DOCTORAL THESIS

Association between temporary housing habitation after the 2011 Japan earthquake and mite allergen sensitization and asthma development

(東日本大震災後の応急仮設住宅に入居歴のある住民を対象とした気管支喘息の有病率およびアレルゲン感作と喘息の発症について)

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Association between Temporary Housing Habitation after the 2011 Japan Earthquake and Mite Allergen Sensitization and Asthma Development

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Keywords

Adult asthma · *Dermatophagoides farinae* · *Dermatophagoides pteronyssinus* · *Aspergillus fumigatus* · Disaster · Great East Japan Earthquake · Temporary housing · Mite-specific immunoglobulin E

Abstract

Introduction: We previously reported an increased prevalence of asthma in adults who lived in temporary housing after the 2011 Great East Japan Earthquake. The goal of the current study was to investigate changes in asthma prevalence and mite-specific immunoglobulin E (IgE) titers in temporary housing residents during 2014–2019. ***Methods:*** By using the Global Initiative for Asthma guidelines, we diagnosed asthma in Ishinomaki city temporary housing residents aged 15 years or older. We then analyzed serum antigen-specific IgE levels to *Dermatophagoides farinae* (*Der f*), *Dermatophagoides pteronyssinus* (*Der p*), and *Aspergillus fumigatus*. ***Results:*** The prevalence of asthma exceeded 20% across all age-groups throughout the study period. The proportion of study participants with a "positive" antigen-specific IgE titer (i.e., ≥0.35 IU_A/mL) was higher in asthmatics than in nonasthmatics for *Der f* and *Der p* but not for *Aspergillus fumigatus*. Among residents ≥50 years old who were diagnosed with asthma, the percentage with a *Der f*-specific IgE titer ≥0.10 IU_A/mL was higher than the proportion with ≥0.35 IU_A/mL. Among study participants, asthma onset occurred before the earthquake, during residence in shelters or temporary housing, and (starting in 2016) after moving out of temporary housing. The *Der p*-specific IgE level was positively correlated with the duration of temporary housing

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($p < 0.05$, $r = 0.41$) and inversely correlated with the time elapsed since moving out of temporary housing ($p < 0.05$, $r = -0.35$). ***Conclusion:*** Mite allergen sensitization was found in both asthmatic and nonasthmatic temporary housing residents after the 2011 Japan earthquake and tsunami; asthma developed even after subjects moved out of temporary housing.

Introduction

In the aftermath of natural disasters, such as floods and tsunamis, waterlogged materials and increased environmental humidity promote increased multiplication of bacteria and fungi, thereby increasing the incidence of infectious diseases and worsening bronchial asthma [1, 2]. Evidence from epidemiologic studies and meta-analyses suggests that exposure to intense indoor dampness and molds is associated with the development or exacerbation of bronchial asthma [3–5].

House dust mites (HDMs), that is, mites found in association with house dust, such as *Dermatophagoides pteronyssinus* (*Der p*) and *Dermatophagoides farinae* (*Der f*), produce allergens that induce immunoglobulin E (IgE)-mediated sensitization and the subsequent development of bronchial hyperresponsiveness [6–9]. HDM-specific IgE antibody titers correlate with airway hyperreactivity [7]. Exposure of sensitized people to *Der p* or *Der f* or *Aspergillus fumigatus* can trigger or exacerbate atopic asthma [6, 9, 10].

Mites feed off spores of fungi and appear to have fungal food preferences, especially for *Alternaria alternata*, *Cladosporium sphaerospermum*, and *Wallemia sebi* [11]. Increased indoor exposure to *Der p* (allergen) and *C. sphaerospermum* (fungus) heightens the risk of development and persistence of atopy and asthma in adults [12]. After the 2010 Great Flood in Bangkok, Thailand, sensitization to dog and *Alternaria* (an indoor fungus) allergens increased during that year and for the next 3 years in children with asthma or allergic rhinitis. However, the trend in sensitization to HDMs showed that although the prevalence of sensitization was high (70% or greater) before the flood, it did not increase after the flood [13].

The Great East Japan Earthquake hit the island nation's east coast at 14:46 on 11 March 2011. This was the strongest earthquake ever recorded in Japan, with a magnitude of 9.0 at the epicenter, and it was followed by a tsunami [14, 15]. These natural calamities were followed by an increased prevalence of bronchial asthma and atopic dermatitis in children [16, 17] and the exacerbation of asthma in adults [15, 18].

The city of Ishinomaki, in eastern Miyagi Prefecture, sustained massive damage [18, 19], and because the earthquake and tsunami destroyed most residents' homes, many had to live in evacuation shelters or temporary housing. In addition, a nuclear accident at the Fukushima Daiichi Nuclear Power Plant after the earthquake and tsunami forced an evacuation, and levels of indoor airborne fungi were found to be increased in the evacuation zone [20]. We previously reported a rare case of allergic bronchopulmonary mycosis in a patient who was exposed to the fungus *Eurotium herbariorum* while living in postearthquake temporary housing in Ishinomaki [21].

While exploring whether disasters, such as earthquakes and tsunamis, lead to the development or exacerbation of bronchial asthma in people who live in temporary housing after such natural calamities, we showed that the prevalence of asthma in residents who were living or had lived in temporary housing in Ishinomaki was 24.9% in 2014 [19] – higher than that reported previously in Japan [22, 23]. In particular, in 45.9% of asthmatics their asthma had begun after they had moved into temporary housing, and 71.4% of asthmatics had exacerbation of their disease after moving into temporary housing. We found that the antigen-specific IgE antibody titer against *Der f* was higher in asthmatic residents than in nonasthmatic residents [19].

Whether long-term living in temporary housing causes health hazards such as asthma has not yet been reported. In the current study, we performed group screening for respiratory and allergic diseases in adults (i.e., age ≥15 years) who were living, or had previously lived for at least 1 year, in temporary housing after the 2011 earthquake and tsunami (by 2019, many of the study participants had moved out of temporary housing). We examined the changes in mite-specific IgE antibody titer and the prevalence of asthma during the screening period of 2014–2019. We assessed whether living in the unique environment of temporary housing was associated with allergen sensitization and the development or exacerbation of asthma.

