学　位　論　文

The association between mechanical ventilation, flue use in heaters and asthma symptoms

(暖房の排気、および室内換気と児童喘息との関連)

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叢　石

Contents

i. List of Publications

1. Shi Cong, Atsuko Araki, Shigekazu Ukawa, Yu Ait Bamai, Syuji Tajima, Ayako Kanazawa, Motoyuki Yuasa, Akiko Tamakoshi, Reiko Kishi. Association of Mechanical Ventilation and Flue Use in Heaters With Asthma Symptoms in Japanese Schoolchildren: A Cross-Sectional Study in Sapporo, Japan. *Journal of Epidemiology* in press.

ii. List of presentations at academic seminars

1. 叢石、荒木敦子、アイツバマイゆふ、竹田智哉、早川敦司、吉岡英治、多島秀司、鵜川重和、岸玲子。小学生の住宅におけるハウスダスト中のエンドトキシン、ならびにβ-グルカン量と住宅特徴に関する調査。第 63 回北海道公衆衛生学会、2011 年 11 月 10−11 日、札幌
2. 叢石、荒木敦子、アイツバマイゆふ、竹田智哉、早川敦司、吉岡英治、多島秀司、鵜川重和、玉腰暁子、岸玲子。小学生の住宅におけるハウスダスト中のエンドトキシン、ならびにβ-グルカン量とアレルギー性疾患に関する調査。第 64 回北海道公衆衛生学会、2012 年 11 月 8−9 日、札幌
3. 叢石、荒木敦子、鵜川重和、アイツバマイゆふ、多島秀司、金澤文子、湯浅資之、玉腰暁子、岸玲子。札幌市内小学生の自宅における暖房、および機械換気の有無と児童の喘息。第 65 回北海道公衆衛生学会、2013 年 11 月 14−15 日、札幌

iii. Preface

Asthma is a common chronic disease among children, and it is characterized by recurrent attacks of breathlessness and wheezing[1]. These attacks may occur from hour to hour or day to day[2]. Asthma is associated with a significant socioeconomic burden, imposing excessive health care costs on the household[3] and resulting in lower school attendance[3,4]. The WHO reported that both the prevalence and burden of asthma and allergic symptoms in children have increased in recent decades in the world[5], and this increasing trend has also been demonstrated in some epidemiologic studies[6-8]. In Japan, the prevalence of asthma in children has been steadily increasing[9,10].

According to one study based on the International Study of Asthma and Allergies in Childhood (ISAAC) Phases One and Three repeat multi-countries cross-sectional surveys, the prevalence of asthma symptoms in 6 to 7 year old Japanese children was 17.4% and 18.2% between 1994-1995 and 2001-2003, respectively. It was also the highest among 8 Asian counties and relatively high globally[11]. One cross-sectional study that took place in 2005 also reported that the prevalence of asthma symptoms was 18.2% among 6-year-old school children in Tokyo[12].

Children spend more time at home than adults, and it is also possible that they are exposed to more pollutants from the indoor environment[13], thus, indoor environmental health is important issue for children. In the past, most households used wood or coal for heating, and numerous studies have reported the use of such solid fuels is associated with asthma symptoms in children[14]. According to data from the WHO, nowadays, solid fuels for heating and cooking are mainly used in developing countries, but not used in developed countries including Japan[15]. From the results of my study that took place in Sapporo, Japan, 88.3% households were using kerosene or gas fuel to heat their homes. However, the association between the use of heaters and asthma symptoms in children in Japan remains unclear.

One study reported that the use of gas heaters for heating homes might be associated with asthma attacks in children[16]. Another study classified heaters into two types: fume emitting heaters and non-fume emitting heaters[17]. In this study, I defined fume-emitting heaters as gas, kerosene, wood, or coal heaters, and non-fume emitting

heaters as electric heaters, and central heating.

To confirm the association between the use of fume emitting heaters and asthma symptoms, the relevant literature has been summarized in Chapter 1. While indoor air pollution from the use of fume emitting heaters might lead to asthma symptoms, the use of flues in heaters and mechanical ventilation might also transfer indoor air pollution to the outside. Thus, in Chapter 2, I present the result of a cross-sectional Japanese study that I undertook in Sapporo, Japan, to investigate the association between mechanical ventilation and flue use in heaters and asthma symptoms in children.

iv. List of Abbreviations

BMI	Body mass index
CI	Confidence interval
CO	Carbon monoxide
CO_2	Carbon dioxide
IgE	Immunoglobulin E
ISAAC	International Study of Asthma and Allergies in Childhood
NO	Nitric oxide
NO_2	Nitrogen dioxide
O_3	Ozone
OR	Odds ratios
PM	Particulate matter
SO_2	Sulfur dioxide
WHO	World Health Organization

v. Chapter 1. Association between heating system and childhood asthma symptoms in previous studies

1.1. Introduction

Epidemiological evidence suggests that environmental factors are major risk factors for asthma in children[18]. Indeed, tobacco smoke[19], carpeting[20], living near main roads[21], and indoor dampness and mold[22-24] are all known to cause or exacerbate asthma and allergic symptoms in school children. In particular, indoor dampness is a well-known strong risk factor for asthma. Recently, it was also reported that outdoor and indoor PM 2.5 levels were associated with asthma symptoms in children[25,26]. In Japan, cedar pollen has also been reported to be strongly associated with asthma symptoms in children[27].

In cold areas, fume emitting heating system might also be associated with asthma symptoms in children. Heating systems consist of various types of heaters. According to whether the heater has fuel combustion or not, heating systems are classified into fume emitting heaters and non-fume emitting heaters[17]. Fume emitting heaters mainly use gas, kerosene, wood, or coal, and non-fume emitting heaters include electric heaters or central heating.

Air pollution from fuel combustion has been reported to be associated with asthma in children. One study suggested that indoor smoke from the combustion of solid fuels such as coal or biomass led to asthma and other respiratory symptoms in children[28]. Fuel combustion mainly originates from cooking and heating in the home. Another study reported that the use of open fires for cooking was associated with increased asthma symptoms in children[29]. Regarding cooking systems, Padhi et al. reported that compared with gas fuels, biomass fuels for cooking were significantly associated with asthma in children, and air pollution levels from cooking such as nitrogen dioxide (NO_2), sulfur dioxide (SO_2), carbon dioxide (CO_2), carbon monoxide (CO), nitric oxide (NO), particulate matter (PM) and ozone (O_3) were significantly higher in from biomass fuels than gas fuels[30].

The association between the use of fume emitting heaters and asthma symptoms in

children in previous studies is unclear. The aim of this chapter is to examine existing knowledge on whether the use of fume emitting heaters is associated with asthma symptoms in children 0-18 years, by summarizing previous studies on heating systems and asthma symptoms.

1.2. Literature search

Data source

I searched for papers published in English up until November 12th 2013, using PubMed database with the MeSH terms "asthma", and "heating" OR "heater" OR "stove". I then screened the literature and limited the results to those studies with a full text available, and subjects that included children 0-18yrs. After screening, I checked the remaining papers using the abstracts and the inclusion criteria listed below.

Inclusion criteria

After checking the abstracts, I selected those papers that investigated the association between heaters and asthma symptoms. Papers that investigated allergic symptoms other than asthma as the outcome were not included. Those studies that assessed stoves for cooking were also not included in this review. Furthermore, those studies that included both adults and children and were not stratified were also excluded.

