Relationships between Mite Allergen Levels, Mold Concentrations, and Sick Building Syndrome Symptoms in Newly Built Dwellings in Japan

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Running head: Dust mite allergens, airborne fungi, and subjective symptoms

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Abstract

This study investigated the possible relationships between exposures to mite allergen and airborne fungi with sick building syndrome (SBS) symptoms for residents living in newly built dwellings. We randomly sampled 5709 newly built dwellings in 6 prefectures from northern to southern Japan. A total of 1479 residents in 425 households participated in the study by completing questionnaire surveys and agreeing to environmental monitoring for mite allergen (Der 1), airborne fungi, aldehydes, and volatile organic compounds. Stepwise logistic regression analyses adjusted for confounders were used to obtain odds ratios (OR) of mite allergen and fungi for SBS symptoms. Der 1 had a significantly high OR for nose symptoms. *Rhodotorula* had a significantly high OR for any symptoms, and *Aspergillus* had significantly high OR for eye symptoms. However, the total colony-forming units had a significantly low OR for throat and respiratory symptoms. *Eurotium* had a significantly low OR for skin symptoms. In conclusion, dust mite allergen levels and indoor airborne *Rhodotorula* and *Aspergillus* concentrations may result in SBS symptoms in newly built dwellings.

Key words: Sick building syndrome; Mite allergen; Der 1; Mold; Colony-forming unit

Practical implications

Various factors can cause sick building syndrome symptoms. This study focused on biological factors such as dust mite allergen and airborne fungi in newly built dwellings in Japan. Dust mite allergen levels were significantly associated with higher rates of nose symptoms, airborne *Rhodotorula* concentrations were significantly associated with higher rates of any symptoms, and *Aspergillus* concentrations were significantly associated with higher rates of eye symptoms. Measures should be taken to reduce mite allergen levels and fungal concentrations in these dwellings.

Introduction

Although sick building syndrome (SBS) is associated with mucosal, skin, and general symptoms that develop primarily in office buildings (Burge, 2004), SBS can also develop in domiciliary environments (Engvall, 2001). SBS in dwellings has been recently highlighted in Japan; some Japanese living in newly built or renovated dwellings began to experience mucosal, skin, and general symptoms in the 1990s. This has been called “sick house syndrome” in Japan, and its cause has often been attributed to chemicals emitted from building materials (Torii, 2002).

However, causes of SBS include various factors other than chemicals. Biological factors, such as molds or mites, also induce SBS symptoms. We reported that dampness was significantly associated with SBS symptoms in solitary houses that were recently built in the Hokkaido Prefecture, a northern island of Japan (Saijo, 2004, Takeda, 2009). In a preliminary survey for this study, we also reported such significant associations in solitary houses that were recently built in many other regions (6 prefectures) of Japan (Kishi, 2009).

Several mechanisms are assumed to cause the dampness effect. Higher humidity in dwellings facilitates mold growth (Garrett, 1998b) and proliferation of dust mites (Bemt, 2006, Garrett, 1998a, Hirsch, 1998), both of which can affect health of residents.

Possible relationships between increased airborne fungal concentrations and SBS symptoms and asthma have been reported (Cooley, 1998, Ross, 2000). However, inverse relationships between airborne fungal concentrations and respiratory symptoms have been reported in primary school children (Kim, 2007). Thus, the effects of airborne fungal concentrations on SBS symptoms have not been fully elucidated, and there are no reports of these effects in newly built dwellings.

Because mite exposure has sensitization and allergic effects, it can aggravate and induce subjective symptoms in people of affected buildings (Bornehag, 2004). Dust mite allergen can cause asthma, rhinitis, and dermatitis (Tupker, 1998) that are defined, in a narrow sense, as specific building-related illnesses when they primarily occur in buildings (Redlich, 1997). However, it would appear that residents who have not been diagnosed with the symptoms are probably treated for SBS (Laumbach, 2005). Therefore, mite allergen exposure should be measured to elucidate its effect on SBS symptoms.

In this study, we used the symptoms query part of the Japanese version of MM040EA, a validated SBS questionnaire (Andersson, 1998, Mizoue, 2001), and measured dust mite allergen levels and airborne fungal concentrations to evaluate the possible associations of mite and mold exposures with SBS symptoms in newly built

dwellings in Japan.

Materials and Methods

Study population and selection of homes

In our previous survey (Kishi, 2009), we randomly sampled 5709 households in dwellings that were ≤6 years old in 6 prefectures from northern to southern Japan: Hokkaido (1240 households), Fukushima (910), Aichi (1070), Osaka (885), Okayama (906), and Fukuoka (698). The household list was obtained from building plan approval applications, which are the official data available for inspections. Preliminary questionnaires on indoor air quality were sent to the households between November 2003 and January 2004, and residents of 2298 households (response rate = 40.3%) responded to the questionnaire. Of these respondents, 1522 residents of 444 households agreed to participate in this study, which was conducted from September to November 2004. Of these participants, 1479 residents in 425 households were used for analyses after eliminating those with missing data. The participation rate for environmental monitoring was 18.5% from the respondents in the preliminary questionnaire survey. Informed consent was obtained from all participants, and the study was approved by the

institutional ethical board for epidemiological studies at Hokkaido University Graduate School of Medicine, the principal investigating institution, and the ethical boards of the regional universities involved with this study.