Materials and Methods

Study Area and Study Population

We performed group screening for respiratory and allergic diseases in adults (age ≥15 years) who (1) currently were living in temporary housing in Ishinomaki (a city in Miyagi Prefecture that had suffered tremendous damage from the tsunami that occurred

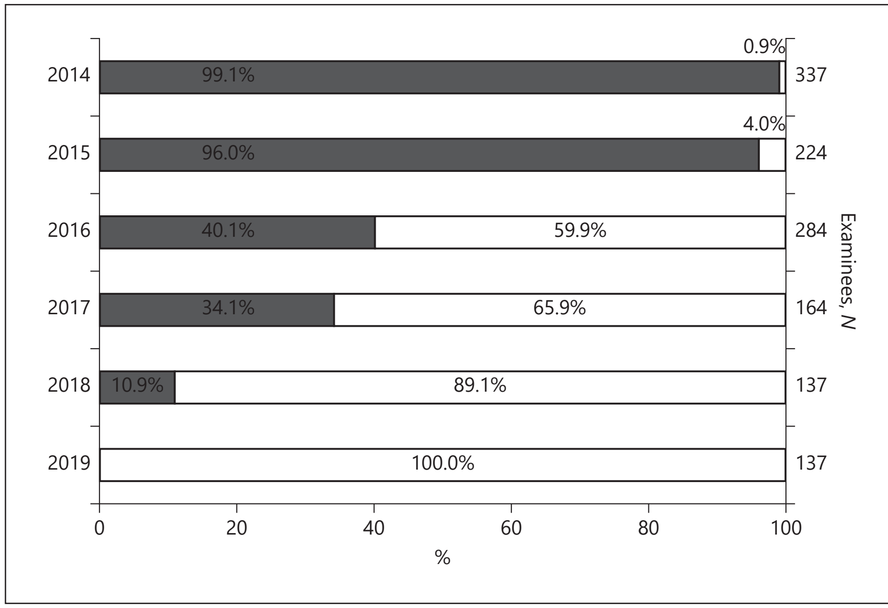


Fig. 1. Year-wise distribution of number of examinees and classification by residence at the time of examination. Gray: examinees living in temporary housing; white: examinees who had moved out of temporary housing.

after the 2011 Great East Japan Earthquake) or (2) had lived there for at least 1 year during 2014–2019. In 2014, we recruited 317 of 4,446 (7.1%) residents in 3 temporary housing complexes [19]. Our surveys during 2015–2019 focused on participants recruited and followed up additional participants and those recruited in 2014 from 1 temporary housing complex, 3 community centers, or the Japanese Red Cross Ishinomaki Hospital in Ishinomaki. Participants were evaluated during a single 6-day survey between June and October 2014 (2 days each in June, July, and October), a 4-day survey each year from 2015 through 2018 between June and July, and a 2-day survey in June 2019. We recruited screening candidates by disseminating information about the survey through posters, leaflets, newspapers, and other media.

Survey Outline

The same 3 respiratory specialists involved in the 2014 survey [19] conducted the screening during 2015–2019 as well. Residents suspected of having asthma or pulmonary emphysema according to the findings of interviews or chest auscultation and X-ray underwent respiratory function tests and, if necessary, airway reversibility tests with inhaled salbutamol. From the test results, we diagnosed asthma or emphysema according to the Global Initiative for Asthma guidelines [24] and identified participants in whom asthma was complicated by pulmonary emphysema (i.e., asthma-COPD overlap). Respiratory symptoms were investigated by using the European Community Respiratory Health Survey (ECRHS) questionnaire [25]. The contents of the questionnaire, including the extent of the damage in the participants' immediate environment at the time of the earthquake and the detailed past medical history of residents, are described in our previous report [19].

This study was funded by a Health and Labor Sciences Research Grant (Research on Health Security Control, H24-Kenki-wakate-001) and International Research Institute of Disaster Science (IRIDeS) co-project 2016. The project was approved by the Ethics Committee of the University Hospital Medical Information Network (UMIN ID: UMIN000014376). The Hospital Ethics Committee approved the study in accordance with the Helsinki Declaration. We obtained written informed consent from each participant every year.

Measures

Spirometry and Airway Reversibility

To diagnose asthma in adults who had lived or were currently living in temporary housing complexes, we examined lung function by using an electric spirometer (Minato Autospiro AS-302, Minato Medical Science Co., Ltd., Osaka, Japan). The forced expiratory volume in 1 s was expressed as percentage of the forced vital capacity. Residents suspected of having asthma underwent bronchodilator testing, which required the administration of 200 μg of salbutamol via a nebulizer (DeVilbiss 646, DeVilbiss Healthcare, Somerset, PA, USA) through tidal breathing. Spirometry was performed at baseline and repeated 15 and 30 min after salbutamol inhalation. Reversibility was defined (according to the Global Initiative for Asthma guidelines [24]) when forced expiratory volume in 1 s increased by ≥200 mL.

Antigen-Specific IgE Antibody Levels

We measured the levels of antigen-specific IgE to 2 allergen sources (HDMs [*Der f* and *Der p*] and *Aspergillus fumigatus* [a fungus]) via IMMULITE 3gAllergy immunoassay (IMMULITE; Siemens Healthcare Diagnostics, Tokyo, Japan) [26]. Levels of specific IgE detected via IMMULITE analysis are expressed in quantitative units (IU_A/mL); the assay has a working range of 0.1–100 IU_A/mL. IMMULITE results were defined as "positive" when IgE values were ≥0.35 IU_A/mL (score 1 or higher) and "weakly positive" when they were ≥0.10 IU_A/mL (score 0).

Statistical Analysis

Data were compared between groups by using the Mann-Whitney U test. Correlation coefficients were obtained by applying Spearman's rank correlation test. Statistical comparison between groups by using two-way ANOVA with repeated measures or with

