareness that smoking can cause negative effect on asthmatics can lead to selection bias, which can possibly explain our finding.

Comments on health associations with the home environment

To study associations between home environment factors and asthma, rhinitis and respiratory infections was the main aim of this thesis. Comments regarding these associations are given below.

Comments on dampness and indoor mould

Dampness in the last 12 months (14.7%) and in the last five years (19.3%) in multi-family buildings were common. Self-reported dampness in multi-family buildings was associated with wheeze and day time attacks of breathlessness among Swedish adults.

In China, the most common dampness problems were damp stains (8.4%) and water damages (9.2%). Presence of water damages was associated with history of allergic asthma in China. Moreover, we found that water damage was associated with allergic rhinitis, and indoor mould was associated with current rhinitis.

A damp foundation defined in our Swedish measurements study includes observed moisture or microbial growth in the foundation/walls. Damp foundations were common in the inspected houses (50.7%). We found that a damp foundation in single-family houses was associated with wheeze.

We found that 26.9% of the inspected single-family houses had a concrete slab foundation constructed before 1991. Moreover, damp foundation was especially common (40.5%) among concrete slab buildings constructed before 1991 (risk constructions due to the overlying thermal insulation), as compared to concrete slab buildings constructed after 1990 (with the thermal insulation under the slab) (6.7%). Concrete slab on the ground with overlying insulation can be easily damaged by moisture as the concrete basement structure can achieve high relative humidity equal to the surrounding soil. Overlying thermal insulation was commonly used for small buildings with concrete slab foundation during 1970's and 1980's. Our Swedish measurements study found that living in houses with a concrete slab foundation constructed before 1991 was a risk factor for current rhinitis.

Totally 29.6% of the inspected single-family houses had a brick façade. Houses with a brick façade can be damp because of rain combined with wind. We found that living in houses with a brick façade was associated with current rhinitis.

In conclusion, dampness is a common problems in dwellings, especially in Swedish single-family houses. The results from in our studies are in agreement with previous review articles concluding that indoor dampness and mould are risk factors for asthma [65, 73] and rhinitis [62].

In our northern Europe study, we found that dampness or mould at home was common at baseline (17.6%) and at follow up (25.7%). Totally 19.1% of the workplace buildings were affected by dampness or mould. We found that dampness or mould at home was associated with onset of asthma symptoms, doctor diagnosed asthma, allergic rhinitis and rhinitis symptoms. Dampness or mould at work was associated with onset of asthma symptoms, doctor diagnosed asthma and rhinitis symptoms. Moreover, dampness and mould at home or at work was related to less remission of asthma symptoms or allergic rhinitis. In conclusion, dampness and mould can be associated with incidence of asthma among adults. This finding is in agreement with the conclusions from a review on residential dampness and mould and development of asthma [61]. We have not found published incidence studies on indoor dampness and incidence of rhinitis among adults. Moreover, our findings on associations between dampness indicators and less remission of asthma symptoms is consistent with a previous RHINE II study [147].

Comments on mould odour

Mould odour at baseline was risk factor for onset of doctor diagnosed asthma and respiratory symptoms in our longitudinal study. One review on residential dampness and mould concluded that mould odour as compared to other dampness indicators, had the strongest association with development of asthma [61]. However, this review included mainly childhood studies. Associations between mould odour at home and asthmatic symptoms among adults has also been shown in a Swedish study [79].

We found that mould odour in Swedish single-family houses detected by inspectors was related to current asthma symptoms in the initial model. However, this association was no longer significant when adding measured air exchange ventilation in the final model. This may indicate that mould odour is an indicator of insufficient ventilation. Poor ventilation can amplify the effect of mould odour. Low ventilation rate at home enhanced the association between mould odour along the skirting board and allergic symptoms among Swedish children [163]. An experimental study showed that increased ventilation level in classrooms was associated with less mould odour reported by university students [164]. In conclusion, the association between mould odour and asthma found in our study was in agreement with one recent review article [61], but this association can be due to lack of ventilation.

