Science of the Total Environment 853 (2022) 158609

Contents lists available at ScienceDirect

Science of the Total Environment

journal homepage: www.elsevier.com/locate/scitotenv

Asthma, allergic rhinitis and atopic dermatitis in association with home environment - The RHINE study

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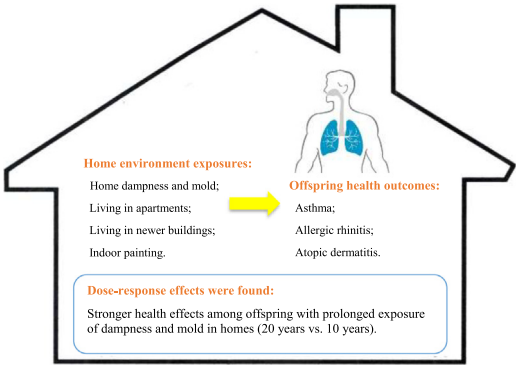
HIGHLIGHTS

- Home dampness and mold were obtained in two follow up investigations cover 20 years.
- Home dampness and mold were associated with offspring asthma and atopic dermatitis.
- There were dose-response effects of dampness and mold on asthma and dermatitis.
- Stronger health effects were found among offspring with 20 years dampness exposure.
- Living in newer buildings and indoor painting were risk factors.

GRAPHICAL ABSTRACT



ARTICLE INFO

Editor: Lidia Minguez Alarcon

Keywords:
Asthma
Allergic rhinitis
Atopic dermatitis
Home environment
Dampness
Indoor painting

ABSTRACT

We studied home environment exposures in relation to asthma, allergic rhinitis and atopic dermatitis among offspring of participants (parents) in the Respiratory Health in Northern Europe (RHINE) study (age ≤ 30 y). Totally 17,881 offspring from Iceland, Norway, Sweden, Denmark and Estonia were included. Home environment exposures, including dampness and mold, type of dwelling, construction year and indoor painting were registered through a questionnaire answered by parents in the first follow up (RHINE II). The parents reported ten years later with in the frame of RHINE III offspring's birth year and offspring's asthma, allergic rhinitis, atopic dermatitis. They also reported dampness and mold at home from RHINE II to RHINE III. The prevalence of offspring's asthma before 10 y, asthma after 10 y, allergic rhinitis at any age and atopic dermatitis at any age were 9.7 %, 4.3 %, 15.6 % and 17.3 %, respectively. Asthma before 10 y was related to any indoor painting at RHINE II (OR = 1.14, 95%CI (1.02, 1.29)). Asthma after 10 y was associated with dampness/mold at home (OR = 1.33–1.62) and living in the newest buildings (constructed in 1986–2001)

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http://dx.doi.org/10.1016/j.scitotenv.2022.158609
Received 9 July 2022; Received in revised form 2 September 2022; Accepted 4 September 2022
Available online 8 September 2022

(OR = 1.30, 95%CI (1.02, 1.66)). Allergic rhinitis was associated with living in newer buildings (constructed in 1961–2001) (OR = 1.16–1.24). Atopic dermatitis was associated with visible mold (OR = 1.35, 95%CI(1.12, 1.62)), dampness/mold at home (OR = 1.18–1.38), living in apartments (OR = 1.22, 95%CI(1.10, 1.35)) and living in newer buildings (constructed in 1961–2001) (OR = 1.14–1.25). There were dose-response effects of dampness and mold on offspring's asthma after 10 y and atopic dermatitis (20 years exposure vs. 10 years exposure). Older offspring had increased risk of developing asthma after 10 y and atopic dermatitis. In conclusion, home dampness and mold, living in apartments, living in newer buildings and indoor painting were associated with offspring's asthma or allergic diseases. Stronger health effects were found among offspring with prolonged exposure of dampness/mold.

1. Introduction

Asthma and rhinitis are common airway diseases globally. Asthma can be due to allergies or infections. It is estimated that asthma prevalence ranges between 1 and 18 % in different part of the world (2017 GINA Report, n.d.). Developed Western countries are reported to have the highest prevalence (Lundback et al., 2016). Atopic rhinitis affects 10–20 % of the population in Europe and the US (Ozdoganoglu and Songu, 2012). Eczema (dermatitis) is a skin disease that occurs more often in children and to much less extent in adults. The International Study of Asthma and Allergies in Childhood (ISAAC) study found that in some countries, >20 % of children were affected (Odhiambo et al., 2009). Atopic dermatitis was only about 1–3 % among adults (Deckert et al., 2014; Eichenfield et al., 2014). Asthma and allergic rhinitis often coexist (Shaaban et al., 2008) and are the most common comorbidities for atopic dermatitis (Chiesa Fuxench, 2017).

We spend the majority of our time indoors, especially at home. Exposures in the home environment can increase risk of asthma and allergic diseases. Home environment related exposure has been shown to be associated with increased incidence of asthma (Quansah et al., 2012; Heinrich, 2011), prevalence of doctor diagnosed asthma (Fisk et al., 2007; Mendell, 2007) and asthma-like symptoms (Fisk et al., 2007; Mendell, 2007; WHO, 2009), impaired lung function (Mendell et al., 2011) as well as increased risk of rhinitis and eczema (Mendell, 2007; Mendell et al., 2011; Jaakkola et al., 2013). The most well documented risk factors in the home environment for asthma and allergic diseases are dampness and mold (Quansah et al., 2012; Heinrich, 2011; Fisk et al., 2007; WHO, 2009; Jaakkola et al., 2013; Wang et al., 2019a) and environmental tobacco smoke (ETS) (Heinrich, 2011; He et al., 2020; Flexeder et al., 2019; Coogan et al., 2015; Lajunen et al., 2013; Thorn et al., 2001; Jaakkola et al., 2003; Hur et al., 2014; Kantor et al., 2016). Chemical emissions in the home environment, especially from new materials, have been suggested to increase the risk of asthma and allergies (Mendell, 2007; Paterson et al., 2021). One review implies that recent painting could be a risk factor for respiratory and allergic effects in children (Mendell et al., 2011).

The Respiratory Health in Northern Europe (RHINE) study is a cohort study on development of asthma and allergic diseases following adults in Northern Europe over two decades (one baseline investigation and two follow up investigations every ten years). We have previously studied onset and remission of asthma and rhinitis in the RHINE cohort in relation to exposures in the home environment, including mold and dampness, smoking, ETS, indoor painting, building year and type of dwellings (Wang et al., 2019a; Wang et al., 2021).

Few studies have investigated indoor dampness exposure over several decades period. Information of dampness and mold exposure at home was obtained in two follow up investigations cover 20 years life span in the RHINE cohort. Moreover, parental reporting of home environment exposures were obtained many years before parental reporting of offspring's health. In the present paper, we aimed to investigate associations between parental report on the home environment in the RHINE cohort and development of asthma, allergic rhinitis and atopic dermatitis in the offspring of the RHINE participants. Our main aim was to study associations between home environment exposures mainly obtained from the first follow up and asthma, allergic rhinitis and atopic dermatitis among offspring from the second follow up.