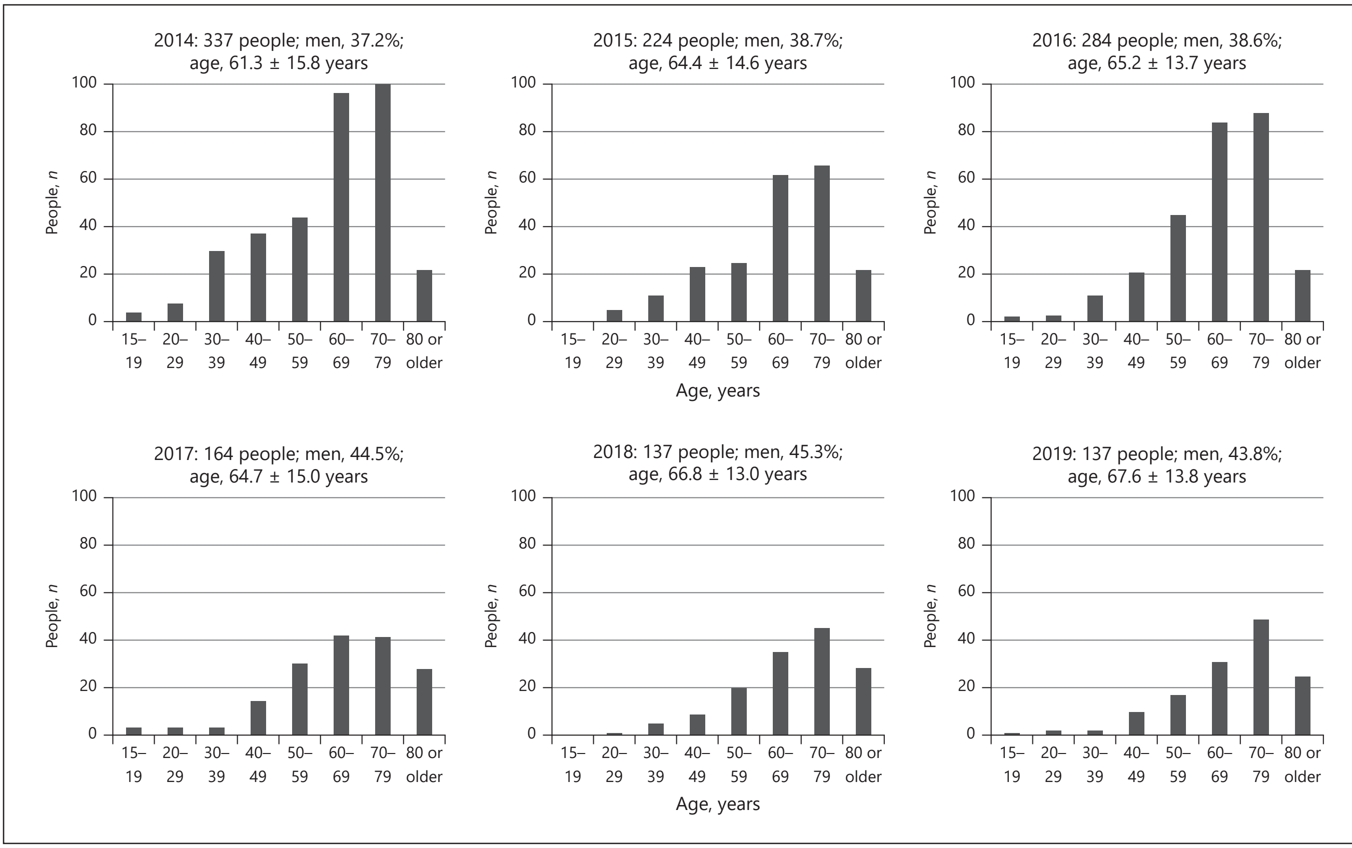


Fig. 2. Age distribution of examinees screened during 2014–2019.

χ^2 testing revealed no significant differences. *p* values <0.05 were considered statistically significant. All statistical analyses were performed by using SPSS for Windows, version 20 (IBM SPSS, Chicago, IL, USA).

Results

Year-Wise Distribution of Number of Examinees and Classification according to Residence at the Time of Examination

We examined the year-wise distribution of the total number of people examined and the percentages of examinees still in temporary housing and those who had moved out (Fig. 1). In both 2014 and 2015, >90% of the examinees resided in temporary housing. However, beginning in 2016, the number of temporary housing residents decreased each year; in 2019, none of the participants was still living in temporary housing.

Age Distribution of Examinees Screened from 2014 through 2019

In 2014, the age (mean ± 1 SD) of examinees was 61.3 ± 15.8 years, and 37.2% of the total population were men, whereas in 2019, the overall average age was 67.6 ± 13.8 years, and 43.8% of examinees were men (Fig. 2). Therefore, throughout the study, examinees included many elderly people and the age distribution peaked in the sixth and seventh decades.

Year-Wise Distribution of Prevalence of Asthma in Examinees Who Were Living or Had Lived in Temporary Housing

Beginning in 2016, the number of people who had moved out of temporary housing gradually increased. We therefore used 2 approaches – diagnoses by the respiratory specialists and assessment of asthma symptoms by using the ECRHS questionnaire (Table 1) – to compare and analyze the prevalence of asthma in examinees once they moved into temporary housing and after they had moved out. The prevalence of asthma according to physi-

Table 1. Year-wise distribution of prevalence of asthma in examinees who were living or had lived in temporary housing

Screening year	Housing status	Prevalence of asthma	
		ECRHS questionnaire	physician diagnosis
2014	Living in or moved out of temporary housing	75/262 (22.3)	84/253 (24.9)
2015	Living in or moved out of temporary housing	44/173 (20.3)	63/157 (28.6)
2016	Living in or moved out of temporary housing	64/220 (22.5)	76/208 (26.8)
	Living in temporary housing	26/88 (22.8)	32/82 (28.1)
	Moved out of temporary housing	38/132 (22.4)	44/126 (25.9)
2017	Living in or moved out of temporary housing	34/130 (20.7)	48/116 (29.3)
	Living in temporary housing	10/47 (17.5)	14/43 (24.6)
	Moved out of temporary housing	24/83 (22.4)	34/73 (31.8)
2018	Living in or moved out of temporary housing	35/102 (25.5)	34/103 (24.8)
	Living in temporary housing	4/11 (26.7)	3/12 (20.0)
	Moved out of temporary housing	31/91 (25.4)	31/91 (25.4)
2019	Living in or moved out of temporary housing	30/107 (21.9)	32/105 (23.4)
	Living in temporary housing	0	0
	Moved out of temporary housing	30/107 (21.9)	32/105 (23.4)

Data are given as number of patients with asthma/number without asthma (% of screened population with asthma). ECRHS, European Community Respiratory Health Survey.

cian diagnosis was similar to that from the ECRHS questionnaire and exceeded 20% across all ages from 2014 through 2019; there were no significant differences between the various age-groups. In addition, according to both diagnostic methods, the prevalence of asthma in examinees who were living in temporary housing did not differ from that in those who had moved out. We examined the prevalence of physician-diagnosed asthma in examinees, by age, from 2014 through 2019 (Fig. 3). Although few examinees were younger than 40 years during 2017–2019, this group tended to have a high prevalence of asthma. In addition, throughout the observation period, the prevalence of physician-diagnosed asthma exceeded 20% in examinees 60–69 years old and was >15% in those who were in the seventh and eighth decades (Fig. 3).