Comments on window pane condensation and moisture load

Window pane condensation indoor in winter can be a sign of insufficient ventilation and high air humidity (RH). Moreover, the temperature on the window surface is an important parameter influencing window pane condensation. The number of glasses on window is related to window surface temperature. Our Chinese study found that two third of the dwellings (67.6%) had single-glass windows. The majority of the Swedish dwellings have double-glass windows.

We found that in Sweden, window pane condensation in multi-family buildings increased the risk of having rhinitis and antibiotic medication for respiratory infections. In China, window pane condensation in winter was associated with a history of allergic rhinitis. A higher moisture load can be associated with window pane condensation. Totally 8.3% of the involved single-family houses had a higher level of moisture load (more than $3g/m^3$), a limited value suggested by the Swedish People's Health Department [91]. We found that a higher moisture load indoor in single-family houses was a risk factor for rhinitis and respiratory infections in Sweden. Our study is the first epidemiological study demonstrating that measured moisture load can be associated with rhinitis. Building constructions, such as walls and ceilings, can be damaged by high moisture load if the dampness barrier inside the wall is not working properly. In conclusion, window pane condensation can be related to rhinitis and respiratory infections. Window pane condensation reported in questionnaire studies can be a proxy variable for high air humidity, and high air humidity can influence respiratory health among occupants in dwellings, especially rhinitis.

Comments on air exchange rate

The Swedish national standard for minimum air exchange rate level is 0.5 per h [91], and more than 80% of the single-family buildings in our study did not fill the standard. Our study found that a low air exchange rate indoor was related to more current asthma symptoms. Most of the published studies on ventilation have focused on the office environment. We have not found any published study on air exchange in home and asthma among adults. Another indicator of ventilation is indoor concentrations of CO_2. The ASHRAE standard recommends that indoor CO_2 level should be not more than 1000 ppm [90]. One Swedish study found association between CO_2 in homes and nocturnal attacks of breathlessness among adults [165].

Comments on ventilation habits

Window opening can influence ventilation, but is also a habit and can be affected by the perception of the indoor environment. We found that higher window opening time was associated with day time attacks of breathlessness and night time attacks of breathlessness among adults living in multi-family buildings in Sweden. One possible reason could be that asthmatics are more prone to improve ventilation by opening window if they get worsening of their asthma by indoor factors. The role of window opening for respiratory health needs to be evaluated in longitudinal studies.

Comments on age of the building

We found that living in Swedish multi-family buildings constructed in 1961-1975 was a risk factor for day time attacks of breathlessness, and living in multi-family buildings constructed in 1976-1985 increased the risk for rhinitis and respiratory infections.

Buildings from 1961-1975 are often poor quality high-rise buildings, with exhaust ventilation only. Presence of dampness and mould has been reported to be common among these buildings [129]. Swedish multi-family buildings from 1976-1985 were affected by energy saving demands. New construction techniques and new building materials were applied during this period [166]. One example is self-level mortar containing the protein casein was used in Swedish buildings during year 1977-1983. One major indoor problem in these buildings was chemical emissions caused by dampness such as ammonia [167], an odorous compound, 2-acetophenone [168] and 2-etyl-1-hexanol to indoor air [169]. More mucosal inflammation, sick building syndrome [169] and asthma [67] were reported among subjects living in buildings with this type of mortar. In conclusion, insufficient ventilation, dampness problems and chemical emissions from new building materials may have explained the increased respiratory illnesses among adults living in buildings constructed from 1961-198 in Sweden.

Comments on type of building

We found that living in rented apartments were related to more rhinitis, wheeze, day time attacks of breathlessness and respiratory infections among

Swedish adults. In agreement with our results, renting was related to more nasal symptoms in multi-family buildings in Stockholm [158]. This study also found high correlations between renting an apartment and lower socio-economic status (SES) [158]. In Sweden, a large number of multi-family apartments are rental. These apartments are mostly owned by the community with similar living standards and rental costs as the private apartments [166], but lower SES can be overrepresented in rented apartments. Thus, rented apartments can be associated with lower SES in our study. In conclusion, persons in rented apartments had more asthma symptoms and rhinitis. If it is due to SES or a poorer indoor environment is unclear.