2. Materials and methods

2.1. Ethics statement

This study was conducted with the approval from the appropriate ethics board at each centre. All participants gave informed consent prior to participation.

2.2. Study design and target population

The European Community Respiratory Health Survey is a multicentre study initially performed in 1989–1992 (ECRHS I study). In the ECRHS I study, a postal questionnaire was sent to selected subjects from each centre through national population registers, including 3000–4000 subjects aged 20–44 y from each centre. The RHINE I study, which is part of the ECRHS I study, includes subjects from seven Nordic countries: Reykjavik in Iceland, Bergen in Norway, Umeå, Uppsala and Gothenburg in Sweden, Aarhus in Denmark and Tartu in Estonia. The participants in the RHINE I study received a postal followed up questionnaire in 1999–2000 (the RHINE II study). All the RHINE I participants were invited to take part in a second follow up in 2010–2012 (the RHINE III study).

There were 21,659 adults participated in RHINE I (response rate 86 %) (Johannessen et al., 2014). The present study population included totally 17,881 offspring from parents who participated in both RHINE II and RHINE III (Fig. 1). We included offspring who were ≤ 30 y at RHINE III. Offspring >30 y were not included in the present study population. The reason to exclude offspring >30 y was that we collected data on dampness situation in their parents' home in the past 20 years, only, and older children had most likely moved out from parents' home since they had their childhood long time ago. Thus, we had no information on their home environment.

2.3. Assessment of offspring's health and age

One question in the RHINE III questionnaire asked “Do you have children (including grown-up children)?”. If the answer was “yes”, one subquestion was followed by asking when each child was born and if the child had (1) Asthma before 10 y (yes/no); (2) Asthma after 10 y (yes/no); (3) Hay fever/rhinitis (allergic rhinitis) (yes/no); (4) Atopic eczema/skin allergies (atopic dermatitis) (yes/no). The age of each child was calculated based on information of birth year and the year when the RHINE III study was performed in each centre.

2.4. Assessment of covariates

There were questions in the RHINE II questionnaire on doctor diagnosed asthma and hay fever/rhinitis of the parent: (1) Ever had asthma diagnosed by a doctor (yes/no); (2) Current hay fever or any other type of allergic nose symptoms (yes/no). Information on education of the parent (primary school/high school/university) was obtained through the RHINE III questionnaire.

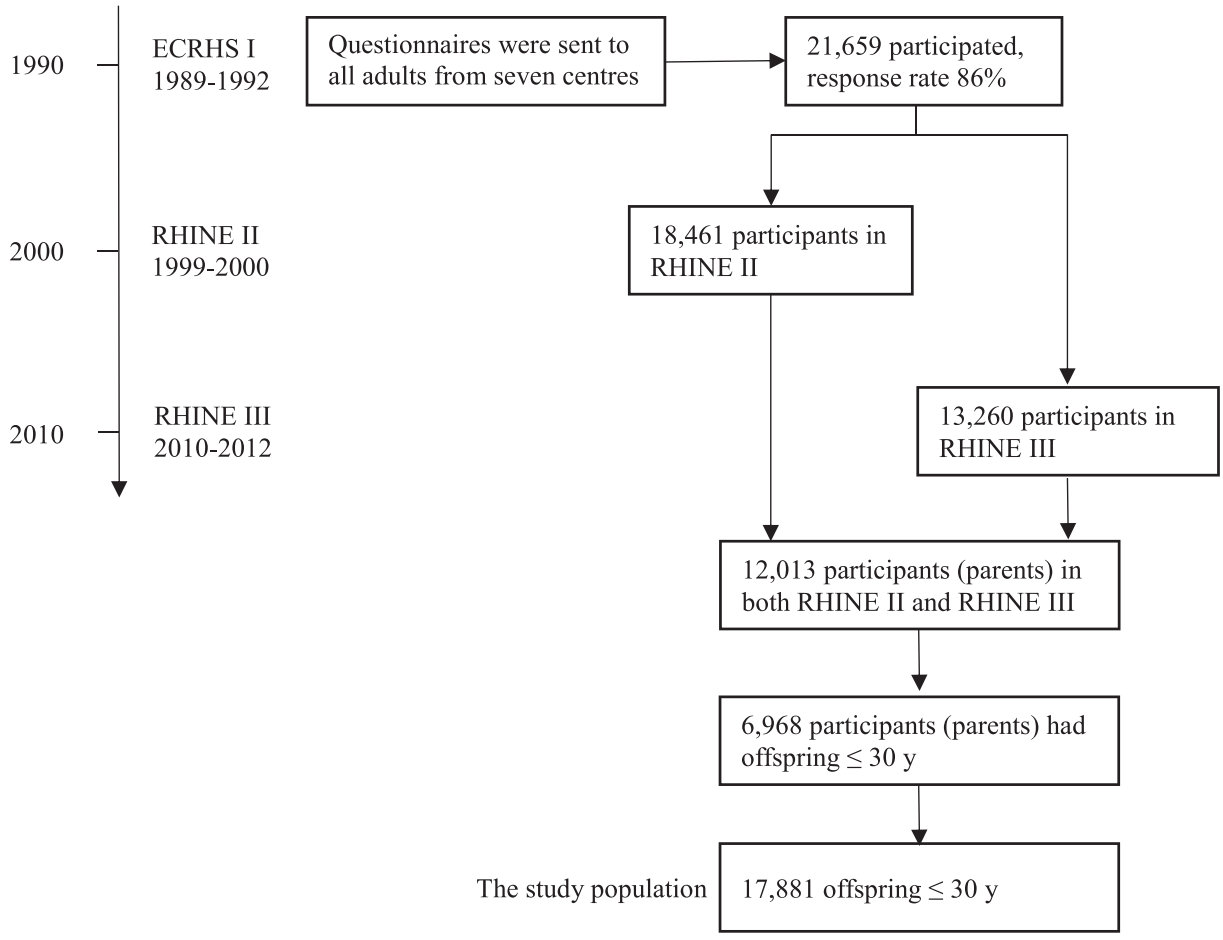

Fig. 1. The flow chart of the study design.