Questionnaire survey

We used 2 types of questionnaires: one for all residents and another for the head of the household or his/her partner. The questionnaire for all residents queried for information on personal characteristics and lifestyle, such as age, gender, current smoking habit, time spent in the dwelling, working hours, and stress levels. Furthermore, the questionnaire contained questions about the history of previous treatments (by a physician) for asthma or allergies. The questionnaire contained the symptoms query part of the Japanese version of MM040EA, a validated questionnaire designed for epidemiological assessments of SBS symptoms (Andersson, 1998, Mizoue, 2001). Symptoms surveyed for the past 3 months included the following: general symptoms (fatigue, feeling heavy-headed, headache, nausea/dizziness, or difficulty concentrating); eye symptoms (itching, burning, or irritation of the eyes); nose symptoms (irritated, stuffy, or runny nose); throat and respiratory symptoms (hoarseness, dry throat, or cough); and skin symptoms (dry or flushed facial skin, scaling/itching of the scalp or

ears, dry, itching, or red-skinned hands). For each symptom, the following answers were possible: “Yes, often (every week);” “Yes, sometimes;” and “No, never.” An additional question that regarded attributing a symptom to the home environment was included in the questionnaire. SBS symptoms were scored as positive if at least one subsymptom was found to occur often (every week)/sometimes and was believed to be attributed to the home environment. In this study, “general symptoms,” “eye symptoms,” “nose symptoms,” “throat and respiratory symptoms,” and “skin symptoms” indicate the abovementioned MM040EA SBS symptoms as positive. In addition, “any symptoms” were defined as at least 1 SBS symptom positive. The questionnaire for children who could not read and/or write was answered by their parent.

The questionnaire for the head of the household or his/her partner contained questions regarding dampness (condensation on window panes or walls, mold growth, moldy odor, slow drying of wet towels in the bathroom, water leakage during the previous 5 years or for a duration the person has lived in the dwelling if 5 years had not passed) and pets in the dwelling. After summing the presence or absence of the 5 dampness indicators, an overall dampness index (0–5) was calculated (Kishi, 2009). Data on the structure and age of the dwellings were obtained from a previous survey conducted in 2003.

Assessment of indoor environmental factors

Indoor airborne fungi were collected on dichloran 18% glycerol agar (DG-18: 20 mL on a 90 mm Petri dish) as a culture medium using an SAS air sampler (AINEX BIO-SAS International Pbi, Italy; catalog number 29842 for standard 90-mm Petri dishes). An air volume of 100 L was sampled at a flow rate of 100 L/min and height of 150 cm above the floor in the living room. The DG-18 medium was incubated at 27°C, fungal colonies were counted, and species were identified morphologically at the Mitsubishi Chemical Medicine Corporation (Tokyo, Japan). The fungal concentrations were expressed as colony-forming units per cubic meter of air (CFU/m^3) after the cultured numbers on the medium were multiplied by 10. A positive hole correction was not applied to correct for coincident spore impaction, since the total number of spore counts on the mediums rarely exceeded 300 colonies (Overberger, 1995).

Dust samples on the floor of the living room were collected at 0.5 m^2/min with a hand vacuum cleaner (HC-V15, National, Japan) equipped with a paper filter. The levels of Der p1 and Der f1 in the dust samples were quantified by ELISA at the LCD Allergic Center (Osaka, Japan); the quantification limit for Der p1 and Der f1 was 0.1 μg/g fine dust. Der 1 levels were calculated by summing the quantified Der p1 and Der

f1 levels. For calculating Der 1, values of Der p1 and Der f1 less than the lower quantification limit were considered to be half of the lower quantification limit.

Indoor air monitoring for aldehydes, acetone, and volatile organic compounds (VOCs) was performed in the living room of each dwelling. Air samples were collected at 100–150 cm above the floor for 24 h with a DSD-DNPH diffusion sampler (Supelco, Japan) for aldehydes and acetone and a VOC-SD diffusion sampler (Supelco) for VOCs. Thirteen aldehydes and acetone were quantified by HPLC, and 29 VOCs were quantified by GC-MS using a previously described method (Takigawa, 2004). The quantification limit for each chemical was 1.0 μg/m^3. Total VOC (TVOC) was calculated as the sum of all VOCs. Because this study dealt with controlling factors for mold and mite risk analyses, only formaldehyde and TVOC were used (Takigawa, 2004). Due to their skewed distributions, formaldehyde and TVOC values were transformed to common logarithmic values. For logarithmic transformations, values less than the lower quantification limit were considered to be half of the lower quantification limit.

Formaldehyde is a major air contaminant in residential and industrial occupational environments and can cause mucosal irritation symptoms (Rumchev, 2002). TVOC is one of the indicators of indoor air chemical environment and is possibly related to

subjective symptoms (Norback, 1990). Therefore, formaldehyde and TVOC concentrations were used as minimum possible confounders of indoor chemical factors in the statistical analyses, though many chemical have been detected in the indoor environment.

Statistical analysis

Statistical analysis was performed using multiple logistic regression. First, crude odds ratios with 95% confidence intervals (OR, 95% CI) for personal and dwelling factors, each fungal concentration, and Der 1 levels for SBS symptoms were calculated. Due to their skewed distributions, fungal concentrations and dust mite allergen levels were transformed to common logarithmic values. For logarithmic transformation, a value of 0 CFU/m^3 for fungus was changed to 0.5 CFU/m^3.