Percentages of Asthmatics and Nonasthmatics with "Positive" Serum Antigen-Specific IgE Levels for Der f, Der p*, or* A. fumigatus

We then calculated the proportions of asthmatics in all age-groups who had a "positive" antigen-specific serum IgE titer (i.e., ≥0.35 IU_A/mL) against *Der f*, *Der p*, or *A. fumigatus*; we similarly determined the percentages of nonasthmatic participants who had "positive" IgE titers against these allergens (Table 2; note that we did not assay *Der p*-specific IgE levels in 2014 and 2015). For *Der f*, the proportion of examinees with "positive" titers was greater among asthmatics than nonasthmatics during 2014, 2017, 2018, and 2019 ($p < 0.01$); for *Der p*, this subpopulation was larger among asthmatics than nonasthmatics in 2017 ($p < 0.05$), 2018 ($p < 0.01$), and 2019 ($p < 0.01$) (Table 2). For *A. fumigatus*, the percentage of examinees with "positive" titers did not differ between asthmatics and nonasthmatics, across all ages. In addition, the proportions of asthmatics with "positive" antigen-specific IgE titers against *Der f* or *Der p* were high and varied between 21.1 and 52.9%, compared with the proportion of asthmatics with a "positive" antigen-specific IgE titer against *A. fumigatus*, which ranged from 2.5 to 8.8%.

Age-Wise Distribution of Serum IgE Levels in Asthmatics and Nonasthmatics

Across all age-groups and years (except 2015), the percentage of asthmatic residents with a serum antigen-specific IgE antibody titer of ≥0.35 IU_A/mL against *Der f* did not differ from that of those with an IgE level ≥0.10 IU_A/mL (Fig. 4a). The proportion of asthmatic residents ≥50 years of age with a serum antigen-specific IgE antibody titer of ≥0.10 IU_A/mL against *Der f* was larger than that of asthmatics with an IgE level ≥0.35 IU_A/mL in 2014 ($p < 0.05$), 2016 ($p < 0.01$), or 2017 ($p < 0.01$) (Fig. 4a). The percentage of nonasthmatic residents with a serum antigen-specific IgE antibody titer of ≥0.10 IU_A/mL against *Der f* was higher than for those with an IgE titer ≥0.35 IU_A/mL against *Der f* in all years except 2015 and across all age-groups. This difference was particularly prominent in the comparison between nonasthmatic residents ≥50 years of age compared with those ≤49 years in 2014, 2016, 2017, or 2018 ($p < 0.01$) (Fig. 4b). In addition, the proportions of examinees with IgE titers ≥0.10 IU_A/mL against *Der f* compared with ≥0.35 IU_A/mL differed for nonasthmatics in their eighth decade in 2014 ($p < 0.05$), in their seventh decade ($p < 0.01$) or eighth decade ($p < 0.05$) in 2016, and in their eighth decade in 2017 ($p < 0.05$) (Fig. 4b).

Timing of Onset of Asthma from 2014 through 2019

In 2014 and 2015, asthma onset occurred either before the earthquake, during stays in shelters, or after moving into temporary housing. In particular, in 2015, asthma onset after moving into temporary housing ac-

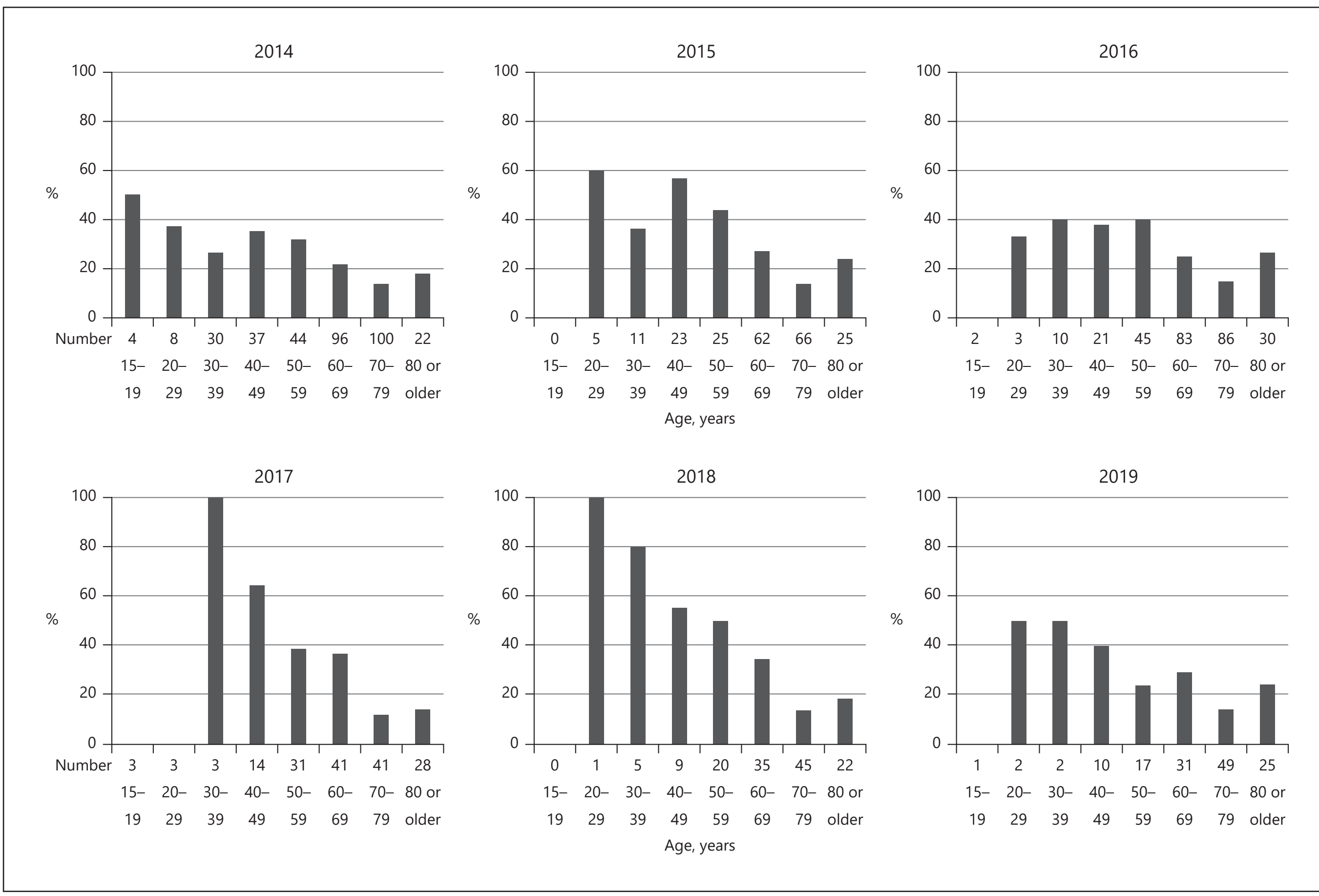
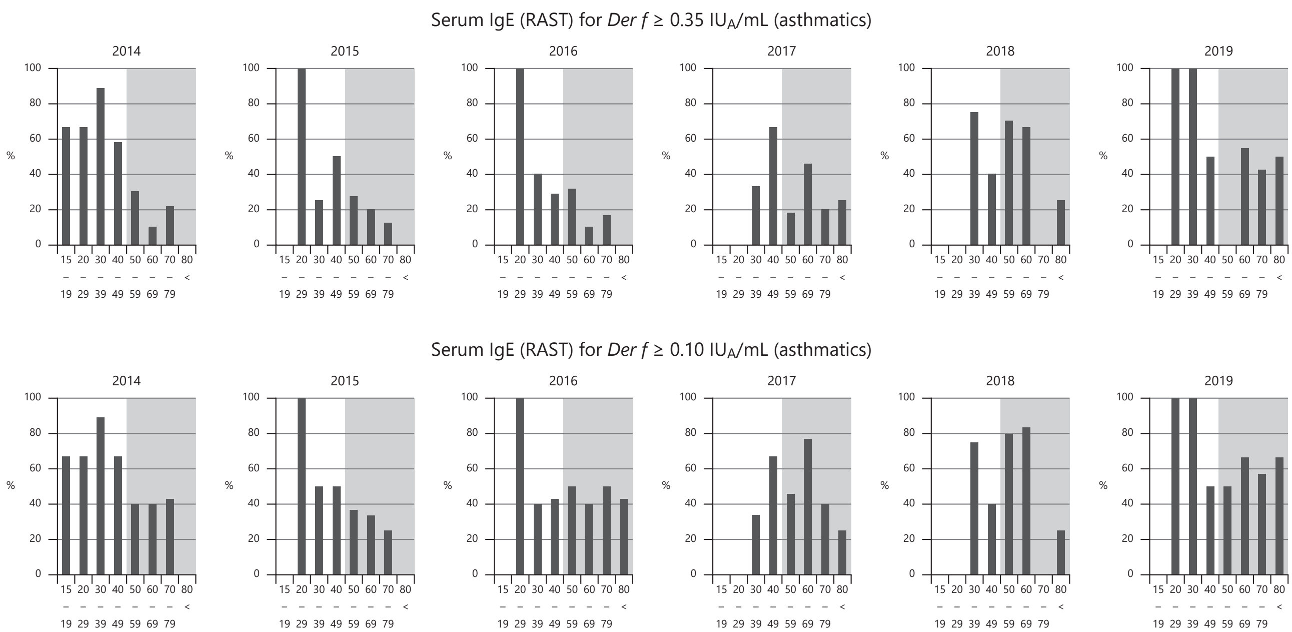