Literature assessment

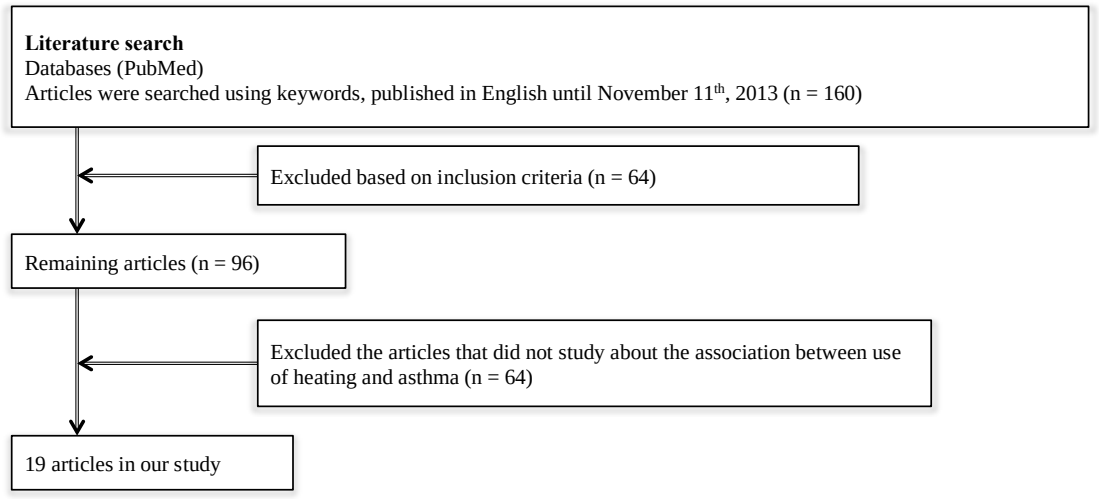
According to differences in the study design, articles were classified into 3 groups: intervention studies, cohort studies, and cross-sectional studies. Furthermore, cross-sectional were classified according to wood or coal, gas and other fuel system. I then investigate the remaining studies using the following 7 items including: "author, publication year", "research place and periods", "participants", "heating fuels", "outcome assessment", "confounding factors" and "results". Finally, I summarized the association between heater-type and asthma symptoms in the results.

1.3. Results

Search results

I searched the PubMed database with “Asthma” in the MeSH terms AND “Heating” OR “Heater” OR “Stove”, and found 160 articles in English. Of these 160 papers, 96 had full papers available and children 0-18yrs as the participants. Finally, 19 papers remained after checking for the inclusion criteria (Figure 1-1). Among these, there were 3 intervention studies, 1 cohort study, and 15 cross-sectional studies. In the 15 articles, 10 studies investigated wood or coal fuel heaters, 7 studies investigated gas heaters, and the remaining 3 studies investigated other fuels including oil, kerosene fuel and multiple fuels.

Figure 1-1 Literature search



Intervention studies

Table 1-1 shows the 3 intervention studies that focused on the association between heating and asthma symptoms. Howden-Chapman et al. reported that the intervention group with more effective heaters such as heat pumps, wood pellet burners or flued gas heaters showed significantly reduced visits to a doctor or pharmacist due to asthma symptom, compared to the control groups that used heating systems which included open fires, plug-in electric heaters or unflued gas heaters[31]. Pilotto et al. reported that difficulty breathing during the day and night, chest tightness during the day, and daytime asthma attacks were significantly reduced in the intervention group which used flued gas heaters or electric heaters, compared with the controls that used unflued gas heaters[32]. After using gas central heating, electric storage heaters, solid fuel central heating or oil-fired central heating to replace coal fires or other heating, wheeze symptoms were decreased in the study of Somerville et al. However, a direct control group was lacking[33]. Two papers also reported that levels of NO_2 were consistently decreased in the interventions, compared with the control groups[31,32].

Table 1-1. Intervention studies

Authors, years	Research place and periods	Participants	Heating fuel	Outcome assessment	Confounding factors	Results
[31]Howden-Chapman P et al. 2008	New Zealand, follow-up from the end of the winter 2005 to the winter 2006	6-12 year old asthmatic children. Interventions: 175; Controls: 174	Interventions: heat pump, wood pellet burner, or flued gas heaters, installed before winter 2006; Controls: unfued gas or plug-in electric heaters	Parents recorded asthma symptoms in daily diaries	Adjusted for outcome at the end of the winter 2005 including respiratory symptoms, lung function, temperature and NO_2.	0.40 fewer visits to a doctor for asthma (0.11 to 0.62), and 0.25 fewer visits to a pharmacist for asthma (0.09 to 0.32) in intervention groups, compared with control groups
[32]Pilotto LS et al. 2004	Australia, over 12 weeks from 1 June to 20 August 2000	Interventions: 45 asthmatic children (mean 8.4 year); Controls: 73 asthmatic children (mean 8.7 year)	Intervention schools: flued gas heaters or electric heaters; Control schools: unflued gas heaters	Telephone interview to parents, asthma symptoms based on the daily diaries	Hay fever and parental education	Difficulty breathing during the day (RR=0.41) and night (RR=0.32), chest tightness during the day (RR=0.45), and daytime asthma attacks (RR=0.39) were significantly reduced in the intervention groups, compared with controls.
[33]Somerville M et al. 2000	UK, baseline questionnaires from June-July 95, follow-up questionnaires from March 96 to December 97	72 children (<16 years) with diagnosed asthma	Intervention: gas central heating (47%), electric storage heaters (37%), solid fuel central heating (12%) and oil-fired central heating (4%); before intervention: coal fire, and other heating	Questionnaires completed by parents	Not adjusted	After intervention all respiratory symptoms were significantly reduced, wheeze by day 2 →1 times and wheeze by night 2→0 times (P<0.001), compared with before intervention

Cohort studies

There was only one cohort study that assessed the association between heaters and asthma symptom in the literature (Table 1-2). In this 7 year follow-up study, it was confirmed that compared with the group not using gas heaters, 7-years-old children in the group that used gas heaters were at risk for asthma, but other heaters such as open fires, and wood, oil, and kerosene heaters were not significantly associated with asthma symptoms[16].

Table 1-2. Cohort studies

Authors, years	Research place and periods	Participants	Heating fuels	Outcome assessment	Confounding factors	Results
[16]Ponsonby AL et al. 2000	Australia, the birth cohort study followed up from 1986 to 1995	863 children	Gas heaters VS no gas heaters	The ISAAC questionnaire completed by parents: asthma, and wheezing in the past 12 months	Active smoking status, and the history of asthma	Gas heaters: RR=1.83 (1.51-2.21) asthma, compared with no use of gas heaters

Wood or coal - cross-sectional studies

Table 1-3 shows 10 papers that reported associations between wood or coal fuel heaters and asthma in children. There were 5 studies that reported an adverse effect of wood or coal heaters on asthma. Compared with other fuel heaters, the use of wood fuel for heating was associated with a 2.2-fold increase in asthma in school children[14]. Coal heating use was significantly associated with asthma (OR = 1.91, 95% CI: 1.06 - 3.45), compared with other fuel heating system[34]. Behrens et al. reported that the use of coal fuel for space heaters was associated with girls' asthma and boys' wheezing compared with other fuels, but the use of wood fuel for space heaters, and the coal or wood for main heating system was not significant[35]. In one study, the use of wood heaters was significantly associated with asthma (OR = 1.22, 95% CI: 1.02-1.45) and wheezing (OR = 1.52, 95% CI: 1.06 -2.15) in Chinese children, compared with other heaters[36]. In another study that also investigated on Chinese children, the proportion of coal heaters use was higher (OR = 1.5, 95% CI: 1.1 – 1.9) in children with asthma, compared with non-asthmatic children[37].