Next, to obtain adjusted OR for SBS symptoms, mite allergen levels, total CFU, and fungal concentrations were introduced separately into the model. We controlled for age (≤19, 20–39, 40–59, ≥60 years), gender, region (2 northern cities, Sapporo and Fukushima, or others), and other personal or dwelling factors significantly related to each symptom. Because time spent in the dwelling had several missing values, the most frequent answer, 12–20 h/day, was assigned to the missing values. The dampness index

was not used for adjustments because it contained fungal exposure factors. Furthermore, smoking was not used because it was only negatively related to skin symptoms and appeared not to have a cause–effect relationship.

For additional adjusted analyses, the abovementioned adjustment factors were forced into the model, and total CFU, fungal concentrations, and mite allergen levels with $P < 0.2$ in the above adjusted analyses were entered into the models in a backward stepwise manner.

A significance level of 5% was applied to all statistical analyses. All analyses used IBM SPSS statistics software for Windows version 18.0 (SPSS Inc., Chicago, USA).

Results

The average age of the analyzed participants was 33 years (range 0−90 years). Females spent longer periods of time in the dwellings and had a lower smoking rate (Table 1). The number of dwellings in the 6 prefectures was as follows: Hokkaido (104), Fukushima (65), Aichi (57), Osaka (78), Okayama (71), and Fukuoka (50). About 80% of the dwellings were wooden; most had been built using the timber framework method (Japanese conventional method) or the two-by-four construction. The most frequent dwelling age category was 1 year (Table 2). SBS symptoms were more frequent in females, and the most frequent symptoms were those of the nose (Table 3).

The median Der 1 level in the living rooms was 1.26 μg/g dust (Table 4). Table 5 shows fungal exposures in the living rooms. *Cladosporium* was identified as the most prevalent fungal genera. Table 6 shows formaldehyde and TVOC concentrations in the living rooms. The median concentrations of formaldehyde and TVOC were 40.6 and 112.3 $\mu g/m^3$, respectively.

Crude analyses (Table 7) showed that Der 1 had a significantly high OR for eye and nose symptoms. Total CFU and *Cladosporium* had a significantly low OR for throat and respiratory symptoms. *Penicillium* had a significantly low OR for skin symptoms. *Aspergillus* had a significantly high OR for eye symptoms and *Rhodotorula* had a

significantly high OR for any or all symptoms. *Candida* and *Cryptococcus* had a significantly high OR for nose symptoms.

Adjusted analyses (Table 8) showed that Der 1 had a significantly high OR for eye and nose symptoms. Total CFU and *Cladosporium* had a significantly low OR for throat and respiratory symptoms. *Penicillium* had a significantly high OR for eye symptoms. *Aspergillus* had a significantly high OR for eye symptoms, and *Rhodotorula* had a significantly high OR for any symptoms. *Eurotium* had significantly low OR for skin, and throat and respiratory symptoms.

Stepwise analyses (Table 9) showed that Der 1 had a significantly high OR for nose symptoms (OR = 1.47; 95% CI: 1.14–1.88). *Aspergillus* had a significantly high OR for eye symptoms (OR = 2.38; 95% CI: 1.29–4.39), and *Rhodotorula* had a significantly high OR for any symptoms (OR = 0.68; 95% CI: 1.09–2.58). However, total CFU had a significantly low OR for throat and respiratory symptoms, and *Eurotium* had a significantly low OR for skin symptoms.

Discussion

Our results indicated relationships between SBS symptoms and Der 1, *Aspergillus,* and *Rhodotorula* for residents living in newly built houses in Japan, even after accounting for adjustments. However, total CFU and *Eurotium* had protective relationships for SBS symptoms in our study. To our knowledge, this is the first study that has investigated the relationships of airborne fungi and mite allergen levels with SBS symptoms among more than 1000 residents in newly built houses.

In a German study, median Der 1 levels were reported to be 0.184, 0.224, and 0.480 μg/g dust at 3 different times in the living rooms (Lau, 2000). In an Italian study, geometric means for Der p1 and Der f1 were 0.15 and 0.83 μg/g dust, respectively (Moscato, 2000). Furthermore, in a Korean study, geometric means for Der p1 and Der f1 were 0.11 and 7.5 μg/g dust, respectively (Nam, 2008) and in a Thai study it was 2.43 μg/g dust for Der 1 (Trakultivakorn, 2004). The mite allergen levels on the floor of the living rooms in our study were somewhat low; however, they appeared comparable with those of previous reports.

As previously described, mite allergen exposure can aggravate and induce subjective symptoms in people of affected buildings (Bornehag, 2004). In this study, the Der 1 concentrations were significantly associated with increased nose symptoms that

primarily occurred in the dwellings. Japan has a high prevalence of allergic rhinitis, and cedar pollen and mites are the predominant allergens associated with allergic rhinitis (Sakashita, 2009). Japanese cedar pollen-induced allergic rhinitis usually develops in spring and early summer, and therefore, the present survey was conducted in the fall to clearly estimate the effects of mite allergen on nose symptoms without interference from cedar pollen.

Mite allergen had no significant effect on throat and respiratory symptoms in this study. Mite allergen is a major allergen associated with bronchial asthma (Richardson, 2005), and people with asthmatic symptoms are probably highly concerned with dust mite allergen avoidance. This may have attenuated the effects of mite allergen exposure on throat and respiratory symptoms in this cross-sectional setting.