Fig. 3. Age-wise prevalence of asthma in examinees (2014–2019). Asthma was diagnosed by respiratory specialists according to the Global Initiative for Asthma guidelines.

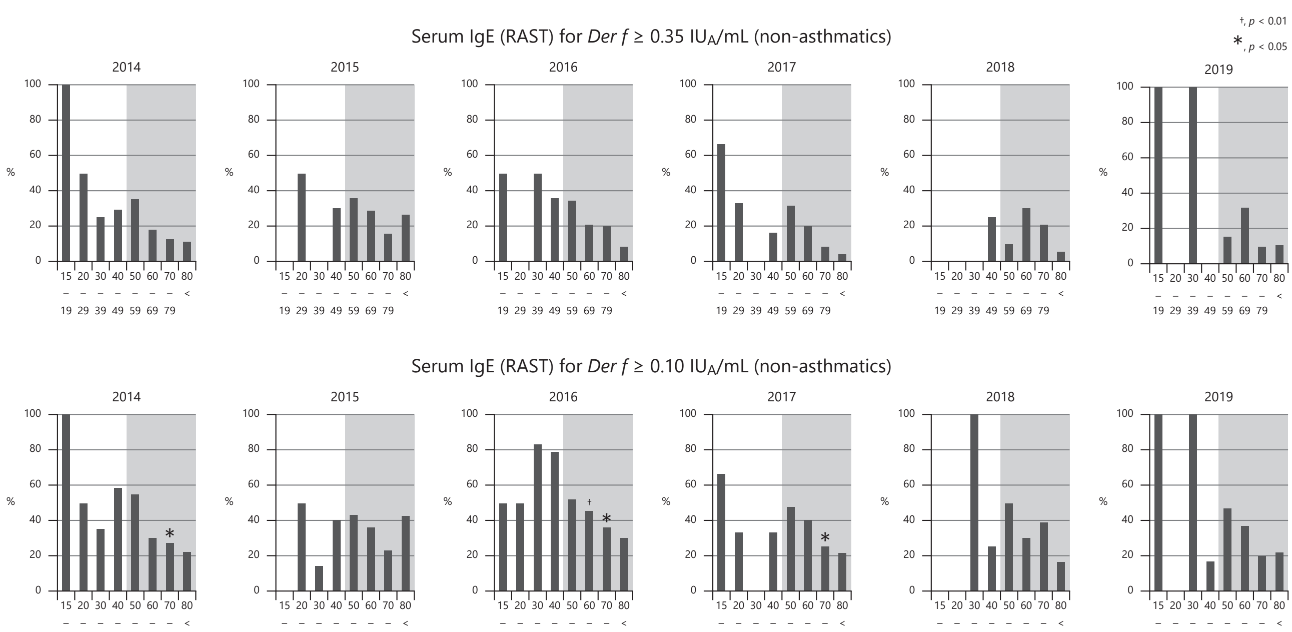
Fig. 4. Age-wise distribution of serum IgE levels (estimated by RAST) to *Der f* of ≥0.35 IU_A/mL compared with serum IgE (RAST) to *Der f* of ≥0.10 IU_A/mL among asthmatics (**a**) and nonasthmatics (**b**). χ^2 testing revealed no significant differences between the values for the 2 groups. Gray shading indicates examinees older than 50 years. p values indicate instances in which the proportion of participants with *Der f* titers of ≥0.10 IU_A/mL is higher than that with ≥0.35 IU_A/mL within the same age-group $^{\dagger}p < 0.01$; $^{*}p < 0.05$. IgE, immunoglobulin E; RAST, radioallergosorbent test; *Der f*, *Dermatophagoides farinae*.