2.5. Assessment of indoor dampness

There were four questions in the RHINE II questionnaire on dampness and mold at home during the past 12 months ("Home" here refers to the home they lived in when they answered the RHINE II questionnaire (current home)): (1) "Water leakage or water damage indoors on walls, floor or ceilings ('water damage')" (yes/no); (2) "Bubbles or yellow discoloration on plastic floor covering or black discoloration of parquet floor ('floor dampness')" (yes/no); (3) "Visible mold growth indoors on walls, floors or ceilings ('visible mould')" (yes/no); (4) "Mold odor in one or several rooms (other than the cellar)" (yes/no); The variable "any dampness" was created based on any "yes" answer to one of the three dampness indicators: water damage, floor dampness or visible mold during the past 12 months. There was one question in the RHINE II questionnaire asked about signs of damp, water leakage or mold in the home during the follow up period from RHINE I to RHINE II (dampness or mold at home from RHINE I to RHINE II) (yes/no) ("Home" here refers to any home they had been living in during this period). Moreover, one question in the RHINE III questionnaire asked about signs of damp, water leakage or mold at home during the follow up period from RHINE II to RHINE III (dampness or mold at home from RHINE II to RHINE III) (yes/no) ("Home" here refers to any home they had been living in during this period). A variable "dampness or mold at home" was created including four alternatives: no dampness/mold from RHINE I to RHINE III; only dampness/mold from RHINE I to RHINE II; only dampness/mold from RHINE II to RHINE III; dampness/mold during both follow up periods (from RHINE I to RHINE III and from RHINE II to RHINE III).

2.6. Assessment of other aspects of home environment

Questions on other aspects of home environment in the RHINE II questionnaire including ("Home" here refers to the home they lived in when they answered the RHINEII questionnaire (current home)): (1) Type of dwelling (detached/semi-detached/apartment/other); (2) Construction year of the building; (3) Any indoor painting in the last 12 months (yes/no); (4) Inside of the home been repainted at any time during the past eight years (painting at home from RHINE I to RHINE II) (yes/no) ("Home" here refers to any home they had been living in during this period).

2.7. Statistical analysis

STATA 15.1 (STATA Corp, Texas, USA) were used for statistical analysis. Correlation analysis (Spearman correlation) was performed to analyse associations between home environment factors. We used two-level logistic regression models (centre, individual) to study associations between home environment factors and offspring's asthma, allergic rhinitis and atopic dermatitis. Parental education, offspring's age, parental doctor diagnosed asthma and parental hay fever in association with offspring's asthma and allergies were analysed in two-level logistic regression models (centre, individual) by keeping all the variables in the same model. Initially we applied a single exposure model including one home environment exposure in each model adjusting for parental education and offspring's age. Mutual adjustment models were then applied including all home environment factors with $p < 0.2$ in previous single exposure models further adjusting for parental education, offspring's age, parental doctor diagnosed asthma

and parental hay fever. As a next step, similar two-level logistic regression models for the single exposure models but stratified for parental doctor diagnosed asthma or hay fever (yes/no) were performed. Finally, extra two-level logistic regression models (centre, individual) for associations between offspring's asthma, allergic rhinitis, atopic dermatitis and dampness/mold, construction year and any indoor painting were performed for older offspring (offspring aged ≥1 y at RHINE II) and younger offspring (offspring aged <1 y at RHINE II). Associations were expressed as odds ratios (OR) with a 95 % confidence interval (CI).

3. Results

There were totally 17,881 offspring aged ≤30 y at RHINE III. Among them, 9.7 % developed asthma before 10 y, 4.3 % developed asthma after 10 y, 15.6 % developed allergic rhinitis and 17.3 % developed atopic dermatitis. The mean age of the offspring was 18 y (ranged 0–30 y). Prevalence of parental doctor diagnosed asthma and hay fever at RHINE II were 8.5 % and 24.8 %, respectively. Around half of the parents participating in the RHINE study had university education (Table 1).

Data on home environment exposures is shown in Table 2. A total of 15.3 % homes had water damage in the past 12 months at RHINE II. Floor dampness at RHINE II (4.1 %), visible mold at RHINE II (7.6 %) and mold odor at RHINE II (3.7 %) were less common. About one third of the homes had dampness or mold problems during the period from RHINE I to RHINE II and from RHINE II to RHINE III. Totally 12.7 % of the homes had dampness during both follow up periods (from RHINE I to RHINE II and from RHINE II to RHINE III). The majority of the dwellings at RHINE II were detached/semi-detached houses (66.2 %), and 32.2 % were apartments. Most of the buildings were constructed in 1961–2001. A total of 40.5 % homes had been painted in the past 12 months at RHINE II. Most of the homes (85 %) had been painted during the period from RHINE I to RHINE II.

The associations between covariates and offspring's asthma, allergic rhinitis and atopic dermatitis are shown in Table 3. Higher parental education level (university vs. primary school) was related to allergic rhinitis and atopic dermatitis in offspring. Negative association was found between offspring's age and offspring's asthma before 10 y. Increased offspring's age was related to higher prevalence of asthma after 10 y and allergic rhinitis among offspring. Both parental doctor diagnosed asthma and parental hay fever were associated with offspring's asthma and allergies.

Correlation analysis (Spearman correlation) showed that there were low correlations between most of the home environment factors (Spearman correlation coefficients <0.6), except the correlations between water damage at RHINE II and any dampness at RHINE II (Spearman correlation coefficient = 0.85).

Home environment in association with asthma, allergic rhinitis and atopic dermatitis among offspring are shown in Table 4. Being exposed to dampness or mold at home (from RHINE I to RHINE II and during both follow up periods), living in other type of dwelling and any indoor painting at RHINE II were associated with offspring's asthma before 10 y. Presence of floor dampness at RHINE II, any dampness at RHINE II and dampness or mold at home (from RHINE I to RHINE II, from RHINE II to RHINE III, only from RHINE II to RHINE III and during both follow up periods) were related to asthma after 10 y among offspring. Dampness or mold at home (from RHINE II to RHINE III and during both follow up periods) and living in newer buildings (constructed in 1961–2001) were related to offspring's allergic rhinitis. All the dampness indicators but not floor dampness at RHINE II were associated with offspring's atopic dermatitis. Moreover, living in apartments and living in newer buildings (constructed in 1961–2001) at RHINE II were related to a higher prevalence of atopic dermatitis among offspring.

Table 5 show associations between home environment and asthma, allergic rhinitis and atopic dermatitis among offspring in mutual adjustment models with extra adjustment for parental doctor diagnosed asthma and parental hay fever. Any dampness at RHINE II was excluded from mutual adjustment models in Model I. Any indoor painting at RHINE II was associated with offspring's asthma before 10 y. Dampness or mold at home (only from RHINE II to RHINE III and during both follow up periods), living in other type of dwelling and living in the newest buildings (constructed in 1986–2001) were related to offspring's asthma after 10 y. Living in newer buildings (constructed in 1961–2001) was associated with allergic rhinitis among offspring. Home environment exposures associated with offspring's atopic dermatitis were visible mold at RHINE II, dampness or mold at home (only from RHINE II to RHINE III and during both follow up periods), living in apartments

Table 2
The prevalence of home environment factors.