Two Japanese studies reported that the most prevalent mold genus in indoor environments was *Cladosporium*, and the second most prevalent was *Penicillium* or *Aspergillus* (Sakai, 2003, Takahashi, 1997). Furthermore, these studies reported the geometric means for indoor total CFU in DG-18 medium as follows: 138/m^3 in Yokohama, 301 and 237/m^3 in the summer in Nagoya, and 88 and 79/m^3 in the winter in Nagoya. Thus, the indoor air fungal concentrations of our study appeared comparable with previous Japanese studies.

In our final model, the indoor airborne *Aspergillus* concentrations were significantly associated with a higher rate of eye symptoms. Indoor airborne *Aspergillus* is considered as one of the causative agents for SBS symptoms (Cooley, 1998), and its primary mechanism is speculated to be allergic reactions (Schwab, 2004). Although we found no significant relationship between *Aspergillus* and throat and respiratory symptoms, the main types of *Aspergillus* allergy symptoms reported were respiratory symptoms. However, because severity of respiratory symptoms appear to provide more of an incentive to be reported (Mari, 2003, Agarwal, 2009), further studies are needed to clarify *Aspergillus* allergy effects on various symptoms in circumstances of relatively low level exposures. In our final model, indoor airborne *Rhodotorula* concentrations were significantly associated with a higher rate of any symptoms. The possibility of its inducing allergic reactions has been reported (Savolainen, 1998, Greenberger, 2004); however, to our knowledge, a relationship between indoor airborne *Rhodotorula* concentrations and subjective symptoms has not been reported.

In our study, indoor airborne total CFU and *Eurotium* were significantly associated with reduced throat and respiratory symptoms. In a Swedish study, total CFU had a significant negative association with asthmatic symptoms in schools; the reason speculated was that higher total CFU indicated higher air ventilation rates, which had

protective effects against asthmatic symptoms. (Kim, 2007) Indeed, outdoor airborne total CFU are higher than indoor airborne total CFU in Japan and other countries (Lee, 2006, Shelton, 2002, Sakai, 2003, Takahashi, 1997). The outdoor airborne *Cladosporium* concentrations were higher than the indoor ones (Lee, 2006, Shelton, 2002, Sakai, 2003, Takahashi, 1997), and *Cladosporium* was a major component of the total CFU. If higher indoor airborne *Cladosporium* concentrations and total CFU represented higher home ventilation rates, which could have an effect on diluting contaminants originating from indoor materials or activities, which may be a reason for the protective association of *Cladosporium* and total CFU on SBS symptoms. However, because significant protective effects were only seen for throat and respiratory symptoms, chance alone may be a reason for the protective effects. In addition, ventilation rates and habits were not evaluated in this study. Further studies are needed to clarify the relationships between ventilation rates, airborne fungal exposure, and SBS symptoms.

Another study has found a protective effect of airborne *Cladosporium* concentrations on allergic sensitization of infants (Osborne, 2006). The authors speculated a Th2 inhibiting mechanism, such as endotoxin (Niven, 2003), but this mechanism may not be applicable to children and details were unknown.

Eurotium is a xerophilic mold, which has higher indoor airborne concentrations than the outdoor onesin Japan (Takahashi, 1997). The possibility of allergy induction by *Eurotium* has been reported (Akiyama, 2001). Thus, the association of *Eurotium* with reduced SBS symptoms in our study was a surprising result. Because *Eurotium* was present in outdoor airborne samples, although at lower concentrations than in indoor airborne samples, the influence of outdoor concentrations and higher ventilation rates may be a reflection of chance. Furthermore, because *Eurotium* is xerophilic and more conspicuous in conditions of low dampness, it may be preferable to prevent SBS symptoms and typical mold growth.

The present study has several limitations. First, the participation rate was relatively low. People who are willing to be involved in an indoor air quality study and open to extensive inspection tend to be those with more severe symptoms (Bornehag, 2006). Therefore, the actual prevalence of SBS may be lower than that shown by our results.

Second, because this was a cross-sectional study, any causal relationships between variables could not be determined. In addition, previous health problems of participants may have altered their lifestyle habits such as cleaning frequency and ventilation time, which would dilute the effects of exposure. And, we only evaluated the living rooms of the dwellings for contaminants. Japanese houses are not large, and most residents seem

to stay in the living rooms for many hours, except for sleep; therefore, we consider that the exposure levels of residents in the living rooms represented the overall exposure levels in the dwellings (Sakaguchi, 2003). Furthermore, we evaluated the airborne fungi at a specific point in time during 1 min sampling period, and evaluated only culturable airborne fungi. It has been reported that shorter sampling period has lower representativeness (Pasanen, 2001). And, seasonal variations could not be evaluated in this study. In particular, the seasonal variations of airborne fungal concentrations may affect the results. Moreover, non-culturable fungi have allergic and toxic effects, and the superiority of evaluating both has been reported (Osborne, 2006). However, air sampling is one of the most common methods to evaluate fungal exposure level in indoor environments, and as the possible health effects caused fungal exposure indoor mainly are suspected to be respiratory symptoms, air sampling is believed to represent the exposure (Holme, 2010). Thus, though airborne fungi measurements with longer sampling time or frequent sampling will be required for further studies, we believe our study is valuable because, to our knowledge, this is the first study of evaluate the relationship of airborne fungi exposure on subjective symptoms in more than four hundred relatively new dwellings.

Third, Sixth, socioeconomic status was not measured. However, because all

households owned newly built detached houses, it was considered that the participants had socioeconomic statuses belonging to the middle class.