However, Nguyen et al. reported that wood heating was associated with decreased asthma symptoms, compared with unvented gas heating and other heating[38]. One study conducted in two cities in Germany reported also that compared with no wood/coal heating, the presence of wood/coal heating was significantly associated with decreased asthma in 5-8 years old children (OR = 0.51, 95% CI: 0.31 – 0.85), but was also associated with increased asthma in 12-15 years old children (OR = 1.38, 95% CI: 1.07 -1.77)[39].

No significant results were reported in a further 3 studies. One study reported no significant association between wood/coal heating and asthma, compared with central heating[7]. Compared with healthy children, wood stove was not significantly associated with asthma[40]. One study reported that coal/wood was not significantly associated with asthma, compared with central and other heating system[41].

Among the 10 papers, only one study was conducted to measure exhaled breath NO, but there was no significant association between levels of NO and the use of wood heating[14].

Table 1-3. Wood or coal – cross-sectional studies

Authors, years	Research place and periods	Participants	Heating fuels	Outcome assessment	Confounding factors	Results
[14]Van Miert E et al. 2012	Belgium, 2006	744 mean age 15-year-old school children, Asthma: 75	Wood VS others	Questionnaires completed by parent: doctor-diagnosed asthma	Age, sex, BMI, birth weight, total serum IgE, the social and medical characteristics, house in rural area, and house built after 1950	Wood fuel for heating and cooking: asthma (OR = 2.2, 95%CI: 1.1-4.4), compared with other fuels
[7]Fedortsiv O et al. 2012	Ukraine, 2010	4871 urban and rural children aged 6-14 years, Asthma: 83	Coal/wood VS central heating	Questionnaires completed by parent: doctor-diagnosed asthma and wheeze during last 12 months	Age, residence, sex, parental education, parental employment, parental allergy, tobacco, housing, household density, dampness and pets	Compared with central heating, coal/ wood was not significantly associated with asthma (OR=0.91) and wheeze (OR=0.59)
[34]Kasznia-Kocot J et al. 2010	Poland, 2005-2006	1,130 children from 13-15 years of age, Wheeze: 143	Coal VS others	Questionnaires completed by parent: wheezing last year	Sickness, sex, parental atopy, socioeconomic status, mold/dampness, tobacco, pneumonia/bronchi inflammation before 3 year, and pets	Coal heating (VS others): asthma (OR=1.91, 95%CI: 1.06-3.45)
[38]Nguyen T et al. 2010	USA, 2002-2003	Children <18 year old. Cases (asthma): 530 Controls (no asthma): 882	Fireplace/wood-burning and unvented gas heating: yes/no	Interview to parents: doctor-diagnosed asthma and still asthma	Age, sex, race/ethnicity, geographic region, education, and percent of the poverty threshold	Fireplace/wood-burning heating: OR=0.6 (0.4-0.8) in case, compared with the children without asthma

Table 1-3. Wood or coal – cross-sectional studies

Authors, years	Research place and periods	Participants	Heating fuels	Outcome assessment	Confounding factors	Results
[35]Behrens T et al. 2005	Germany, 1995-2000	6996 children aged 6-7 years in two cross-sectional studies	Main heating: gas, coal, oil, wood, and electric; Space heating: gas, coal, oil, and wood	ISAAC questionnaire completed by parents: last 12 months asthma	Social economic status, parental atopy, cooking with gas, space heating, passive smoking and truck traffic	Main heating: not significant Space heating: Coal (VS others): asthma in girls (OR=13.46, 95%CI, 1.76-103.14), and not significant in boys; wheeze in boys (OR=2.56, 95%CI, 1.0-6.55) and not significant in girls; Wood (VS others): not significant
[36]Qian Z et al. 2004	China, 1993-1996	7058 school children living in the four Chinese cities	Coal VS others	Questionnaires completed by parents: doctor diagnosed asthma and wheeze	Age, sex, and the eight study districts	Heating coal smoke (VS others) wheeze: OR=1.22(1.02-1.45); asthma OR=1.52(1.06-2.15)
[37]Zheng T et al. 2002	China, January 1999	6-10 years school children. Cases (asthma): 403; Controls (no asthma): 806	Coal: yes or no	Questionnaires completed by parents: diagnosed asthma	Adjusted for sex, age, ethnicity, parents' history of allergies, full-term pregnancy, and duration of being breastfed (0, 1-12, >12 months)	Coal for heating in children with asthma: (OR=1.5, 95%CI: 1.1-1.9), compared with the children without asthma

Table 1-3. Wood or coal – cross-sectional studies

Authors, years	Research place and periods	Participants	Heating fuels	Outcome assessment	Confounding factors	Results
[39]Duhme H et al. 1998	Germany, 1994 and 1995	5-8 years olds: 3741 children in Münster, 2857 children in Greifswald; 12-15 years olds: 4003 and 3153, respectively	Coal/wood VS others	ISAAC: asthma symptoms in the last 12 months, 5-8 yrs children reported by parents, and 12-15 yrs children by self-report	Age and sex	5-8 years: wood/coal (yes/no) in first year: OR=0.51 (0.31-0.85) in Münster, and wood or coal at present and in Greifswald were no significant; 12-15 years: wood/coal (yes/no) OR=1.38 (1.07-1.77) in Münster, and in Greifswald no significant
[40]Maier WC et al. 1997	USA, February-June 1994	925 primary school students aged 5-9-year, Asthma: 106; Current wheezing: 66; normal: 73	Wood, kerosene, and wood	ISAAC questionnaires completed by parents: doctor-diagnosed asthma, current wheezing in the past 12 months	Not adjusted	Wood stove: doctor-diagnosed asthma was not significantly, compared with normal population; current wheezing was not significantly, compared with normal population
[41]Von Mutius E et al. 1996	Germany, September 1989 to July 1990	1958 school-children aged 9-11 years, Asthma: 89 Current asthma: 53	Coal/wood VS central heating and other	Questionnaires completed by parents: either asthma or recurrent "asthmatic" or "spastic" bronchitis	Socioeconomic status, number of adults living in the household, number of siblings, family history of atopic diseases, passive smoking, dampness, and presence of a cat or dog in the home	Coal/wood was not significantly associated with asthma, compared with other heating

Gas - cross-sectional studies

Seven papers referred to the association between the use of gas heating and asthma symptoms. Four studies reported that the use of gas heaters was significantly associated with asthma symptoms. Belanger et al. reported that compared with other fuel heating systems, using gas heating in multi-family housing was associated with asthma symptoms including the likelihood of wheezing (OR = 2.27), shortness of breath (OR = 2.33), and chest tightness (OR = 4.34), but was not significant in single-family housing[42]. Compared with healthy children, the use of unvented gas geyser for water heating was significantly associated with asthmatic children (OR = 3.01, 95% CI: 1.21 -7.56), but the use of vented gas geysers was not significant[43]. The use of a gas stove or oven was also reported to be associated with asthma, compared with no use[44]. Garrett et al. reported that compared with other heaters, the use of a gas stove was associated with asthma (OR =2.11, 95% CI: 1.06 -4.72), and also associated with respiratory symptoms (OR = 2.24, 95% CI: 1.04 -4.82) after adjusting for parental allergy, parental asthma, sex, and indoor NO_2 concentration[45].