Home exposures		%
Dampness indicators		
Water damage[a]		15.3
Floor dampness[a]		4.1
Visible mold[a]		7.6
Mold odor[a]		3.7
Any dampness[a]		20.0
Dampness or mold at home from RHINE I to RHINE II		29.5
Dampness or mold at home from RHINE II to RHINE III		29.4
Dampness or mold at home	No dampness/mold	54.3
	Only dampness/mold from RHINE I to RHINE II	16.8
	Only dampness/mold from RHINE II to RHINE III	16.2
	Dampness/mold during both follow up periods	12.7
Other home exposures		
Type of dwelling[a]	Detached/semi-detached	66.2
	Apartment	32.2
	Other	1.6
Construction year[a]	−1960	34.9
	1961–1975	21.9
	1976–1985	20.3
	1986–2001	23.0
Any indoor painting[a]		40.5
Painting at home from RHINE I to RHINE II		85.0

[a] Exposure at RHINE II.

Table 1
The prevalence of asthma, allergic rhinitis and atopic dermatitis among offspring and parental doctor diagnosed asthma, parental hay fever and parental education (n = 17,881).

		n	%	Mean (SD)	Min-Max
Offspring's asthma before 10 y (offspring ≤30 y at RHINE III)		1740	9.7		
Offspring's asthma after 10 y (offspring between 10 and 30 y at RHINE III)		651	4.3		
Offspring's allergic rhinitis (offspring ≤30 y at RHINE III)		2796	15.6		
Offspring's atopic dermatitis (offspring ≤30 y at RHINE III)		3090	17.3		
Offspring's age (RHINE III)				18 (7.4)	0–30
Parental doctor diagnosed asthma (RHINE II)		1301	8.5		
Parental hay fever (RHINE II)		3798	24.8		
Parental doctor diagnosed asthma or hay fever (RHINE II)		4335	28.4		
Parental education (RHINE III)	Primary school	1363	7.7		
	High school	7144	40.2		
	University	9283	52.2		

Table 3
Associations between asthma, allergic rhinitis and atopic dermatitis among offspring and covariates.

Home exposures		Offspring's asthma before 10 y		Offspring's asthma after 10 y		Offspring's allergic rhinitis		Offspring's atopic dermatitis	
		OR(95%CI)[a]	p	OR(95%CI)[a]	p	OR(95%CI)[a]	p	OR(95%CI)[a]	p
Parental education (RHINE III)	Primary school	1.00		1.00		1.00		1.00	
	High school	1.01(0.81,1.26)	0.922	1.16(0.84,1.60)	0.371	1.10(0.92,1.32)	0.283	1.19(0.99,1.42)	0.065
	University	0.99(0.80,1.23)	0.918	1.03(0.75,1.43)	0.839	1.28(1.07,1.52)	**0.007**	1.29(1.08,1.55)	**0.005**
Offspring's age (RHINE III)[b]		0.86(0.80,0.92)	**<0.001**	1.52(1.30,1.78)	**<0.001**	1.71(1.60,1.82)	**<0.001**	0.99(0.94,1.06)	0.866
Parental doctor diagnosed asthma (RHINE II)		2.01(1.71,2.37)	**<0.001**	1.92(1.50,2.46)	**<0.001**	1.21(1.05,1.40)	**0.010**	1.24(1.07,1.43)	**0.004**
Parental hay fever (RHINE II)		1.26(1.11,1.42)	**<0.001**	1.51(1.25,1.82)	**<0.001**	2.32(2.10,2.55)	**<0.001**	1.61(1.47,1.78)	**<0.001**

Bold values indicate $p < 0.05$.

[a] Two-level logistic regression models (centre, individual), including parental education (RHINE III), offspring's age (RHINE III), parental doctor diagnosed asthma (RHINE II) and parental hay fever (RHINE II) in the same model. The results were expressed as odds ratio (OR) with 95 % confidence interval (CI).

[b] The ORs were expressed per 10 y increase for offspring's age.

and living in newer buildings (constructed in 1961–2001). Similar extra mutual adjustment models including any dampness at RHINE II but not water damage, floor dampness or visible mold at RHINE II in the models (Model II) showed that any dampness at RHINE II was related to offspring's atopic dermatitis.

Stratified analyses for parental doctor diagnosed asthma or hay fever (yes/no) are presented in Table 6, showing home environment in association with offspring's asthma, allergic rhinitis and atopic dermatitis. Most of the associations remained in "yes" group or both groups. Some associations were only among "no" group: mold odor at RHINE II in relation to

Table 4
Associations between asthma, allergic rhinitis and atopic dermatitis among offspring and home environment factors.

Home exposures		Offspring's asthma before 10 y		Offspring's asthma after 10 y		Offspring's allergic rhinitis		Offspring's atopic dermatitis	
		OR(95%CI) [a]	p	OR(95%CI)[a]	p	OR(95%CI)[a]	p	OR(95%CI)[a]	p
Dampness indicators									
Water damage[b]		1.10 (0.95,1.27)	0.214	1.23 (0.98,1.54)	0.070	1.01 (0.89,1.14)	0.937	1.27 (1.14,1.42)	**<0.001**
Floor dampness[b]		1.13 (0.88,1.45)	0.329	1.66 (1.17,2.37)	**0.005**	1.02 (0.82,1.27)	0.884	1.14 (0.93,1.40)	0.199
Visible mold[b]		1.16 (0.96,1.42)	0.133	0.98 (0.70,1.37)	0.907	1.12 (0.94,1.32)	0.198	1.56 (1.35,1.80)	**<0.001**
Mold odor[b]		1.09 (0.82,1.43)	0.563	1.01 (0.64,1.60)	0.969	0.98 (0.77,1.25)	0.849	1.30 (1.06,1.60)	**0.013**
Any dampness[b]		1.11 (0.98,1.27)	0.112	1.28 (1.05,1.57)	**0.015**	1.05 (0.94,1.18)	0.369	1.32 (1.19,1.46)	**<0.001**
Dampness or mold at home from RHINE I to RHINE II		1.09 (0.97,1.22)	0.153	1.20 (1.001,1.44)	**0.049**	1.02 (0.93,1.13)	0.652	1.20 (1.09,1.31)	**<0.001**
Dampness or mold at home from RHINE II to RHINE III		1.14 (1.02,1.27)	**0.021**	1.46 (1.23,1.72)	**<0.001**	1.13 (1.03,1.24)	**0.009**	1.40 (1.29,1.53)	**<0.001**
Dampness or mold at home	No dampness/mold	1.00		1.00		1.00		1.00	
	Only dampness/mold from RHINE I to RHINE II	1.02 (0.87,1.19)	0.818	0.95 (0.74,1.22)	0.696	0.97 (0.86,1.10)	0.663	1.05 (0.93,1.19)	0.404
	Only dampness/mold from RHINE II to RHINE III	1.03 (0.88,1.20)	0.733	1.30 (1.02,1.64)	**0.031**	1.12 (0.99,1.27)	0.075	1.24 (1.10,1.40)	**<0.001**
	Dampness/mold during both follow up periods	1.18 (1.01,1.39)	**0.042**	1.71 (1.35,2.17)	**<0.001**	1.15 (1.003,1.32)	**0.045**	1.59 (1.38,1.76)	**<0.001**
Other home exposures									
Type of dwelling[b]	Detached/semi-detached	1.00		1.00		1.00		1.00	
	Apartment	1.09 (0.96,1.23)	0.169	1.15 (0.94,1.41)	0.175	0.97 (0.87,1.07)	0.541	1.17 (1.06,1.28)	**0.002**
	Other	1.50 (1.02,2.21)	**0.039**	1.50 (0.86,2.61)	0.155	0.73 (0.49,1.07)	0.107	1.01 (0.72,1.43)	0.937
Construction year[b]	−1960	1.00		1.00		1.00		1.00	
	1961–1975	1.13 (0.97,1.31)	0.110	1.15 (0.91,1.45)	0.231	1.16 (1.03,1.32)	**0.015**	1.13 (1.01,1.27)	**0.040**
	1976–1985	1.05 (0.89,1.22)	0.581	0.86 (0.67,1.11)	0.237	1.15 (1.01,1.30)	**0.032**	1.12 (0.99,1.27)	0.069
	1986–2001	0.90 (0.77,1.05)	0.193	1.19 (0.95,1.50)	0.136	1.19 (1.06,1.35)	**0.005**	1.12 (1.00,1.26)	0.050
Any indoor painting[b]		1.14 (1.02,1.27)	**0.022**	0.98 (0.83,1.17)	0.858	1.00 (0.91,1.09)	0.985	1.05 (0.96,1.15)	0.257
Painting at home from RHINE I to RHINE II		1.13 (0.96,1.34)	0.148	0.93 (0.72,1.20)	0.577	0.93 (0.82,1.06)	0.275	1.11 (0.97,1.26)	0.121