Forth, we were not able to clarify the sources of the airborne fungi in these relatively new dwellings. The sources of indoor airborne fungi which have been reported are outdoor air, pets, carpets, water damaged materials and damped materials, etc (Li, 2004, Ren, 2001). The new materials are also possible sources (Li, 2004), and some dwellings in the present study had condensation on window panes or walls, mold growth, moldy odor, and/or water leakage.

Fifth, though it has been reported that fungi have pathogenic effects through allergic reactions, microbial VOC (MVOC) emissions and their inflammatory components (glucans) (Li, 2004), the pathogenic mechanisms of fungi were not able to be clarified in the present study.

Finally, a BIO-SAS sampler was selected for this study because it is easy to use and portable (battery availability). Furthermore, it has a high flow rate of 100 L/min and can have a high impact efficiency (Whyte, 2007). However, a high flow rate may cause more fungal injuries due to drying of viable spores (Verhoeff, 1990). The sampling duration can also affect the sampling performance. Long sampling durations can reduce the analytical detection limit compared with short sampling durations, although long

durations can also cause more fungal injuries due to drying of viable spores and mechanical damage from shear and impaction forces (Saldanha, 2008). Longer nozzle-to-agar distances increase the cutoff sizes (d_{50}) (Whyte, 2007) . However, the agar amount in the Petri dishes used in this study, 20 mL, was that commonly used in studies because the instruction manual did not suggest an ideal agar amount. Thus, underestimations of fungal amounts may have occurred, although the method for airborne fungi evaluation was standardized in all 6 regions. Thus, we believe that the relationship between airborne fungi and SBS symptoms could be properly evaluated.

In conclusion, dust mite allergen levels and indoor airborne *Aspergillus* and *Rhodotorula* concentrations were significantly related to SBS symptoms in newly built dwellings. We should take measures to reduce the mite allergen levels and fungal concentrations in dwellings. Further studies are needed to clarify seasonal variations for the effects of biological contaminants, including nonviable fungi, and their effects in various types of dwellings. Furthermore, it will be necessary to investigate whether increased indoor airborne *Cladosporium* concentrations and total CFU actually have protective relationships for symptoms in particular environments.

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Table 1 Characteristics of participants (n = 1479)

Characteristics	All (n = 1479)		Female (n = 770)		Male (n = 709)	
	n	(%)	n	(%)	n	(%)
Age (years)						
≤9	326	22.0	159	20.6	167	21.7
10–19	186	12.6	100	13.0	86	11.2
20–29	77	5.2	32	4.2	45	5.9
30–39	323	21.8	132	17.1	191	24.8
40–49	243	16.4	134	17.4	109	14.2
50–59	144	9.7	57	7.4	87	11.3
≥60	180	12.2	96	12.5	84	10.9
Current smoker	180	12.2	30	3.9	150	21.2
History of allergy or asthma	713	48.2	383	49.7	330	46.5
Time in the dwelling (h/day)						
<12	394	26.6	82	10.6	312	44.0
12–20	835	56.5	490	63.6	345	48.7
≥20	239	16.2	190	24.7	49	6.9
Unknown	11	0.7	8	1.0	3	0.4

Table 2 Numbers of dwellings and participants with regard to dwelling characteristics

	Number of dwellings (n = 425)		Number of participants (n = 1479)	
	n	(%)	n	(%)
City				
Sapporo	104	24.5	343	23.2
Fukushima	65	15.3	238	16.1
Nagoya	57	13.4	191	12.9
Osaka	78	18.4	283	19.1
Okayama	71	16.7	260	17.6
Kitakyushu	50	11.8	164	11.1
Age of dwelling (years)				
<1	7	1.6	23	1.6
1–<2	108	25.4	392	26.5
2–<3	92	21.6	310	21.0
3–<4	77	18.1	272	18.4
4–<5	59	13.9	203	13.7
5–<6	58	13.6	200	13.5
6–<7	22	5.2	75	5.1
7–<8	2	0.5	4	0.3
Size of household				
1–2	92	21.6	176	11.9
3–4	258	60.7	903	61.1
5–8	75	17.6	400	27.0
Number of rooms				
2–4	76	17.9	239	16.2
5–6	270	63.5	825	55.8
7–12	74	17.4	302	20.4
Unknown	4	0.9	13	0.9
Wooden house	339	79.8	1150	77.8
Pets at home	103	24.2	377	25.5
Dampness index				
0	76	17.9	232	15.7
1	90	21.2	294	19.9
2	160	37.6	581	39.3
3	74	17.4	280	18.9
4	21	4.9	80	5.4
5	4	0.9	12	0.8

Table 3 Prevalence of sick building syndrome symptoms in females and males

Type of symptoms	Females (n = 769)		Males (n = 710)		All (n = 1479)	
	n	(%)	n	(%)	n	(%)
Skin symptoms	42	5.5	18	2.5	60	4.1
Eye symptoms	29	3.8	22	3.1	51	3.4
Nose symptoms	65	8.5	50	7.0	115	7.8
Throat and respiratory symptoms	62	8.1	40	5.6	102	6.9
General symptoms	20	2.6	9	1.3	29	2.0
Any symptoms	128	16.8	82	11.5	210	14.2

Table 4 Der 1 levels in living rooms (μg/g dust) (n = 425)

	GM*	Median	Min.	25th percentile	75th percentile	Max.	Identification rate (%)
Der p1	0.20	<0.1	<0.1	<0.1	0.55	144.80	46.8
Der f1	0.98	0.84	<0.1	0.28	4.11	200.00	86.1
Der 1 (Der p1 + Der f1)	1.69	1.26	<0.1	0.44	6.73	200.05	89.4