Three studies reported no significant association between the use of gas heating and asthma symptom. Compared with wood and other fuel heating systems, unvented gas fireplaces/stoves were not significantly associated with asthma[38]. Compared with not using gas heating, the use of gas fuel for main and space heating was not associated with asthma or wheezing in boys or girls[35]. Similarly is was also reported that gas stoves were not significantly associated with asthma and wheezing, compared with other heaters[40].

In two studies, NO_2 levels were also measured. One study reported that mean NO_2 concentrations were 8.6 ppb in homes with electric heaters and 25.9 ppb in homes with gas stoves, and the levels of NO_2 were significantly associated with wheezing and chest tightness[42] in children. Another study reported that levels of NO_2 were associated with increased respiratory symptoms, but this was not statistically significant ($P = 0.09$)[45].

Table 1-4. Gas – cross-sectional studies

Authors, years	Research place and period	Participants	Heating fuels	Outcome assessment	Confounding factors	Results
[38]Nguyen T et al. 2010,	USA, 2002-2003	Children younger than 18 year old. Cases (asthma): 530 Controls (no asthma): 882	Unvented gas heating: yes/no; Fireplace/wood-burning heating: yes/no	Interview to parents: doctor-diagnosed asthma and still asthma	Age, sex, race/ethnicity, geographic region, education, and percent of the poverty threshold	Unvented gas heating: not significantly in case, compared with children without asthma
[42]Belanger K et al. 2006	USA, 1997-1999	728 children with asthma was younger 12 years old	Gas VS other	Enrollment visit the asthmatic children through asking their mother: wheeze, cough, shortness breath of breath, chest tightness	Age, ethnicity, mold, water leaks, maintenance medication use, and season of sampling	Among children in multifamily housing, exposure to gas stoves increased likelihood of wheeze (OR=2.27; 95% CI, 1.15-4.47), shortness of breath (OR, 2.33; 95% CI, 1.12-5.06), and chest tightness (OR, 4.34; 95% CI, 1.76-10.69), compared with no use of gas stove, but not significant in single-family housing

Table 1-4. Gas – cross-sectional studies

Authors, years	Research place and period	Participants	Heating fuels	Outcome assessment	Confounding factors	Results
[43]Mommers M et al. 2005	Germany, 1997	7-8-year-old children. Cases: 781 children with respiratory symptoms Controls: 781 normal children	Unvented gas geyser for water heating VS others; Vented gas geyser for water heating VS others	The ISAAC questionnaire completed by parents: asthma symptoms	Sex, smoking during pregnancy, ETS, presence of pets, mold or damps pots in the home, wall-to-wall carpeting, presence of insulation measures, hearth or open fire place, gas cooking, organic waste removal, way of heating, SES and country of residence.	Compared with normal children, the use of unvented gas geyser was associated with increased asthma (OR=3.01, 95%CI: 1.21-7.56), but the use of vented gas geyser was not significant
[35]Behrens T et al. 2005	Germany, 1995-2000	6996 children aged 6-7 years in two cross-sectional studies	Main heating: gas, coal, oil, wood, and electric; Space heating: gas, coal, oil, and wood	ISAAC questionnaire completed by parents: last 12 months asthma or wheeze	Social economic status, parental atopy, cooking with gas, space heating, passive smoking and truck traffic	Main heating and space heating: Wheeze and asthma was not associated significantly in boys and in girls using gas heating, compared with no use of gas heating
[44]Lanphear BP et al. 2001	USA, 1988-1994	8257 children aged < 6 years, Doctor-diagnosed asthma: 491	A gas stove or oven for heat VS others	Questionnaires reported by parents: doctor-diagnosed asthma	Sex, race, poverty status, education of head of family, ever breastfed, received care in neonatal intensive care unit, birth weight, cat in home, urban residence, and age of house	The use of a gas stove or oven for heat was associated with asthma (OR=1.8, 95% CI: 1.02-3.2), compared with no use of a gas stove or oven

Table 1-4. Gas – cross-sectional studies

Authors, years	Research place and period	Participants	Heating fuels	Outcome assessment	Confounding factors	Results
[45]Garrett MH et al. 1998	Australia, 1994-1995	148 children between 7 and 14 years of age, Asthma: 53	Gas VS others	Respiratory symptoms included wheeze was recorded in 1994-1995; Asthma was diagnosed by doctor	Asthma: parental allergy, parental asthma, sex and presence of pets; Respiratory symptoms: parental allergy, parental asthma, sex and NO_2 levels	Gas heating: asthma was associated with gas stove (OR=2.11, 95%CI: 1.06-4.72); respiratory symptoms was associated with gas stove (OR=2.24, 95%CI: 1.04-4.82)
[40]Maier WC et al. 1997	USA, February-June 1994	925 primary school students aged 5-9-year, Asthma: 106; Current wheezing: 66; normal: 73	Wood, kerosene, and wood	ISAAC questionnaires completed by parents: doctor-diagnosed asthma, current wheezing in the past 12 months	Not adjusted	Gas stove use was not significantly associated with doctor-diagnosed asthma and current wheezing, adjusted PR was 0.9 and 0.9, respectively, compared with other heaters

Other fuels - cross-sectional studies

Oil fuels in heating systems were not significantly associated with asthma and wheezing in boys and girls, compared with other fuels[35]. Kerosene stove use was also not significantly associated with asthma and wheezing, compared with other fuels[40]. In one study, heating systems were classified into fume emitting and non-fume emitting heaters, and fume emitting heating systems included flued gas, unflued gas, open fire, wood stove, and kerosene heaters; non-fume emitting included central heating, electric, and reverse cycle heaters. There was no association between the current use of fume emitting heaters and any asthma symptoms compared with non-fume emitting heaters, but a significant association occurred between fume emitting heaters during the first year of life and current wheezing among 8-11 years old children[17].

Table 1-5 Other fuels – cross-sectional studies

Authors, years	Research place and periods	Participants	Heating fuels	Outcome assessment	Confounding factors	Results
[35]Behrens T et al. 2005	Germany, 1995-2000	6996 children aged 6-7 years in two cross-sectional studies	Main heating: gas, coal, oil, wood, and electric; Space heating: gas, coal, oil, and wood	ISAAC questionnaire completed by parents: last 12 months asthma or wheeze	Social economic status, parental atopy, cooking with gas, space heating, passive smoking and truck traffic	Oil (VS others): wheeze and asthma was not associated significantly in boys and in girls using oil heating, compared with no use of oil heating
[17]Phoa LL et al. 2004	Australia, in 2002	627 schoolchildren aged 8-11 years, Current wheeze: 160; Current wheeze: 62; Diagnosed asthma: 207	Fume emitting heaters (flued gas, unflued gas, open fire, wood stove, and kerosene) VS non-fume emitting (central, electric, and reverse cycle heating)	Questionnaires completed by parents: ever had asthma or wheeze, wheeze + AHR, and diagnosed asthma	Atopy, maternal smoking current, smokers in child's first year of life, smoking in other family members currently, parental asthma, the use of gas cookers currently, sex, and the use of fume emitting heaters in child's first year of life	No association between the current the use of fume emitting heaters and any of the asthma outcomes. Compared with non-fume emitting heaters, fume emitting heaters during the first year of life was associated with recent wheeze (RR=1.44, 95%CI: 1.11-1.86), and recent wheeze + AHR (RR=2.08, 95%CI: 1.31-3.31), other symptoms was not significant
[40]Maier WC et al. 1997	USA, February-June 1994	925 primary school students aged 5-9-year, Asthma: 106; Current wheezing: 66; normal: 73	Wood, kerosene, and wood	ISAAC questionnaires completed by parents: doctor-diagnosed asthma, current wheezing in the past 12 months	Not adjusted	Kerosene stove use (VS other heating) was not significantly associated with doctor-diagnosed asthma and current wheezing