(For figure see next page.)



Der f ≥ 0.35 IU$_A$/mL vs ≥ 0.10 IU$_A$/mL	2014 (*n* = 75)	2015 (*n* = 58)	2016 (*n* = 68)	2017 (*n* = 45)	2018 (*n* = 34)	2019 (*n* = 29)
All ages	ns	ns	$p < 0.01$	ns	ns	ns
15–49 years	ns	ns	ns	ns	ns	ns
50 years and older	$p < 0.05$	ns	$p < 0.01$	$p < 0.01$	ns	ns

a



Der f ≥ 0.35 IU$_A$/mL vs ≥ 0.10 IU$_A$/mL	2014 (*n* = 256)	2015 (*n* = 154)	2016 (*n* = 216)	2017 (*n* = 115)	2018 (*n* = 95)	2019 (*n* = 104)
All ages	$p < 0.01$	ns	$p < 0.01$	$p < 0.01$	$p < 0.01$	$p < 0.05$
15–49 years	ns	ns	$p < 0.05$	ns	ns	ns
50 years and older	$p < 0.01$	ns	$p < 0.01$	$p < 0.01$	$p < 0.01$	ns

b

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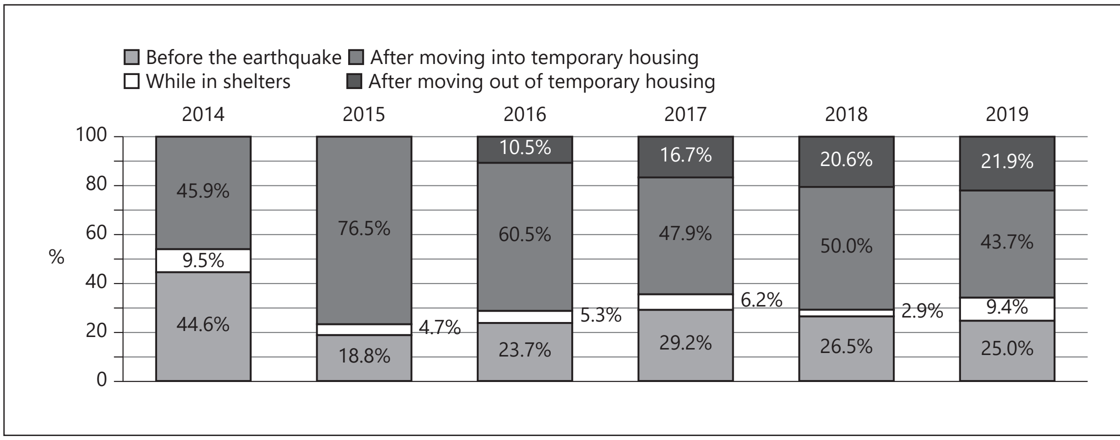

Fig. 5. Timing of onset of asthma from 2014 through 2019. Vertical stripes: before the earthquake; solid white: during stays in shelters; diagonal stripes: after moving into temporary housing; solid black: after moving out of temporary housing. There were 84 examinees with asthma in 2014, 63 in 2015, 76 in 2016, 48 in 2017, 44 in 2018, and 32 in 2019. In 2014, there were 10 subjects in whom the onset of asthma was unknown, and in 2015 there was one.

counted for 76.5% of all cases – the highest percentage during the study period (2014–2019). Thereafter, the percentage of asthma cases that occurred after moving into temporary housing varied between 60.5% (in 2016) and 43.7% (in 2019). Beginning in 2016, in addition to the previously described 3 subsets of asthma onset (i.e., before the earthquake, during stays in shelters, and after moving into temporary housing), people also developed asthma after moving out of temporary housing; this subpopulation accounted for 10.5% (in 2016) to 21.9% (in 2019) of all examinees during 2016–2019 (Fig. 5).

Correlation between Der f- *or* Der P-*specific IgE Antibody Level and Time Elapsed since Moving into or out of Temporary Housing*

The *Der f*-specific serum IgE level in examinees in 2019 was correlated positively with the time elapsed since moving into temporary housing ($p < 0.05$, $r = 0.36$) (Fig. 6a, left panel) but not with the time elapsed since moving out of temporary housing (Fig. 6a, right panel). Similarly, the *Der p*-specific IgE antibody level was positively correlated with the time elapsed since moving into temporary housing ($p < 0.05$, $r = 0.41$) (Fig. 6b, left panel) and inversely correlated with the time elapsed since moving out of temporary housing ($p < 0.05$, $r = -0.35$) (Fig. 6b, right panel).

Discussion

The prevalence of current asthma and asthma symptoms, such as wheezing, among Japanese adults (age, 20–79 years) is 10.1% [22]. The prevalence of lifetime asthma increased from 5.1 to 6.7% and that of current asthma increased from 1.5 to 3.4% during the years 1999–2006 among adults in Fujieda, Japan [23].

In our survey (2014–2019), notwithstanding the fact that the number of medical examinations differed among years, the prevalence of physician-diagnosed asthma among adults aged ≥15 years who had lived for at least 1 year in temporary housing exceeded 20% across all age-groups – more than double the rate reported previously in Japan. Our results also show that the prevalence of asthma did not differ between residents still living in temporary housing and those who had moved out of temporary housing; this therefore implies that moving out of temporary housing does not reduce the prevalence of asthma (Table 1).

In the 2014 survey we reported [19], the rates of depression among victims of the Great East Japan Earthquake were more than double those among victims of the 1995 Great Hanshin-Awaji Earthquake [27], but there were no significant differences in mental stress-related illnesses between asthmatics and nonasthmatics. The development and exacerbation of asthma in our survey population may not have been directly related to the effects of postearthquake mental stress.