*GM: geometric mean

1 Table 5 Total colony-forming units (CFU) and fungal genera CFU in living rooms (n =
2 425)

	GM* (CFU/m^3)	Median (CFU/m^3)	Min. (CFU/m^3)	25th percentile (CFU/m^3)	75th percentile (CFU/m^3)	Max. (CFU/m^3)	Identification rate (%)
Total CFU	247.9	260	0	160	445	3370	98.6
Genera							
Cladosporium	91.9	120	0	60	260	2440	92.0
Penicillium	12	20	0	0	50	2490	74.8
Aspergillus	2.7	0	0	0	10	950	46.1
Alternaria	1.5	0	0	0	10	100	32.3
Rhodotorula	1.1	0	0	0	0	330	20.0
Eurotium	0.9	0	0	0	0	310	17.2
Aureobasidium	0.7	0	0	0	0	50	8.7
Candida	0.7	0	0	0	0	220	7.3
Cryptococcus	0.6	0	0	0	0	120	7.1

3 *GM: geometric mean

Table 6 Concentrations of formaldehyde and total volatile organic compounds (TVOC) in living rooms (n = 425)

	GM*	Median	Min.	25th percentile	75th percentile	Max.
Formaldehyde (μg/m^3)	31.2	40.6	<1.0	29.0	57.7	202.8
TVOC (μg/m^3)	121.5	112.3	16.0	67.8	203.6	1770.9

*GM: geometric mean

Table 7 Crude odds ratios for personal and dwelling factors, mites, and fungi for sick building syndrome symptoms

	Any	Skin	Eye	Nose	Throat and respiratory	General
	OR (95% CI) P value	OR (95% CI) P value	OR (95% CI) P value	OR (95% CI) P value	OR (95% CI) P value	OR (95% CI) P value
Age						
≤19	2.89 (1.50–5.55) 0.001	1.72 (0.65–4.58) 0.277	2.26 (0.78–6.58) 0.135	3.21 (1.35–7.61) 0.008	1.70 (0.74–3.92) 0.211	0.79 (0.24–2.59) 0.694
20–39	3.37 (1.74–6.53) <0.001	1.75 (0.64–4.75) 0.276	1.60 (0.52–4.92) 0.416	2.96 (1.22–7.14) 0.016	2.75 (1.21–6.26) 0.016	0.67 (0.19–2.40) 0.539
40–59	2.07 (1.05–4.10) 0.037	1.10 (0.39–3.23) 0.834	0.93 (0.28–3.13) 0.905	1.66 (0.66–4.20) 0.281	1.49 (0.62–3.55) 0.369	1.17 (0.36–3.77) 0.796
≥60	Reference	Reference	Reference	Reference	Reference	Reference
Female	1.53 (1.14–2.06) 0.005	2.22 (1.27–3.90) 0.005	1.23 (0.70–2.15) 0.480	1.22 (0.83–1.79) 0.312	1.47 (0.97–2.22) 0.067	2.08 (0.94–4.60) 0.070
Two northern cites	1.78 (1.33–2.39) <0.001	1.94 (1.16–3.27) 0.021	1.28 (0.73–2.25) 0.388	1.30 (0.89–1.91) 0.176	2.15 (1.43–3.23) <0.001	1.26 (0.60–2.64) 0.538
Current smoker	0.30 (0.48–1.25) 0.300	0.24 (0.06–0.99) 0.049	0.61 (0.22–1.70) 0.341	0.75 (0.39–1.42) 0.375	1.06 (0.58–1.94) 0.854	0.25 (0.03–1.88) 0.179
History of allergy or asthma	2.26 (1.67–3.06) <0.001	3.60 (1.48–5.56) 0.001	3.26 (1.72–6.17) <0.001	4.06 (2.59–6.37) <0.001	1.65 (1.10–2.49) 0.016	1.54 (0.73–3.27) 0.260
Time in the dwelling (h)						
<12 (n = 394)	Reference	Reference	Reference	Reference	Reference	Reference
12–20 (n = 835)	1.52 (1.04–2.21) 0.030	2.10 (1.00–4.37) 0.048	2.00 (0.91–4.34) 0.086	1.45 (0.91–2.46) 0.110	1.56 (0.91–2.68) 0.109	1.34 (0.53–3.44) 0.537
≥20 (n = 239)	1.94 (1.23–3.08) 0.005	2.26 (0.94–5.45) 0.069	2.11 (0.82–5.42) 0.122	1.98 (1.09–3.59) 0.025	2.55 (1.37–4.76) 0.003	1.67 (0.53–5.22) 0.382