1.4. Discussion

Assessment of the effect of fume emitting heaters on asthma in children

In the 19 reviewed papers, fume emitting fuel heaters included coal, wood, gas, kerosene, and oil heaters. In the intervention studies, the results were consistent in all 3 studies regarding the fact that asthma symptoms were significantly decreased in the home[31,33] and in the classroom[32], after changing the previous heating system to an improved heating system. In one study, decreased asthma symptoms were found after fume emitting coal heaters were replaced with non-fume emitting electric storage heaters and gas, solid, oil central heaters, although it was a time-series study[33]. In the remaining two studies[31,32], the heaters in the intervention group included fume emitting and non-emitting heaters, thus it was difficult to assess the effect of fume emitting heaters on asthma symptoms. Furthermore, they did not set one fuel heater as a reference to compare other another fuel heaters, thus, I did not know which fuel was actually associated with asthma in children.

In the 7 years follow-up cohort study[16], the use of fume emitting gas heater at baseline was a risk for asthma symptoms in children.

In the cross-sectional studies examining the use of coal or wood heating, after controlling for reasonable confounding factors, 5 studies reported a positive significant association between coal or wood fuel heating and asthma, while 4 other studies did not find any significant association, however, two studies reported inconsistent results. One study[38] reported the use of wood-burning heaters was significantly associated with decreased asthma symptoms, compared with other fuel heating systems, which contained unvented gas heaters. Another study explained an inverse association between the use of wood or coal heating and asthma in 5-8 years old children. The authors proposed that exposure to wood or coal heating in early childhood may lead to respiratory infections, which subsequently might have a protective effect on the development of atopic symptoms[39].

In cross-sectional studies on gas heaters, results were consistent in that the use of gas heaters was a risk for asthma symptoms with the exception of three studies that

showed no significant results. Kerosene[40] and oil[35] fuel was not significantly associated with asthma in children. One study found a significant association between current asthma and fume emitting heaters use during the first year of life, although not significant with current fume emitting heaters use[17].

Considering the results of previous studies, the use of fume emitting heaters including wood, coal, and gas heaters might be a risk for asthma in children <18 years of age. Kerosene was not associated with asthma symptoms in all 19 studies, but one study reported that the use of kerosene heating was strongly associated with asthma in children and adults, compared with other fuel (mainly wood) heating system[46]. In all 19 studies, there was no evidence to show that the use of kerosene heating is associated with asthma symptoms in children.

Association between heating fuels and asthma symptoms

Regarding which fuel use is more associated with asthma symptoms, compared with other fuels. In the 19 studies, gas, coal, wood, oil, kerosene, and electric fuels were mentioned. However, few studies set one fuel heater as a reference to compare another fuel heater, thus, I did not know which fuel was actually associated with asthma in children One study reported an association between coal/wood heating and asthma, compared with central heating, but it was not significant[7]. One intervention study reported that compared with unflued heaters, the use of electric or flued heaters significantly decreased asthma symptoms[32]. In all 19 studies, no study reported that electric heaters were associated with asthma symptoms. This might be explained by the fact that electric heaters are not a burning stove, and do not emit fumes. Thus, it might be associated with lower asthma symptoms than other fuel heaters.

Flue use in heaters

I also tried to summarize the association between the use of flued or unflued heaters and asthma. However, no study reported the effect of flued heater on asthma, compared with unflued heater directly. In cross-sectional studies, compared with the use of a vented gas geyser, using an unvented gas geyser showed a higher risk for

asthma symptoms in children[43]. In the intervention studies, two studies suggested that flue use in heaters decreased asthma symptoms in children[31,32]. Thus, flue use in heaters might decrease the adverse impact of fume emitting fuel heater on asthma, due to pollutants from heaters being emitted to the outside by flue use.

Mechanism of the effect of fume emitting heater on asthma symptoms

Indoor levels of NO_2 are thought to be related to the use of fuel heaters[31,32,45] and asthma symptoms[42,45]. Respiratory symptoms were significantly associated with the use of gas heater, after adjustment for levels of NO_2[45]. The use of gas heaters might emit other harmful substance other than NO_2. One study reported that biomass fuels for cooking were significantly associated with levels of NO_2, SO_2, CO_2, CO, NO, PM and O_3[30]. Thus, other pollutants emitted from fuel heaters might be associated with asthma symptoms in children.

The WHO reported that indoor dampness was associated with fuel heater use in the home[47]. One study reported that unflued gas heaters might release water vapors during the combustion process and might be related to dampness, which leads to asthma symptoms[16]. Dampness and mold problems in the home environment are associated with asthma symptoms in children[22-24]. Thus, the association between the use of fuel heaters and asthma might be partly explained by indoor dampness.

Assessment of asthma symptoms

In these studies, most studies used questionnaires to assess asthma in children, such as the well-known ISAAC questionnaire, in addition, there were other questionnaires that asked whether a doctor-diagnosed asthma or asthma symptoms. Several studies also interviewed parents to ask about asthma symptoms in their children. Due to the assessment of asthma by parents in most studies, it might exist misestimate in previous studies. However, the misestimating might not be great. For example, the ISAAC questionnaire[48] as “Have you had wheezing or whistling in the chest in the 12 months.” Parents could therefore distinguish asthma symptom by the sound of wheezing or whistling in the chest.

Confounding factors

In the 19 studies, two studies did not control for confounding factors, and did not conduct multivariate regression analyses to assess any association between heaters and asthma[33,40]. Most studies controlled for confounding factors to assess the effect of heaters on asthma symptoms. Basic characteristics were adjusted for in multivariate regression analyses such as age, ethnicity, sex, parental history of allergies, number of siblings, socioeconomic status, birth weight, different study districts, lung function, serum IgE levels, parental education status and employment, etc. Several environmental factors were also controlled for. These mainly included tobacco smoke, indoor dampness, truck traffic, house location, presence of pets, presence of wall-to-wall carpeting, cooking with gas, etc.

Remaining unsolved issues

Firstly, most studies included several different types of heaters, however, there was a lack of a detailed classification of heating fuel, and did not set one fuel heater as a reference to compare other fuel heaters. It was therefore difficult to know which fuel heater was associated with a higher prevalence of asthma symptoms than other fuel heaters.

Secondly, having ventilation also can decrease air pollution in the house. Several have studies suggested that improving indoor ventilation was an important method to reduce indoor air pollution from cooking[49,50]. Improved ventilation can decrease mean indoor NO_2 levels emitted from gas stoves[51,52], and ventilation might decrease indoor pollution[53]. Furthermore, flue use might decease the pollution from fume emitting fuel heaters[31,32]. However, no study reported the combined effect of flue use and ventilation on asthma symptoms.