Bold values indicate $p < 0.05$.

[a] Two-level logistic regression models (centre, individual), including one single home environment factor in each model and adjusting for parental education (RHINE III) and offspring's age (RHINE III). The results were expressed as odds ratio (OR) with 95 % confidence interval (CI).

[b] Exposure at RHINE II.

Table 5
Associations between asthma, allergic rhinitis and atopic dermatitis among offspring and home environment factors in mutual adjustment models.

	Home exposures		Offspring's asthma before 10 y		Offspring's asthma after 10 y		Offspring's allergic rhinitis		Offspring's atopic dermatitis	
			OR(95%CI)	p	OR(95%CI)	p	OR(95%CI)	p	OR(95%CI)	p
Model I[a]	Dampness indicators									
	Water damage[c]				1.03 (0.78,1.36)	0.835			1.13 (0.98,1.30)	0.088
	Floor dampness[c]				1.38 (0.92,2.06)	0.120			0.96 (0.76,1.20)	0.717
	Visible mold[c]		1.04 (0.83,1.31)	0.710			0.97 (0.80,1.18)	0.790	1.35 (1.12,1.62)	**0.001**
	Mold odor[c]								0.97 (0.76,1.24)	0.818
	Dampness or mold at home	No dampness/mold	1.00		1.00		1.00		1.00	
		Only dampness/mold from RHINE I to RHINE II	0.98 (0.83,1.15)	0.776	0.93 (0.70,1.23)	0.596	0.97 (0.85,1.12)	0.705	0.98 (0.85,1.12)	0.745
		Only dampness/mold from RHINE II to RHINE III	0.98 (0.83,1.15)	0.808	1.33 (1.04,1.69)	**0.023**	1.11 (0.98,1.27)	0.107	1.18 (1.04,1.34)	**0.008**
		Dampness/mold during both follow up periods	1.07 (0.89,1.28)	0.484	1.62 (1.23,2.13)	**0.001**	1.15 (0.99,1.34)	0.070	1.38 (1.19,1.59)	**<0.001**
	Other home exposures									
	Type of dwelling[c]	Detached/semi-detached	1.00		1.00		1.00		1.00	
		Apartment	1.11 (0.97,1.27)	0.115	1.17 (0.95,1.45)	0.136	1.01 (0.91,1.13)	0.807	1.22 (1.10,1.35)	**<0.001**
		Other	1.47 (0.96,2.27)	0.080	1.79 (1.01,3.17)	**0.047**	0.77 (0.51,1.17)	0.223	1.02 (0.70,1.49)	0.915
	Construction year[c]	−1960	1.00		1.00		1.00		1.00	
		1961–1975	1.13 (0.96,1.31)	0.136	1.14 (0.90,1.45)	0.279	1.19 (1.04,1.35)	**0.009**	1.14 (1.01,1.29)	**0.037**
		1976–1985	1.07 (0.91,1.27)	0.395	0.91 (0.70,1.18)	0.484	1.16 (1.01,1.32)	**0.032**	1.16 (1.02,1.32)	**0.024**
		1986–2001	0.95 (0.80,1.12)	0.512	1.30 (1.02,1.66)	**0.035**	1.24 (1.09,1.41)	**0.001**	1.25 (1.10,1.41)	**0.001**
	Any indoor painting[c]		1.14 (1.02,1.29)	**0.026**						
	Painting at home from RHINE I to RHINE II		1.07 (0.89,1.29)	0.491					1.12 (0.98,1.29)	0.095
Model II[b]	Any dampness		1.02 (0.87,1.21)	0.761	1.04 (0.80,1.34)	0.786			1.19 (1.05,1.36)	**0.008**

Bold values indicate $p < 0.05$.

[a] Model I: two-level logistic regression models (centre, individual), including all home environment factors with $p < 0.2$ in Table 4 in each model and adjusting for parental education (RHINE III), offspring's age (RHINE III), parental doctor diagnosed asthma (RHINE II) and parental hay fever (RHINE II). The results were expressed as odds ratio (OR) with 95 % confidence interval (CI). Any dampness at RHINE II, dampness or mold at home from RHINE I to RHINE II and dampness or mold at home from RHINE II to RHINE III were excluded from the mutual adjustment models.

[b] Model II: two-level logistic regression models (centre, individual), including all home environment factors with $p < 0.2$ in Table 4 in each model and adjusting for parental education (RHINE III), offspring's age (RHINE III), parental doctor diagnosed asthma (RHINE II) and parental hay fever (RHINE II). The results were expressed as odds ratio (OR) with 95 % confidence interval (CI). Water damage at RHINE II, floor dampness at RHINE II, visible mold at RHINE II, dampness or mold at home from RHINE I to RHINE II and dampness or mold at home from RHINE II to RHINE III were excluded from the mutual adjustment models.

[c] Exposure at RHINE II.

more atopic dermatitis, and any indoor painting at RHINE II in relation to more atopic dermatitis.

Associations between asthma, allergic rhinitis, atopic dermatitis and dampness/mold, construction year and indoor painting among older offspring are shown in Table 7. Any dampness at RHINE II was associated with offspring's atopic dermatitis. Dampness or mold at home (only from RHINE II to RHINE III and during both follow up periods) was associated with offspring's asthma after 10 y and offspring's atopic dermatitis.