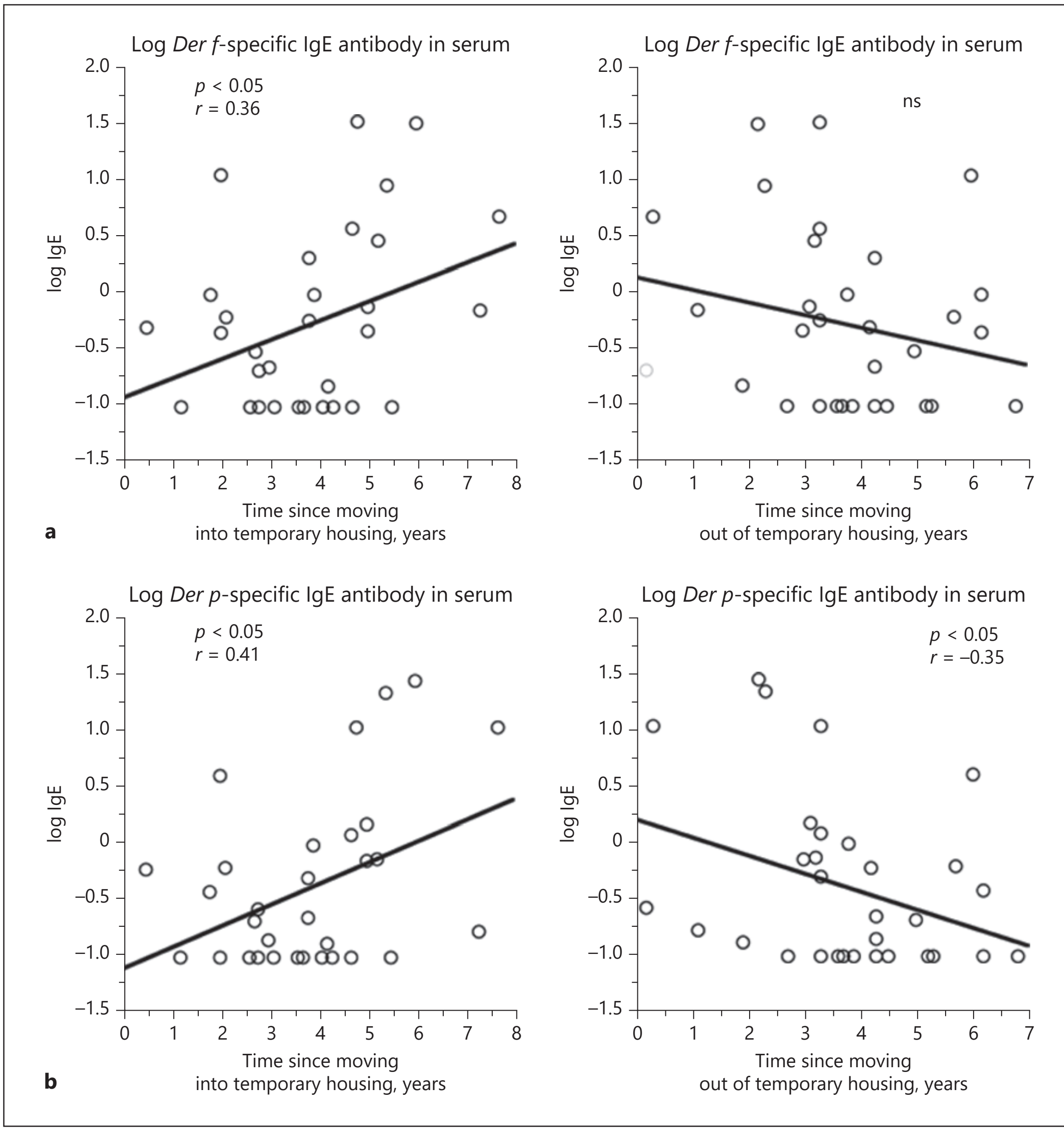

Fig. 6. a Correlation between log *Der f*-specific IgE antibody levels in serum in examinees in 2019 and time elapsed since moving into (left panel) or out of (right panel) temporary housing. *Der f*-specific IgE antibody level at the time of examination in 2019 was correlated with duration of temporary housing ($p < 0.05$, $r = 0.36$) (left panel) but not with time elapsed since moving out of temporary housing (right panel). **b** Correlation between log *Der p*-specific IgE antibody levels in serum in examinees in 2019 and time elapsed since moving into (left panel) or out of (right panel) temporary housing. Correlation coefficients were obtained by using Spearman's rank correlation test. *Der f*, *Dermatophagoides farinae*; IgE, immunoglobulin E.

After Hurricane Katrina in New Orleans in 2005, *Alternaria* antigen was detected in dust from 98% of flooded houses, with 58% having high concentrations (i.e., >10 μg/g), but *Der p* 1 concentrations exceeding 2 μg/g were detected in only 9% of all flooded houses [28]. One report suggests that most homes have greater quantities of *Der f* allergen than *Der p* allergen and that *Der f* is better adapted for living in drier climates [29]. The percentage of the population with a "positive" *Der f* titer was almost the same as that with a "positive" *Der p* titer in our findings (Table 2).

Table 2. Numbers of examinees (asthmatics and nonasthmatics) in all age-groups who had, or did not have, a "positive" serum antigen-specific IgE level (i.e., ≥0.35 IU_A/mL) against *Der f*, *Der p*, or *Aspergillus fumigatus*

Year		Asthmatics	Nonasthmatics	*p* value
2014	Participants, *n*	84	253	
	Der f	29; 53 (35.4)	48; 199 (19.4)	<0.01
	Der p	nd	nd	nd
	Aspergillus fumigatus	4; 78 (4.9)	7; 240 (2.8)	ns
2015	Participants, *n*	63	157	
	Der f	19; 41 (31.7)	36; 121 (22.9)	ns
	Der p	nd	nd	nd
	Aspergillus fumigatus	2; 58 (3.3)	6; 151 (3.9)	ns
2016	Participants, *n*	76	208	
	Der f	17; 59 (22.4)	47; 161 (22.6)	ns
	Der p	16; 60 (21.1)	49; 159 (23.6)	ns
	Aspergillus fumigatus	3; 73 (4.0)	6; 202 (2.9)	ns
2017	*n*	48	116	
	Der f	17; 31 (35.4)	18; 96 (15.8)	<0.01
	Der p	16; 32 (33.3)	18; 96 (15.8)	<0.05
	Aspergillus fumigatus	3; 45 (6.3)	7; 107 (6.1)	ns
2018	*n*	34	103	
	Der f	18; 16 (52.9)	19; 84 (18.4)	<0.01
	Der p	18; 16 (52.9)	17; 86 (16.5)	<0.01
	Aspergillus fumigatus	3; 31 (8.8)	6; 97 (5.8)	ns
2019	*n*	32	104	
	Der f	15; 17 (46.9)	17; 87 (16.3)	<0.01
	Der p	13; 19 (40.6)	14; 90 (13.5)	<0.01
	Aspergillus fumigatus	4; 28 (2.5)	4; 100 (3.8)	ns

Data are given as the number of participants with a "positive" titer; the number of those with a "negative" titer (% of screened population with a "positive" titer). IgE, immunoglobulin E; *Der f*, *Dermatophagoides farinae*; *Der p*, *Dermatophagoides pteronyssinus*; RAST, radioallergosorbent test; nd, not determined; ns, not significant. $p < 0.05$ (χ^2 testing) was considered statistically significant.