Thirdly, it remains unknown whether the effect of fume emitting heaters on asthma symptoms is mediated by dampness. Unflued gas heaters might release water vapor during the combustion process and asthma symptoms might be partly explained by dampness[16]. Dampness problems might be associated with the growth of mold, fungi,

and bacteria; the release of volatile organic compounds; the breakdown of building materials, and house dust mite[47,54], and such pollutants might lead to asthma symptoms. Mold may be the most important risk factors for asthma symptoms, and many previous epidemiological studies have provided evidence that asthma symptoms in children are associated with dampness and mold problems in home building[22-24].

Forth, in the 19 reviewed studies, there were only two studies conducted in Asia[36,37], with the remaining 17 studies being conducted in USA, Europe, and Oceania. In Japan, heating use status, types of heaters, and the association between the use of heaters and asthma symptoms in children remains unknown.

1.5. Conclusions

According to these previous studies, the use of fume emitting fuel heaters for heating was associated with asthma symptoms in children. These heaters included coal, wood and gas heaters. It was suggested that levels of NO_2 were associated with the use of fume emitting fuel heaters and asthma symptoms in children. The use of electric heaters might be not associated with asthma symptoms in children, compared with fume emitting heaters. Most previous studies assessed asthma symptoms with questionnaires or ISAAC questionnaires by parents. In most cross-sectional studies, confounding factors were controlled for by multivariate regression analysis, such as basic information on children, and several environmental factors that included tobacco smoke, indoor dampness, truck traffic, house location, presence of pet, presence of wall-to-wall carpeting, etc.

The association between kerosene heaters and asthma symptoms in children remains unknown. Flue use in heaters may decrease asthma symptoms in children. However, no study reported the combined effect of flue use and ventilation on asthma symptoms. Furthermore, in Japan, heating use status, types of heaters, and the association between the use of heater and asthma symptoms in children remains unknown.

vi. Chapter 2. The association between mechanical ventilation, flue use in heaters and asthma symptoms in Japanese schoolchildren - A cross-sectional study in Sapporo, Japan

2.1. Introduction

Numerous studies have reported that the use of gas, coal, or wood heaters is associated with asthma symptoms in children[14,34,43,45]. The World Health Organization states that over three billion people in developing countries are dependent on solid fuel for heating and cooking; however, no household in Japan uses solid fuels[15]. In fact, according to data of this study on this survey of schoolchildren, about 90% of households used fume emitting heaters such as kerosene, or gas heaters. In Sapporo city, Japan, it is common practice to use fuel heaters during the winter for heating the house, but the association between such heating system and asthma symptoms remains unknown. Furthermore, the houses in Sapporo city are typically airtight[55], and using fume emitting fuel heater might be a severe problem regarding asthma attacks in children in winter.

Three interventional studies suggested that replacing unflued heaters with flued heaters decreased asthma symptoms[31,32,56]. In addition, mechanical ventilation (ventilation) in the home is a useful method of decreasing indoor air pollution[57]. However, it remains unclear whether ventilation systems are actually beneficial for decreasing the influence of fume emitting heaters on asthma symptoms.

The World Health Organization has reported that dampness and mold are the most important factors in the indoor environment that increase the prevalence of respiratory symptoms, allergies, and asthma[47]. Unflued gas heaters might release water vapor during the combustion process and asthma symptoms might be partly explained by dampness[16]. Dampness was associated with the use of fume emitting heaters[47], and the association of the use of fume emitting heaters and asthma symptoms might be mediated by dampness.

There are two aims in this chapter, which are as follows:

Firstly, this study aimed to determine whether an association exists between the

combination of ventilation and flue use in heaters and asthma symptoms among 1st–6th grade (6–12-year-old) Japanese school children in Sapporo who were exposed to fuel heaters during the winter in poorly aerated houses.

Secondly, to determine whether an association between the combination of ventilation and flue use in heaters and asthma symptoms is mediated by dampness.

2.2. Material and Methods

Study participants

This cross-sectional study was conducted in Sapporo city, Japan. Thirty-five of Sapporo's 202 public elementary schools were selected and invited to join in this study through the assistance from Sapporo Board of Education and Sapporo City Head Teachers' Association. Finally, 12 schools that located in eight out of ten wards in Sapporo agreed to join in this study, after the headmasters were informed about the items of this survey. A total of 6393 children in grades 1 to 6 (6 to 12 years old) received the questionnaire from their teachers, with instructions for their parents to complete the questionnaires between November 29th 2008 and January 30th 2009. Classroom teachers collected the questionnaires from the children, within 5 to 8 days from their distribution. The details have been also described in a previous study[58].

Definition of asthma symptoms

Asthma symptoms were defined using the Japanese Version[59] of the International Study of Asthma and Allergies in Childhood (ISAAC) questionnaire[48]. I classified participants as having "current asthma symptoms" when they answered "Yes" to the question, "Has your child had wheezing or whistling in the chest in the last 12 months?" For "ever had asthma symptoms", it was a response of "yes" to the question "Has your child ever had wheezing or whistling in the chest at any time in the past?"

Assessment of heating systems and mechanical ventilation status

I assessed heating system and mechanical ventilation by asking three questions that investigated the use of heating fuels, heater flue use, and ventilation status.

Regarding heating fuels used, I asked: “What heating fuels do you use in your house?” and participants could choose one or more of the following: “kerosene”, “gas”, “electric”, or “others”. According to the answers, heating fuel was redefined as follows: “electric”, meaning the use of electric heater only in the house; “kerosene”, meaning the use of any kind of kerosene heater; “gas”, meaning the use of any kind of gas heater but not a kerosene heater; “others”, meaning the use of other types of fuel heaters only or using other fuels in the presence of electric heater.

Regarding heater flue I asked: “Are you using unflued heaters that have no vent pipe to the outside?” Participants could answer “Yes” or “No”. Next, heating fuels and heater flue status were combined and classified into electric heaters, flued heaters (not including electric heaters), and unflued heaters (not including electric heaters).

Ventilation status was assessed by the question “Which rooms in your house have mechanical ventilation?” and possible answers were “living room”, “children’s bedroom”, “kitchen”, “bathroom”, “toilet”, and “other sites”. For the analysis, ventilation status in the living room and/or children’s bedroom was used to define the presence of mechanical ventilation (ventilation). Finally, the status of heating system and ventilation was classified into five groups: “electric heaters (only)”, “flued heaters with ventilation”, “flued heaters without ventilation”, “unflued heaters with ventilation”, and “unflued heaters without ventilation”.

Assessments of indoor dampness

The best indicators of dampness were suggestions that included the presence of water leakage, the presence of visible mold, or a perception of moldy odor[54]. Thus, the presence of visible mold (yes/no), the perception of moldy odor (yes/no), the presence of water leakage within the past 5 years (yes/no), and condensation on the windowpanes (yes/no) were evaluated in the questionnaires. I defined absence of indoor dampness as none of the four dampness indicators existing in the house, and the presence of indoor dampness was when at least one of the four dampness indicators existed in the house.

Assessments of other aspects of house environment

Other parameters were also evaluated in the questionnaires completed by parents: residence <200 meters from a main road (yes/no), presence of wall-to-wall carpeting in the house (yes/no), presence of furry animals and/or birds in the house (yes/no), presence of a smoker in the house (yes/no). Additional information was also collected, including sex (boy/girl), age (6–12), school grade (1^{th}–6^{th}), whether the child was a first-born, and parental history of allergies (both parents, mother only, father only, or neither).