Age of dwelling (year)						
0–1	Reference	Reference	Reference	Reference	Reference	Reference
2–3	1.13 (0.77–1.66)	0.75 (0.37–1.54)	2.00 (0.88–4.53)	0.94 (0.57–1.56)	1.12 (0.67–1.88)	0.95 (0.33–2.76)
	0.532	0.439	0.098	0.806	0.667	0.825
4–7	1.68 (1.15–2.46)	1.71 (0.90–3.23)	2.32 (1.02–5.29)	1.60 (0.99–2.59)	1.34 (0.79–2.25)	2.10 (0.84–5.70)
	0.007	0.100	0.046	0.056	0.278	0.108
Wooden house	0.80 (0.55–1.15)	1.40 (0.80–2.49)	0.74 (0.36–1.54)	0.81 (0.53–1.32)	0.58 (0.33–1.02)	0.91 (0.37–2.25)
	0.230	0.249	0.423	0.404	0.061	0.839
Pets at home	1.11 (0.80–1.54)	1.37 (0.79–2.40)	0.71 (0.35–1.44)	1.03 (0.67–1.60)	1.44 (0.93–2.21)	1.32 (0.59–2.93)
	0.553	0.264	0.329	0.878	0.101	0.490
Population density**	1.03 (0.88–1.22)	1.02 (0.75–1.38)	1.03 (0.76–1.41)	0.93 (0.71–1.23)	1.11 (0.94–1.34)	1.04 (0.70–1.55)
(n = 1466)	0.703	0.923	0.833	0.620	0.195	0.854
Dampness index**	1.42 (1.24–1.61)	1.27 (1.01–1.60)	1.41 (1.10–1.81)	1.66 (1.39–1.97)	1.27 (1.06–1.51)	1.37 (0.99–1.90)
	<0.001	0.042	0.006	<0.001	0.010	0.056
Formaldehyde*	1.85 (1.21–2.84)	1.17 (0.64–2.16)	1.93 (0.81–4.62)	1.48 (0.89–2.46)	1.64 (0.93–2.91)	1.77 (0.59–5.32)
	0.005	0.609	0.139	0.130	0.087	0.312
TVOC*	1.17 (0.78–1.77)	0.68 (0.32–1.44)	1.19 (0.55–2.56)	1.07 (0.63–1.83)	1.99 (1.15–3.44)	1.43 (0.52–3.94)
	0.441	0.315	0.656	1.795	0.013	0.486
Der 1*	1.12 (0.93–1.35)	1.10 (0.80–1.53)	1.45 (1.02–2.07)	1.39 (1.09–1.77)	1.04 (0.80–1.34)	1.20 (0.76–1.92)
	0.224	0.555	0.039	0.007	0.792	0.438
Total CFU*	0.86 (0.61–1.21)	0.69 (0.39–1.23)	1.73 (0.84–3.54)	0.81 (0.52–1.25)	0.57 (0.37–0.88)	0.73 (0.32–1.67)
	0.389	0.210	0.136	0.340	0.011	0.458
*Cladosporium**	0.94 (0.74–1.20)	0.79 (0.52–1.20)	1.64 (0.99–2.74)	0.88 (0.64–1.21)	0.65 (0.47–0.90)	0.73 (0.41–1.32)
	0.620	0.264	0.057	0.440	0.008	0.297
*Penicillium**	0.94 (0.70–1.25)	0.57 (0.33–0.99)	1.60 (0.95–2.71)	0.96 (0.66–1.40)	0.95 (0.64–1.42)	0.74 (0.35–1.56)
	0.664	0.047	0.078	0.824	0.816	0.423
*Aspergillus**	1.15 (0.79–1.69)	0.78 (0.37–1.66)	2.34 (1.29–4.23)	1.45 (0.91–2.32)	0.89 (0.51–1.56)	2.01 (0.90–4.49)

	0.469	0.513	0.005	0.116	0.678	0.088
*Alternaria**	0.89 (0.54–1.15)	1.01 (0.47–2.56)	0.69 (0.25–1.91)	1.13 (0.61–2.10)	1.11 (0.55–2.08)	0.70 (0.19–2.65)
	0.636	0.828	0.478	0.696	0.832	0.600
*Rhodotorula**	1.97 (1.32–2.93)	1.92 (0.99–3.68)	1.79 (0.87–3.68)	1.17 (0.65–2.11)	1.52 (0.86–2.67)	1.91 (0.77–4.75)
	0.001	0.050	0.112	0.594	0.147	0.166
*Eurotium**	0.80 (0.43–1.49)	0.21 (0.04–1.31)	0.87 (0.27–2.79)	0.70 (0.30–1.65)	0.71 (0.29–1.76)	1.50 (0.45–5.00)
	0.481	0.095	0.814	0.417	0.458	0.510
*Aureobasidium**	0.60 (0.19–1.91)	0.27 (0.20–3.77)	0.21 (0.01–4.48)	1.28 (0.37–4.51)	0.62 (0.13–3.12)	1.54 (0.16–14.99)
	0.389	0.322	0.316	0.698	0.565	0.710
*Candida**	1.40 (0.72–2.74)	0.56 (0.10–3.12)	1.60 (0.50–5.09)	2.12 (1.02–4.43)	1.58 (0.67–3.72)	2.15 (0.57–8.04)
	0.323	0.512	0.430	0.045	0.296	0.256
*Cryptococcus**	1.91 (0.84–4.31)	1.76 (0.44–6.96)	2.21 (0.57–8.57)	2.56 (1.01–6.48)	1.96 (0.69–5.63)	2.34 (0.42–12.96)
	0.122	0.424	0.251	0.047	0.209	0.330

*OR was calculated using 1 unit change (aftercommon log-transformation)