The development and exacerbation of asthma have been reported to be associated with the presence of inhaled allergens, such as HDMs, in both children and adults [6–10]. Our 6-year screening study revealed that HDMs – but not *Aspergillus fumigatus* – were the allergens typically associated with asthma. The proportion of nonasthmatics with serum antigen-specific IgE antibody titers for *Der f* ≥0.10 IU_A/mL (defined as "weakly positive" and indicated as a score of 0 was larger than that of nonasthmatics with serum antigen-specific IgE antibody titers for *Der f* ≥0.35 IU_A/mL (defined as "positive" and indicated as a score of (1) across all age-groups and years, except 2015 (Fig. 4b). However, whether a score of 0, which indicates detection of IgE antibody titer, is clinically significant has not yet been sufficiently verified.

The percentages of asthmatics with serum antigen-specific IgE antibody titers against *Der f* of ≥0.10 IU_A/mL and those with IgE titers of ≥0.35 IU_A/mL were similar across all age-groups and years, except 2016 (Fig. 4a). Our results show that, compared with asthmatics, nonasthmatics showed greater weak sensitization to HDMs (defined as antigen-specific IgE antibody titers to *Der f* of ≥0.10 IU_A/mL) over the 6-year observation period. Furthermore, a greater proportion of asthmatic residents ≥50 years of age had "weakly positive" *Der f* serum IgE titers than "positive" titers in 2014, 2016, and 2017 (Fig. 4a). These results indicate that both asthmatic and nonasthmatic adults ≥50 years of age are more susceptible to weak sensitization to *Der f* than are adults ≤49 years of age who are former or current residents of temporary housing.

It is unclear what proportion of HDM-sensitized but otherwise healthy people go on to develop asthma. In a previous study [30], mite-specific IgE antibody (≥0.35 IU_A/mL) was detected in 21.8% of 234 patients who had a mean age of 29.4 ± 6.4 years and no history of respiratory disease. In addition, the mite-specific IgE antibody titer was correlated with increased airway hyperresponsiveness ($r = 0.52$, $p < 0.018$) [30]. Of 308 students who were nonsmokers and had no history of allergic disease, 34.2% had a mite-specific IgE radioallergosorbent test score of 2 or higher [31]. In an analysis of total serum IgE levels throughout childhood, 469 subjects (age, 1–20 years) were nonatopic, defined as having a negative response to 5 airborne antigens (HDM, cat, dog, mixed grass, and birch pollen) and 4 food allergens (cow milk, hen eggs, wheat, and soy); 15.2% of these nonatopic participants had high total IgE levels [32].

The prevalence of asthma in our study population did not necessarily decrease after people moved out of temporary housing. In fact, new cases of asthma were diagnosed not only after examinees moved into temporary housing but also after they moved out; these latter cases occurred every year since 2016. This suggests that sensitization to HDM allergens while living in temporary housing led to the development of asthma due to these environmental factors after residents had moved out.

Serum antigen-specific IgE antibody titers for *Der p* $\geq$0.10 IU_A/mL assayed in 2019 were positively correlated with the duration of temporary housing and negatively correlated with the time elapsed since moving out of temporary housing. These findings indicate that HDM sensitization intensifies when temporary housing is prolonged and that sensitization becomes weaker once residents move out. This pattern implies that HDM sensitization can be decreased by moving out of temporary housing, thereby reducing HDM allergen exposure. We considered that allergen sensitization could be increased or asthma could newly develop, owing to the difference in mite allergen exposure in the living environment after moving out of temporary housing. Although prolonged occupancy of temporary housing is rare, this study is useful in explaining 1 mechanism of allergic sensitization and asthma development.

Owing to allergen avoidance through environmental improvement after floods, asthma symptoms in children can diminish [33] and respiratory function improve [34]. Similarly, we reported in a case presentation that the temporary housing environment in Ishinomaki city has improved greatly, thereby decreasing fungal exposure and ameliorating symptoms of allergic bronchopulmonary mycosis [21]. A meta-analysis showed that bronchial hyperresponsiveness decreased after mite-impermeable mattress covers were provided to patients previously exposed to high levels of *Der* 1 [35]. Allergen avoidance through changes in the living environment after an earthquake might similarly ameliorate asthma exacerbation or development.

This study showed asthma prevalence rates in temporary housing residents over a 6-year period after the Great East Japan Earthquake. Moreover, HDM allergen sensitization was found in nonasthmatics as well as asthmatics; asthma developed even after residents had moved out of temporary housing; and, in some cases, *Der p*-specific IgE antibody titers decreased after residents moved out of temporary housing. Future interventional studies for allergen avoidance by residents with a history of temporary housing are warranted to verify the usefulness of environmental maintenance in reducing HDM allergen levels and diminishing the symptoms of asthma, as well as to determine the long-term prognosis of asthma.

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Statement of Ethics

The project was approved by the Ethics Committee of the University Hospital Medical Information Network (UMIN ID: UMIN000014376). The Hospital Ethics Committee approved the study in accordance with the Helsinki Declaration. We obtained written informed consent from each participant every year.

Conflict of Interest Statement

None of the authors has a conflict of interest to disclose. The work was not funded by a grant or any other external source of financial support.

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Author Contributions

Naomi Tsurikisawa analyzed participants' data and takes responsibility for the overall content of the paper. Naomi Tsurikisawa, Maiko Watanabe, and Masaru Yanai negotiated with the administration in conducting the medical examinations. Chiyako Oshikata, Masatsugu Ishida, and Naomi Tsurikisawa diagnosed asthma residents. Chiyako Oshikata analyzed participants' data and wrote the first draft. Naomi Tsurikisawa, Chiyako Oshikata, Maiko Watanabe, Seiichi Kobayashi, Masaru Yanai, Yoichi Kamata, Takeshi Kaneko, and Shinichi Kuriyama conceived the idea of this study and participated in discussions. Kazuhiro Hashimoto, Naoki Kobayashi, Rumi Konuma, and Akiko Yamazaki helped with height and weight measurements, blood pressure measurements, interviews, and lung function measurements.

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