Statistical analysis

Categorical variables are presented as number of children (percentage). The X^2 test was used to analyze the association of asthma symptoms with participant characteristics and house environment, and the association between house environment and indoor dampness. Logistic regression analyses were used to calculate odds ratios (ORs) and 95% confidence intervals (95% CIs) for the effects of house heating systems and ventilation on asthma symptoms. Electric heaters were used as a reference and categorized as non-fume-emitting, regardless of ventilation. All analyses were performed using the JMP version 10.0 for Windows (SAS Institute Inc., Cary, NC, USA). Statistical significance was defined as a two-side *P* value of <0.05.

I controlled extensively for potential confounders in the multivariate models. I chose these confounders based on the results of my study (i.e. they were statistically associated with asthma symptoms), or on known risk factors in previous studies[19-24]. In model 1, I adjusted for children's characteristics such as sex, school grade, schools and parental history of allergies. In model 2, I adjusted for house environmental factors such as residence <200 meters from a main road, presence of wall-to-wall carpeting in the house, and presence of smoker in the house, in addition to model 1. In model 3, I adjusted for indoor dampness, in addition to model 2. Finally, I conducted a stratified analysis according to indoor dampness after adjusting for the covariates shown in model 2, because indoor dampness is a well-known strong risk factor for

asthma.[11-13] In this study, I used four dampness indicators to assess indoor dampness status including visible mold, perception of moldy odor, water leakage within the past 5 years, and condensation on the windowpanes.

Ethical Considerations

This study was approved by the ethical board for epidemiological studies at the Hokkaido University Graduate School of Medicine and conformed to the principles outlined in the Declaration of Helsinki of 1975, as revised in 1983. The study was conducted after obtaining the relevant informed consent from participants' parents.

2.3. Results

In total, the parents of 4445 (69.5%) children replied to the questionnaires. After excluding questionnaires with incomplete data on sex, school grade, parental history of allergies, use of heating fuels, heater flue, ventilation, and asthma symptoms, 3874 (60.6%) children were evaluated, of 496 and 1197 reported current asthma symptoms and ever had asthma symptoms, resulting in a prevalence of 12.8% and 30.9%, respectively.

Table 2-1. Different types of heating fuel in the 3874 households

	n	%
Single fuel (n = 3507)		
Electric only	331	8.5
Kerosene only	2536	65.5
Gas only	523	13.5
Other	117	3.0
Multiple fuels (n = 367)		
Kerosene + electric	228	5.9
Kerosene + gas	46	1.2
Kerosene + other	4	0.1
Gas + electric	58	1.5
Gas + other	3	0.1
Other + electric	7	0.2
Kerosene + gas + other	1	0.0
Kerosene + gas + electric	20	0.5

Other means unknown fuels except electric, kerosene, and gas

Table 2-1 shows the different types of heating fuel in the 3874 households. In 3507 households (90.5%) single heating fuel was used, and in the remaining 367 (9.5%) households multiple heating fuels were used. The detailed distribution of heating fuels was 331 (8.5%) “electric only”, 2536 (65.5%) “kerosene only”, 523 (13.5%) “gas only”, 117 (3.0%) “other”, 228 (5.9%) “kerosene + electric”, 46 (1.2%) “kerosene + gas”, 4 (0.1) “kerosene +other”, 58 (1.5%) “gas + electric”, 3 (0.1%) “gas + other”, 7 (0.2%) “other +electric”, 1 (0%), “kerosene + gas + other” and 20 (0.5) “kerosene + gas + electric” heaters. Among the 3874 households, 2835 households (73.2%) used kerosene heaters, 644 households (16.7%) used electric heaters, 651 households (16.8%) used gas heaters, and 132 households (3.4%) used other fuel heaters. Other fuels were not recorded clearly.

Table 2-2 compares participants with and without asthma symptoms and reveals that current asthma symptoms and ever had asthma symptoms tended to occur more frequently in boys and in children with a parental history of allergies. The prevalence of current asthma symptoms and ever had asthma symptoms in boys versus girls was 15.6% versus 10.1%, and 35.8% versus 26.1%, respectively. The distribution of the prevalence of current asthma symptoms was also statistically different for each school grade, with 13.4%, 14.0%, 16.0%, 10.4%, 13.2%, and 9.7% for grades 1 to 6, respectively. In the 12 schools, the prevalence of current asthma symptoms and ever had asthma symptoms varied from 6.6% to 15.3%, and 21.8% to 36.0%, respectively.

The association between asthma symptoms and the home environment is shown in table 2-3. The following variables were associated with current asthma symptoms in children: use of kerosene and gas fuel heaters, use of unflued heaters, absence of ventilation in the living room or bedroom, presence of wall-to-wall carpeting, a smoker in the house, visible mold, moldy odor, water leakage, and condensation on windowpanes. For ever had asthma symptoms, it was: absence of ventilation in the living room or bedroom, residence <200 meters from a main road, presence of wall-to-wall carpeting, a smoker in the house, water leakage, and condensation on windowpanes.

Table 2-2. Associations between asthma symptoms and participant characteristics

Variable	n (%)	Current asthma symptoms		P-value	Ever had asthma symptoms		P-value
		Yes	No		Yes	No	
		n (%)	n (%)		n (%)	n (%)	
Participants		496 (12.8)	3378 (87.2)		1197 (30.9)	2677 (69.1)	
Sex							
Boys	1900 (49.0)	297 (15.6)	1603 (84.4)	<0.001	681 (35.8)	1219 (64.2)	<0.001
Girls	1974 (51.0)	199 (10.1)	1775 (89.9)		516 (26.1)	1458 (73.9)	
School grade							
1st	635 (16.4)	85 (13.4)	550 (86.6)	0.006	202 (31.8)	433 (68.2)	0.59
2nd	656 (16.9)	92 (14.0)	564 (86.0)		196 (29.9)	460 (70.1)	
3rd	655 (16.9)	105 (16.0)	550 (84.0)		204 (31.2)	451 (68.8)	
4th	689 (17.8)	72 (10.4)	617 (89.6)		224 (32.5)	465 (67.5)	
5th	612 (15.8)	81 (13.2)	531 (86.8)		194 (31.7)	418 (68.3)	
6th	627 (16.2)	61 (9.7)	566 (90.3)		177 (28.2)	450 (71.8)	
Parental history of allergies							
Both parents	994 (25.7)	197 (19.8)	797 (80.2)	<0.001	432 (43.5)	562 (56.5)	<0.001
Mother only	946 (24.4)	158 (16.7)	788 (83.3)		343 (36.3)	603 (63.7)	
Father only	531 (13.7)	69 (13.0)	462 (87.0)		184 (34.6)	347 (65.4)	
Neither parents	1403 (36.2)	72 (5.1)	1331 (94.9)		238 (17.0)	1165 (83.0)	
First-born child							
Yes	2074 (53.5)	269 (13.0)	1805 (87.0)	0.512	669 (32.3)	1405 (67.7)	0.072
No	1759 (45.4)	224 (12.7)	1535 (87.3)		520 (29.6)	1239 (70.4)	
Schools							
School 1	462 (11.9)	64 (13.8)	398 (86.2)	0.049	141 (30.5)	321 (69.5)	<0.001
School 2	173 (4.5)	24 (13.9)	149 (86.1)		57 (33.0)	116 (67.0)	
School 3	519 (13.4)	73 (14.1)	446 (85.9)		180 (34.7)	339 (65.3)	
School 4	177 (4.6)	23 (13.0)	154 (87.0)		49 (27.7)	128 (72.3)	
School 5	209 (5.4)	32 (15.3)	177 (84.7)		74 (35.4)	135 (64.6)	
School 6	333 (8.6)	36 (10.8)	297 (89.2)		78 (23.4)	255 (76.6)	
School 7	364 (9.4)	39 (10.7)	325 (89.3)		124 (34.1)	240 (65.9)	
School 8	81 (2.1)	9 (11.1)	72 (88.9)		18 (22.2)	63 (77.8)	
School 9	441 (11.4)	67 (15.2)	374 (84.8)		146 (33.1)	295 (66.9)	
School 10	413 (10.6)	49 (11.9)	364 (88.1)		116 (28.1)	297 (71.9)	
School 11	431 (11.1)	62 (14.4)	369 (85.6)		155 (36.0)	276 (64.0)	
School 12	271 (7.0)	18 (6.6)	253 (93.4)		59 (21.8)	212 (78.2)	

Values are expressed as numbers (percentage). *P* values were calculated using the χ^2 test.