Similar analyses among younger offspring were performed (Table S1). Any dampness at RHINE II was associated with offspring's asthma after 10 y. Dampness or mold at home during both follow up periods was associated with offspring's atopic dermatitis. Moreover, living in the newest buildings (constructed in 1986–2001) was negatively related to offspring's asthma before 10 y.

4. Discussion

The present study suggested that risk factors in home environment were related to offspring's asthma, allergic rhinitis and atopic dermatitis. Dampness and mold at home were associated with increased prevalence of offspring's asthma after 10 y and atopic dermatitis. We found dose-response effects of dampness and mold exposure in homes on offspring's asthma after 10 y and atopic dermatitis, suggesting stronger health effects of prolonged dampness/mold exposure in home environment. Older offspring had increased risk of developing asthma after 10 y and atopic dermatitis. As compared to living in detached/semi-detached houses, living in apartments was related to atopic dermatitis among offspring. Living in newer buildings (constructed in 1961–2001) was associated with higher prevalence of asthma after 10 y, allergic rhinitis and atopic dermatitis in offspring (vs. constructed before 1961). Moreover, we found that indoor painting was associated with increased risk of offspring's asthma before 10 y.

4.1. Prevalence of offspring's asthma and allergies

One out of ten offspring developed asthma before 10 y in our study, while only 4.3 % of the offspring developed asthma after 10 y. ISAAC study showed a prevalence of asthma between 7 and 20 % among children aged 6–7 y and between 8 and 31 % among children aged 13–14 y (Asher et al., 2006). The high prevalence of asthma in early life and decreasing

Table 6
Associations between asthma, allergic rhinitis and atopic dermatitis among offspring and home environment factors, stratified for parental doctor diagnosed asthma or hay fever.

Home exposures			Parental doctor diagnosed asthma or hay fever (yes)		Parental doctor diagnosed asthma or hay fever (no)	
			OR(95%CI)[a]	p	OR(95%CI)[a]	p
Dampness indicators						
Water damage[b]		Offspring's atopic dermatitis	1.52(1.26,1.83)	**<0.001**	1.15(1.00,1.33)	0.050
Floor dampness[b]		Offspring's asthma after 10 y	1.78(1.06,2.98)	**0.029**	1.53(0.94,2.51)	0.089
Visible mold[b]		Offspring's atopic dermatitis	1.66(1.32,2.10)	**<0.001**	1.44(1.19,1.74)	**<0.001**
Mold odor[b]		Offspring's atopic dermatitis	1.17(0.84,1.61)	0.356	1.32(1.002,1.73)	**0.048**
Any dampness[b]		Offspring's asthma after 10 y	1.28(0.94,1.75)	0.122	1.20(0.91,1.58)	0.187
		Offspring's atopic dermatitis	1.59(1.34,1.87)	**<0.001**	1.16(1.01,1.32)	**0.032**
Dampness or mold at home	No dampness/mold	Offspring's asthma before 10 y	1.00		1.00	
	Only dampness/mold from RHINE I to RHINE II		1.03(0.80,1.33)	0.794	0.96(0.79,1.17)	0.703
	Only dampness/mold from RHINE II to RHINE III		1.15(0.90,1.47)	0.266	0.93(0.76,1.14)	0.469
	Dampness/mold during both follow up periods		1.35(1.04,1.74)	**0.023**	1.04(0.84,1.30)	0.693
	No dampness/mold	Offspring's asthma after 10 y	1.00		1.00	
	Only dampness/mold from RHINE I to RHINE II		1.18(0.80,1.75)	0.401	0.80(0.57,1.13)	0.203
	Only dampness/mold from RHINE II to RHINE III		1.47(1.02,2.14)	**0.041**	1.17(0.86,1.61)	0.313
	Dampness/mold during both follow up periods		1.87(1.29,2.71)	**0.001**	1.54(1.13,2.11)	**0.007**
	No dampness/mold	Offspring's allergic rhinitis	1.00		1.00	
	Only dampness/mold from RHINE I to RHINE II		0.88(0.72,1.08)	0.210	1.01(0.86,1.19)	0.911
	Only dampness/mold from RHINE II to RHINE III		1.16(0.95,1.42)	0.137	1.03(0.87,1.22)	0.740
	Dampness/mold during both follow up periods		1.18(0.95,1.47)	0.125	1.05(0.87,1.26)	0.628
	No dampness/mold	Offspring's atopic dermatitis	1.00		1.00	
	Only dampness/mold from RHINE I to RHINE II		1.04(0.85,1.28)	0.700	1.03(0.88,1.21)	0.685
	Only dampness/mold from RHINE II to RHINE III		1.16(0.95,1.42)	0.153	1.25(1.07,1.45)	**0.004**
	Dampness/mold during both follow up periods		1.66(1.35,2.04)	**<0.001**	1.46(1.24,1.71)	**<0.001**
Other home exposures						
Type of dwelling[b]	Detached/semi-detached	Offspring's asthma before 10 y	1.00		1.00	
	Apartment		1.02(0.83,1.25)	0.853	1.13(0.97,1.32)	0.129
	Other		1.48(0.80,2.73)	0.207	1.51(0.91,2.48)	0.109
	Detached/semi-detached	Offspring's atopic dermatitis	1.00		1.00	
	Apartment		1.35(1.15,1.59)	**<0.001**	1.07(0.95,1.21)	0.269
	Other		0.93(0.53,1.63)	0.811	1.00(0.64,1.55)	0.997
Construction year[b]	−1960	Offspring's allergic rhinitis	1.00		1.00	
	1961–1975		1.17(0.96,1.43)	0.125	1.17(0.998,1.37)	0.053
	1976–1985		1.15(0.94,1.42)	0.176	1.12(0.95,1.32)	0.181
	1986–2001		1.34(1.10,1.64)	**0.003**	1.11(0.95,1.31)	0.197
	−1960	Offspring's atopic dermatitis	1.00		1.00	
	1961–1975		1.46(1.19,1.78)	**0.001**	1.00(0.86,1.16)	0.982
	1976–1985		1.34(1.08,1.65)	**0.007**	1.01(0.87,1.18)	0.888
	1986–2001		1.26(1.03,1.54)	**0.024**	1.08(0.93,1.25)	0.294
Any indoor painting[b]		Offspring's asthma before 10 y	1.04(0.87,1.25)	0.657	1.20(1.04,1.38)	**0.011**

Bold values indicate $p < 0.05$.

[a] Two-level logistic regression models (centre, individual), including one single home environment factor in each model and adjusting for parental education (RHINE III) and offspring's age (RHINE III). The results were expressed as odds ratio (OR) with 95 % confidence interval (CI).

[b] Exposure at RHINE II.

trend of asthma symptoms in children during later childhood has been confirmed in the ISAAC study (Lai et al., 2009). The prevalence of asthma in later childhood/adulthood found in our study is somewhat lower as compared to most of previous studies from Europe (Lundback et al., 2016).