Comments on renovation and materials

Redecoration and new furniture in Chinese homes were risk factors for rhinitis symptoms among adults in China. These two variables were related to each other according to the factor analysis. In China, new furniture is often accompanied with redecoration. Redecoration and new furniture can cause chemical emissions. Formaldehyde and volatile organic compounds (VOC) emissions from furniture and decorating process has been studied [95, 104]. Two previous Chinese cross-sectional studies have shown that home renovation was related to an increase of allergic rhinitis among women [100] and asthma among children [105]. Another Chinese study including mainly adults found that home renovation was a risk factor for allergic rhinitis [99]. In conclusion, renovation and new furniture in China can be associated with adult rhinitis.

In contrast, new indoor painting was negatively associated with current asthma in our Swedish study, which is opposite results as a previous study from Sweden [94]. Newly painted surfaces at home was positively associated with nocturnal breathlessness among adults in Sweden [94]. The reason for the opposite finding in our study is unclear. In developed countries like Sweden, indoor paints become more and more environmental friendly and produces less and less chemical emissions. Painting is often included in part of a major renovation in buildings, with strategies of minimizing dust, house dust mites, moulds, etc., and therefore can lead to a better indoor environment, especially regarding dust contamination.

Comments on pets and cockroaches

Our study found that pet keeping was associated with rhinitis among Chinese adults. A total of 5.1% of the participants had cats at home and 6.9% had dogs. Cat and dog epithelium are common indoor allergens in rural areas in China [170]. A multi-centre cross-sectional from China concluded that pet ownership was related to increased prevalence of chronic rhinosinusitis among adults [171]. One study in Qatar found that adult allergic rhinitis was more common among those with domestic animals as compared with those without [172]. In conclusion, pet keeping can be associated with adult rhinitis. However, the time window of exposure to pets can be important. Effects of exposure to furry pets can be different in childhood. A population-based study in North Europe demonstrated that exposure to pets at birth and during childhood was related to less allergic rhinitis in adulthood [173].

Our Chinese study found that the presence of cockroaches increased the risk of having rhinitis symptoms. Cockroaches are common in dwellings in China. Totally 93% of household samples from south China contained cockroach allergens [174]. Moreover, exposure to cockroaches was a risk factor for wheeze among Chinese adolescents [175]. Another Chinese study found that around 20-24% of the adult patients recruited from allergy centres from southern China had positive skin prick tests (SPT) for American cockroach and German cockroach [176]. In conclusion, cockroach allergens at home can be associated with adult rhinitis.

Comments on ETS

ETS at home was negatively associated with respiratory health both in Sweden and in China. In Sweden, ETS exposure was associated with current asthma. In China, non-smoking Chinese females had more current rhinitis if their husbands were current smokers. Our findings are in agreement with previous review articles. A review concluded that ETS at home is one of the most consistently risk factors for asthma among adults [177]. It was concluded in a systematic review that passive smoking is a risk factor for allergic rhinitis among adults [45]. In conclusion, ETS may increase risk of asthma symptoms and rhinitis in adults. There is a need to reduce ETS exposure, especially in Chinese homes.

Comments on climate zone

We found that participants from colder climate zones in Sweden had more wheeze and night time attacks of breathlessness. Our results are in agreement with a previous Swedish study among conscripts [178]. A higher prevalence of asthma was associated with a colder outdoor climate among conscripts [178]. In conclusion, climate zone may influence the prevalence of asthma symptoms among adults. Less ventilation could be one possible explanation as the desire to save energy in this part of Sweden could be high.