**OR of per 1 number increasing

1 Table 8 Adjusted odds ratios for mites and fungi for sick building syndrome symptoms

	Any[a]	Skin[b]	Eye[c]	Nose[d]	Throat and respiratory[e]	General[f]
	OR (95% CI) P value	OR (95% CI) P value	OR (95% CI) P value	OR (95% CI) P value	OR (95% CI) P value	OR (95% CI) P value
Der 1*	1.16 (0.96–1.41) 0.136	1.12 (0.80–1.57) 0.501	1.45 (1.01–2.10) 0.046	1.47 (1.14–1.88) 0.003	1.08 (0.83–1.41) 0.553	1.16 (0.73–1.85) 0.532
Total CFU*	0.81 (0.58–1.15) 0.239	0.67 (0.38–1.18) 0.160	1.60 (0.79–3.25) 0.192	0.75 (0.48–1.18) 0.213	0.51 (0.33–0.79) 0.003	0.74 (0.33–1.67) 0.467
*Cladosporium**	0.90 (0.70–1.15) 0.380	0.78 (0.52–1.178) 0.229	1.54(0.93–2.58) 0.096	0.84 (0.61–1.15) 0.273	0.63 (0.46–0.87) 0.005	0.81 (0.45–1.45) 0.472
*Penicillium**	0.94 (0.70–1.27) 0.687	0.59 (0.34–1.03) 0.062	1.69 (1.01–2.84) 0.047	1.01 (0.69–1.49) 0.950	0.90 (0.60–1.37) 0.614	0.74 (0.34–1.57) 0.426
*Aspergillus**	1.22 (0.82–1.82) 0.322	0.83 (0.39–1.79) 0.637	2.38 (1.29–4.39) 0.006	1.49 (0.92–2.43) 0.105	0.97 (0.55–1.73) 0.92	2.06 (0.91–4.65) 0.081
*Alternaria**	0.62 (0.36–1.05) 0.077	0.77 (0.32–1.86) 0.559	0.53 (0.18–1.55) 0.243	0.99 (0.51–1.92) 0.966	0.77 (0.38–1.53) 0.450	0.59 (0.15–2.37) 0.461
*Rhodotorula**	1.66(1.08–2.55) 0.020	1.60 (0.80–3.19) 0.185	1.70 (0.80–3.64) 0.170	1.07 (0.58–1.99) 0.823	1.15 (0.63–2.08) 0.658	1.97 (0.75–5.15) 0.168
*Eurotium**	0.49 (0.24–1.01) 0.054	0.08 (0.01–0.62) 0.015	0.73 (0.20–2.70) 0.636	0.50 (0.19–1.33) 0.165	0.35 (0.12–0.99) 0.048	1.36 (0.38–4.86) 0.637
*Aureobasidium**	0.79 (0.24–2.54) 0.686	0.34 (0.03–4.66) 0.420	0.21 (0.01–4.34) 0.313	1.35 (0.38–4.73) 0.643	1.07 (0.21–5.39) 0.933	1.57 (0.15–16.07) 0.706
*Candida**	0.93 (0.46–1.89) 0.831	0.35 (0.06–2.17) 0.261	1.17 (0.35–3.92) 0.801	1.74 (0.80–3.80) 0.165	1.09 (0.45–2.67) 0.844	2.07 (0.53–8.31) 0.292
*Cryptococcus**	1.68 (0.70–4.04) 0.246	1.34 (0.32–5.59) 0.690	2.37 (0.57–9.78) 0.235	2.59 (0.95–7.07) 0.064	1.44 (0.47–4.42) 0.525	2.22 (0.38–12.97) 0.375

*transformed to common logarithmic values
[a]Adjusted for age, gender, regions, history of allergy, time spent in the dwelling, age of dwelling, log formaldehyde
[b]Adjusted for age, gender, regions, history of allergy, time spent in the dwelling
[c]Adjusted for age, gender, regions, history of allergy, age of dwelling
[d]Adjusted for age, gender, regions, history of allergy, time spent in the dwelling
[e]Adjusted for age, gender, regions, history of allergy, time spent in the dwelling, log TVOC
[f]Adjusted for age, gender, regions

1 Table 9 Adjusted odds ratios for mites and fungi for sick building syndrome symptoms in stepwise models

	Any[a]	Skin[b]	Eye[c]	Nose[d]	Throat and respiratory[e]	General[f]
	OR (95% CI) P value	OR (95% CI) P value	OR (95% CI) P value	OR (95% CI) P value	OR (95% CI) P value	OR (95% CI) P value
Der 1*	not selected		not selected	1.47 (1.14–1.88) 0.003		
Total CFU		not selected			0.55 (0.15–0.85) 0.008	
*Cladosporium**			not selected			
*Penicillium**		0.63 (0.37–1.08) 0.093	not selected			
*Aspergillus**			2.38 (1.29–4.39) 0.006	not selected		2.06 (0.91–4.65) 0.081
*Alternaria**	not selected					
*Rhodotorula**	1.68 (1.09–2.58) 0.019	not selected	not selected			not selected
*Eurotium**	0.48 (0.23–1.00) 0.051	0.09 (0.01–0.66) 0.019		not selected	0.42 (0.14–1.20) 0.105	
*Aureobasidium**						
*Candida**				not selected		
*Cryptococcus**				not selected		

*transformed to common logarithmic values
[a]Adjusted for age, gender, regions, history of allergy, time spent in the dwelling, age of dwelling, log formaldehyde
[b]Adjusted for age, gender, regions, history of allergy, time spent in the dwelling
[c]Adjusted for age, gender, regions, history of allergy, age of dwelling
[d]Adjusted for age, gender, regions, history of allergy, time spent in the dwelling
[e]Adjusted for age, gender, regions, history of allergy, time spent in the dwelling, log TVOC: because total CFU and *Cladosporium* were highly correlated, Total CFU that had a higher P value was entered into the stepwise analyses
[f]Adjusted for age, gender, regions
Not selected: eliminated in backward stepwise analysis