Allergic rhinitis (15.6 %) and atopic dermatitis (17.3 %) in offspring were common in our study. ISAAC study reported that the prevalence of allergic rhinitis among children aged 13–14 y in Western Europe were between 15 and 16 % in most of the studied countries (Asher et al., 2006), which is compatible to our results. The prevalence of eczema symptoms in the study were between 4 and 11 % among 13–14 y children in Western Europe (Asher et al., 2006), which is much lower as compared to our prevalence of atopic dermatitis in offspring. However, we had no information on time of diagnosis of allergic rhinitis and atopic dermatitis in our study.

4.2. Dampness and mold in association with offspring's asthma and allergies

We found that dampness and mold at home were important risk factors for asthma in later childhood (after 10 y). This is in agreement with previous findings, since several reviews have demonstrated exposure to dampness and mold growth in home environment as the most consistent risk factor for asthma-related symptoms (Fisk et al., 2007; WHO, 2009), doctor diagnosed asthma (Fisk et al., 2007) and incidence of asthma (Quansah et al., 2012; Heinrich, 2011).

The associations between mold and dampness and atopic dermatitis in offspring found in our study are in agreement with findings from previous multicentre studies on eczema (Weinmayr et al., 2013; Wang et al., 2019b).

Dampness and mold are most likely to be constant risk factors in indoor environment, since moisture damage and mold growth can exist under a long period. Our study adds new evidence of the negative effect of dampness and mold in home environment on asthma and allergic diseases.

4.3. Timing and dose-response effects of dampness and mold exposure

The present study showed dose-response effects of dampness and mold exposure on asthma after 10 y and atopic dermatitis in offspring, indicated by increased likelihood of developing asthma after 10 y and atopic dermatitis among offspring exposed to dampness/mold at home both from RHINE I to RHINE II and from RHINE II to RHINE III. Our results suggested that prolonged exposure to dampness/mold in home environment can have stronger health effects in offspring. As compared to dampness/mold exposure during the first follow up period, stronger health effects were found among offspring with such exposure in the home environment during the

Table 7
Asthma, allergic rhinitis and atopic dermatitis among offspring ≥1 y at RHINE II (n = 14,717) in relation to dampness/mold, construction year and indoor painting.

Home exposures		Offspring's asthma before 10 y		Offspring's asthma after 10 y		Offspring's allergic rhinitis		Offspring's atopic dermatitis	
		OR(95%CI) [a]	p	OR(95%CI)[a]	p	OR(95%CI)[a]	p	OR(95%CI)[a]	p
Any dampness[b]		1.14 (0.98,1.32)	0.095	1.22(0.99,1.50)	0.057	1.02 (0.91,1.15)	0.704	1.37 (1.23,1.54)	**<0.001**
Dampness or mold at home	No dampness/mold	1.00		1.00		1.00		1.00	
	Only dampness/mold from RHINE I to RHINE II	1.09 (0.92,1.29)	0.338	0.96(0.74,1.24)	0.745	0.96 (0.84,1.10)	0.584	1.10 (0.97,1.26)	0.147
	Only dampness/mold from RHINE II to RHINE III	1.01 (0.85,1.21)	0.896	1.28 (1.003,1.62)	**0.047**	1.12 (0.98,1.28)	0.085	1.24 (1.08,1.42)	**0.002**
	Dampness/mold during both follow up periods	1.12 (0.93,1.35)	0.227	1.67(1.31,2.12)	**<0.001**	1.09 (0.95,1.26)	0.216	1.52 (1.32,1.75)	**<0.001**
Construction year[b]	−1960	1.00		1.00		1.00		1.00	
	1961–1975	1.07 (0.90,1.26)	0.436	1.15(0.92,1.45)	0.226	1.13 (0.99,1.28)	0.065	1.11 (0.97,1.26)	0.126
	1976–1985	0.99 (0.83,1.17)	0.885	0.84(0.65,1.09)	0.189	1.13 (0.99,1.29)	0.061	1.07 (0.94,1.22)	0.324
	1986–2001	0.91 (0.77,1.08)	0.300	1.15(0.91,1.45)	0.247	1.12 (0.98,1.28)	0.084	1.09 (0.96,1.25)	0.185
Any indoor painting[b]		1.12 (0.99,1.27)	0.065	1.00(0.84,1.19)	0.994	1.00 (0.91,1.10)	0.930	1.05 (0.95,1.16)	0.368

Bold values indicate $p < 0.05$.
[a] Two-level logistic regression models (centre, individual), including one single factor in each model and adjusting for parental education (RHINE III) and offspring's age (RHINE III). The results were expressed as odds ratio (OR) with 95 % confidence interval (CI).
[b] Exposure at RHINE II.

second follow up period. Moreover, our results on stratified analyses among offspring (older offspring vs. younger offspring) indicated stronger health effects of dampness and mold exposure in older offspring.

4.4. Type of dwelling in association with offspring's asthma and atopic dermatitis

Associations were found between living in other types of dwelling and offspring's asthma after age 10 and between living in apartments and offspring's atopic dermatitis in our study (vs. living detached/semi-detached houses). We have previously investigated type of dwelling in relation to parents' asthma and allergies but found no health associations (Wang et al., 2021). A Swedish birth cohort study showed that living in relatively new apartment buildings and single-family homes with crawl space/concrete slab foundation were associated with recurrent wheezing in very young children (Emenius et al., 2004). One study from US reported that public housing was associated with childhood asthma (vs. private housing) (Northridge et al., 2010). One Swedish study suggested that older houses and single family houses had more dampness problems (Hägerhed-Engman et al., 2009). One study from UK found no difference between single and multi-family houses regarding fungal and bacterial communities in house dust samples, but increased microbial richness was associated with suburban homes (vs. urban homes) (Dannemiller et al., 2016).

4.5. Building age in association with offspring's asthma and allergies

We found that living in newer buildings (constructed in 1961–2001) was related to more allergic rhinitis and atopic dermatitis in offspring as compared to living in buildings constructed before 1961. Living in the newest buildings (constructed in 1986–2001) was associated with offspring's asthma after 10 y (vs. constructed before 1961). Age of building is one important characteristic associated with indoor environment. Building materials and techniques used in construction section can change in different construction periods. We have previously published the results on building age and parental asthma and rhinitis, and found that living in the oldest buildings (built before 1961) increased onset of parental physician diagnosed asthma and nocturnal cough, and living in the newest buildings (built in 1986–2001) increased the risk of onset of parental nocturnal breathlessness and rhinitis (Wang et al., 2021). One Swedish study found that, as compared to buildings built before 1960, asthma exacerbation and rhinitis were more common among occupants living in newer buildings (Wang et al., 2014; Wang et al., 2017a; Wang et al., 2017b). One multicentre study from China suggested that adult asthma and allergic rhinitis were associated with living in older buildings, but no association was found for eczema (Wang et al., 2019b). Old buildings have been shown to be related more dampness problems (Hägerhed-Engman et al., 2009), higher level of mite allergen (Salehi et al., 2011) and overall indoor fungi (Fu et al., 2020). The reason that newer buildings increased the risk of offspring's asthma and allergies in our study is unclear. Housing characteristics/home environment factors that were not included in the present study, such as new buildings materials and insufficient ventilation can have affected offspring's asthma and allergies.