Comments on urbanization and exposure to traffic exhausts

We found that rhinitis among Swedish adults and respiratory infections were more common among those living in areas with a higher population density (persons/km^2). Infections can be easily spread among people in high population density areas because of the crowded environments. Population density is often considered as a proxy variable for degree of urbanization. Higher degree of urbanization can be associated with severe air pollution due to heavy traffic. We found that living near a main road or highway (<200 meters) was related to more rhinitis symptoms among Chinese adults. Another Chinese study found that living or working in a place near traffic artery had negative impact on non-allergic rhinitis among adults [179]. Similar results were shown in a Swedish study, where adults living in homes located within 100 meters from a high traffic road had a higher prevalence of allergic rhinitis [122]. One study from in Italy found that NO_2 exposure which is mainly from traffic air pollution, was associated with prevalence of adult allergic rhinitis [180]. Unfortunately, we did not collect traffic related air pollution data from Chongqing. However, according to one previous study, outdoor average concentrations of CO, NO_2 and PM_{10} that measured at high way toll gates in Chongqing, China, were all exceeded indoor air quality standards [181]. In conclusion, urbanization and traffic-related air pollution (TRAP) can be risk factors for rhinitis and respiratory infections among adults.

Conclusions and implications

The increase of asthma and allergic diseases is an important global issue. We can expect a considerable increase of asthma and allergic diseases in the future in China as well as in other middle-income countries. It is important to identify environmental risk factors influencing this increase and to identify and strengthen protective factors to counteract the increase. This thesis has contributed to increased knowledge on important risk factors for asthma, rhinitis and respiratory infection among adults in the home environment in northern Europe and China. The united airway hypothesis has suggested that asthma and rhinitis have a similar origin related to mucosal airway inflammation. However, this does not mean that the environmental risk factors are the same for asthma and rhinitis, since water solubility of gas pollutants and particle size of particles can influence the deposition of the air pollution in the airways. We found that some environmental risk factors we more related to asthma while others were more related to rhinitis and respiratory infections.

We found that living in homes with dampness/mould, environmental tobacco smoke (ETS), and with low measured air exchange rate (in Sweden) were risk factors for asthma symptoms. Moreover, living in homes constructed from 1961-1975 and buildings located in a colder climate zone were risk factors for asthma symptoms in the Swedish study.

Living in homes with dampness/mould, window pane condensation in winter, ETS, cockroaches (in China), indoor pets (in China) and with elevated exposure to traffic air pollution (in China) were risk factors for rhinitis. Moreover, the studies in Sweden demonstrated that the type of building construction and the location of the building could influence the prevalence of rhinitis. Living in homes constructed from 1976-1985, with a concrete slab with overlying insulation, with a high indoor air humidity (measured as moisture load) and living in more urbanized areas were associated with an increased risk of rhinitis. Living in homes with dampness/mould, with a brick façade, window pane condensation in winter, a high moisture load, and living in more urbanized areas were risk factors for respiratory infections.

Our studies confirm that building dampness and indoor mould are consistent environmental risk factors in the home environment, in Sweden, northern Europe as well as in China, related to both asthma, rhinitis and respiratory infections. Moreover, a low ventilation flow in the building (poor ventilation at home) can increase the risk of asthma symptoms. Further longitudinal home environment studies on asthma, rhinitis and respiratory infections are needed, especially in China and other parts of Asia. In these studies, it is important to study incidence as well as remission of respiratory illness, since environmental risk factors can influence the prevalence of diseases in two ways, by increasing the incidence and decreasing the remission. In the Chinese study, we found that daily cleaning of the home and frequently putting the beddings outside to be exposed to sunshine, were protective factors for current rhinitis. More intervention studies are needed on preventive measures in the home to be able to give scientifically based advices on how to improve respiratory health by improving the home environment.

A major challenge in the future is to combine the global demand for a better life and a higher living standard in poor and middle-income countries with a sustainable development of the global society. A sustainable development includes both energy saving aspects linked to the global warming, protecting the ecosystems and saving natural resources. However, since humans spend most of their life indoors, and most of the time in the home environment, we cannot achieve a sustainable development unless we include the creation of a good indoor environment in homes and in workplace buildings in this development.

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