4.6. Indoor painting in association with offspring's asthma

Any indoor painting at RHINE II was associated with offspring's asthma before 10 y in our study. We found that any indoor painting at RHINE II was related to offspring's asthma before 10 y among offspring without parental asthma or hay fever. Moreover, there was borderline significance between any indoor painting at RHINE II and offspring's asthma before 10 y in offspring >1 y at RHINE II.

Our result that indoor painting as a risk factor for offspring's asthma is in agreement with previous studies. It was demonstrated in one review that recent painting is one common risk factor for children' respiratory and allergic diseases (Mendell et al., 2011). Another review suggested that domestic painting was associated with asthma-like symptoms especially in children but the evidence was weak to infer causality (Canova et al., 2013). Only one adult study was included in the review (Canova et al., 2013), which showed that exposure to newly painted surfaces in dwellings (especially painted wood details and kitchen painting) was associated with increased prevalence of adult asthma (Wieslander et al., 1997). One birth cohort study from Taiwan suggested that exposure to indoor painting/renovation during pregnancy was one of the studied perinatal factors that predicting of asthma development at 5 y (Wen et al., 2015). Thus, being exposed to emissions from indoor painting can trigger respiratory illnesses. Emissions from painting usually lead to short-term chemical exposures in indoor environment. Most of the chemical exposures from indoor painting disappear in few months. Future prospective studies are needed to investigate effects of indoor painting on respiratory health.

4.7. Health associations for stratified analyses of parental asthma or hay fever

Stratified analysis for parental asthma or hay fever showed that most of the associations for offspring's asthma and allergic rhinitis remained in both groups or among the group of offspring with parental asthma or hay fever. However, two associations were found only among offspring without parental asthma or hay fever: mold odor at RHINE II was related to more atopic dermatitis; and any indoor painting at RHINE II was related to offspring's asthma before 10 y. Our results indicated that risk factors in home environment can have stronger effects on respiratory health especially among those with parental atopy.

4.8. Strengths

There are several strengths in the present study. It is a multicentre study including a large number of offspring from the RHINE participants, ensuring high statistical power. Reporting bias is less likely since the home environment exposures were obtained before offspring's health outcomes. Most of the exposures were reported in a separate questionnaire answered 10 years before reporting on offspring's asthma and allergies. The exposure data covered a range of 10–20 years living environment. We have asked dampness and mold exposure in every home parents had lived in during both follow up periods, not only the current dwelling. Moreover, indoor painting exposure covered every dwelling parents lived in during the period from RHINEI to RHINE II. Our study adds new evidence that early life home environment exposures can be related to development of asthma and allergic diseases later in life.

4.9. Limitations

Some limitations exist in our study. It included only questionnaire data, no objective exposure measurements were available. There was no information on offspring's gender, and no information on other indoor renovation activities besides painting. We have no information on when the offspring moved out from parents' home. Information on home environment and offspring's asthma and allergies were reported by offspring's parents. Data on construction year and type of dwelling were only available regarding the home parents lived in when they answered the RHINE II questionnaire. We have previously studied in this study population on agreement of reporting of offspring' asthma, comparing parental reported (RHINE) and self-reported asthma in the RHINESSA generation study (Kuiper et al., 2018). The agreement was good for parental report of offspring's early onset asthma and moderate for parental report of offspring's later onset asthma (offspring's own answers were defined as gold standard) (Kuiper et al., 2018). We have no information on the duration of dampness and mold problems in homes that reported by parents. Nevertheless, dampness and mold in dwellings are often one persistent issue and can last for a long time.

The RHINE study were performed in cities with a lung clinic, which means that most families lived in cities. This can be the reason for many academic parents were included. One previous article based on RHINE data found an urban-rural gradient in adult asthma and showed a protective effect of livestock farm upbringing on asthma development and an urban-rural gradient (Timm et al., 2015).

Moreover, we have no information on ventilation system, heating system, indoor cleaning methods and furry pets in homes. Pet keeping in relation to and asthma/allergy is a complicate question due to selection effects related to occurrence of the diseases. One review indicated no clear associations between pet keeping and asthma/allergy (Chen et al., 2010). Another limitation is that ETS was not studied, the main reason is that there was no information on environmental tobacco smoke from RHINE I to RHINE III.

Outdoor air pollution can have negative effects on asthma/allergies. However, it was shown in one previous article that outdoor air pollution in northern Europe cities is generally low and no annual mean outdoor exposures exceeded the recommended EU-values (Kuiper et al., 2020). The study suggested that parental exposure to air pollution can influence the risk of asthma and allergies in future offspring (Kuiper et al., 2020). The ECRHS study found that traffic related air pollution was lower in northern Europe cities as compared to other parts of Europe (Jacquemin et al., 2009). The study suggested that traffic-related pollution can cause asthma symptoms and possibly asthma incidence in adults (Jacquemin et al., 2009). We did not analyse traffic density related question since this information was only available in RHINE III.

Level of medication is one aspect that can influence asthma and allergies. According to one previous article based on RHINE data, asthma medication has increased from 3.6 % to 7.6 % from RHINE I to RHINE III (Janson et al., 2018). However, we have no medication information for offspring. Moreover, quality of life was not studied in the RHINE study.

5. Conclusions

The present study suggested that presence of dampness and mold at home was consistently associated with offspring's asthma and atopic dermatitis. There were dose-response effects of indoor dampness and mold exposure on offspring's asthma and atopic dermatitis, suggesting stronger health effects of prolonged dampness/mold exposure in homes. Stronger health effects of dampness and mold exposure were found in older offspring. Living in apartments (vs. detached/semi-detached houses), living in newer buildings constructed in 1961–2001 (vs. constructed before 1961) and indoor painting were associated with offspring's asthma or allergic diseases. Reducing moisture and mold damage at home can be benefit for occupants with asthma and allergies. More perspective studies are needed to investigate the effects of building characteristics and other indoor environment exposures on development of atopic diseases.

Supplementary data to this article can be found online at https://doi.org/10.1016/j.scitotenv.2022.158609.

CRediT authorship contribution statement

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Data availability

The authors do not have permission to share data.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgments

The work was supported by the Icelandic Research Council, the Swedish Heart and Lung Foundation, the Vårdal Foundation for Health Care and Allergic Research, the Swedish Association Against Asthma and Allergy, the Swedish Council for Work Life and Social Research, the Swedish AFA Insurance (No. 467801100), the Bror Hjerpstedt Foundation, the Norwegian Research Council, the Norwegian Asthma and Allergy Association, the Danish Lung Association and the Estonian Science Foundation.

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