Missing data are not displayed.

Table 2-3. Associations between asthma symptoms and the home environment

Variable	Current asthma symptoms		P-value	Ever had asthma symptoms		P-value
	Yes	No		Yes	No	
	n (%)	n (%)		n (%)	n (%)	
Use of heating fuels						
Electric	27 (8.2)	304 (91.8)	0.045	91 (27.5)	240 (72.5)	0.481
Gas	74 (12.7)	510 (87.3)		187 (32.0)	397 (68.0)	
Kerosene	379 (13.4)	2456 (86.6)		883 (31.2)	1952 (68.8)	
Others	16 (12.9)	108 (87.1)		36 (29.0)	88 (71.0)	
Heater flue						
Flued heaters	361 (12.0)	2659 (88.0)	0.004	916 (30.3)	2104 (69.7)	0.153
Unflued heaters	135 (15.8)	719 (84.2)		281 (32.9)	573 (67.1)	
Ventilation						
Present	302 (11.9)	2231 (88.1)	0.025	755 (29.8)	1778 (70.2)	0.044
Absent	194 (14.5)	1147 (85.5)		442 (33.0)	899 (67.0)	
Residence <200 meters from a main						
Yes	397 (13.5)	2545 (86.5)	0.057	954 (32.4)	1988 (67.6)	0.001
No	95 (10.5)	808 (89.5)		236 (26.1)	667 (73.9)	
Wall-to-wall carpeting in the house						
Yes	318 (14.4)	1885 (85.6)	0.002	720 (32.7)	1483 (67.3)	0.022
No	177 (10.7)	1480 (89.3)		473 (28.6)	1184 (71.4)	
Furry animals or birds in the house						
Yes	115 (11.9)	853 (88.1)	0.458	285 (29.4)	683 (70.6)	0.452
No	381 (13.1)	2523 (86.9)		911 (31.4)	1993 (68.6)	
Smoker in the house						
Yes	269 (14.6)	1576 (85.4)	0.004	608 (33.0)	1237 (67.0)	0.008
No	227 (11.2)	1798 (88.8)		589 (29.1)	1436 (70.9)	
Visible mold						
Yes	198 (14.3)	1187 (85.7)	0.015	444 (32.1)	941 (67.9)	0.397
No	295 (11.9)	2187 (88.1)		750 (30.2)	1732 (69.8)	
Moldy odor						
Yes	49 (23.6)	159 (76.4)	<0.001	79 (38.0)	129 (62.0)	0.076
No	447 (12.2)	3211 (87.8)		1115 (30.5)	2543 (69.5)	
Water leakage within the past 5 years						
Yes	85 (19.2)	357 (80.8)	<0.001	165 (37.3)	277 (62.7)	0.003
No	408 (11.9)	3012 (88.1)		1026 (30.0)	2394 (70.0)	
Condensation on the windowpanes						
Yes	305 (15.0)	1726 (85.0)	<0.001	672 (33.1)	1359 (66.9)	0.004
No	189 (10.3)	1646 (89.7)		521 (28.4)	1314 (71.6)	
Indoor dampness						
Absent	158 (10.1)	1401 (89.9)	<0.001	443 (28.4)	1116 (71.6)	<0.001
Present	338 (14.6)	1977 (85.4)		754 (32.6)	1561 (67.4)	

Values are expressed as numbers (percentage). *P* values were calculated using the χ^2 test.

Ventilation means mechanical ventilation in the living room or bedroom.

Missing data are not displayed.

Compared with the use of electric heaters, the use of gas and kerosene heaters was associated with current asthma symptoms (Table 2-4). Furthermore, the use of unflued heaters was associated with current asthma symptoms compared with the use of flued heaters, as was the absence of ventilation compared with the presence of ventilation. After adjusting for potential confounders, including sex, school grade, schools, parental history of allergies, residence <200 meters from a main road, presence of wall-to-wall carpeting in the house, presence of a smoker in the house, and indoor dampness in model 3, the use of kerosene heaters (OR = 1.58; 95% CI, 1.03-2.49) and unflued heaters (OR = 1.29; 95% CI, 1.02-1.63) remained significantly associated with current asthma symptoms, compared with electric heaters and the use of flued heaters. No significant association was found after adjustment in the case of ever had asthma symptoms.

Table 2-5 shows the association between asthma symptoms and combination of heating systems and ventilation. After adjusting for potential confounding factors in Model 3, the use of flued heaters without ventilation (OR = 1.62; 95% CI, 1.03-2.64) was significantly associated with current asthma symptoms. The use of unflued heaters was also significantly associated with current asthma symptoms in the presence (OR = 1.77; 95% CI, 1.09-2.95) or absence of ventilation (OR = 2.23; 95% CI, 1.31-3.85) compared with the use of electric heaters. Only the use of unflued heaters without ventilation was significantly associated with ever had asthma symptoms (OR =1.47; 95% CI, 1.01-2.14).

Table 2-4. Multivariate analyses for association between heating systems and mechanical ventilation (ventilation) and asthma symptoms

Variable	n (%)	Asthma symptoms	Crude OR (95% CI)	Model 1 OR[a] (95% CI)	Model 2 OR[b] (95% CI)	Model 3 OR[c] (95% CI)
Current asthma symptoms						
Use of heating fuels						
Electric	331 (8.5)	27 (8.2)	1.00	1.00	1.00	1.00
Gas	584 (15.1)	74 (12.7)	1.63 (1.04-2.64)*	1.75 (1.08-2.91)*	1.57 (0.97-2.62)	1.45 (0.89-2.43)
Kerosene	2835 (73.2)	379 (13.4)	1.74 (1.18-2.67)*	1.94 (1.29-3.04)*	1.75 (1.15-2.74)*	1.58 (1.03-2.49)*
Other	124 (3.2)	16 (12.9)	1.67 (0.85-3.18)	1.90 (0.94-3.74)	1.78 (0.88-3.50)	1.62 (0.80-3.20)
Heater flue (except electric						
Flued heaters	2775 (78.3)	343 (12.4)	1.00	1.00	1.00	1.00
Unflued heaters	768 (21.7)	126 (16.4)	1.39 (1.11-1.73)*	1.36 (1.08-1.71)*	1.32 (1.04-1.65)*	1.29 (1.02-1.63)*
Ventilation						
Present	2533 (65.4)	302 (11.9)	1.00	1.00	1.00	1.00
Absent	1341 (34.6)	194 (14.5)	1.25 (1.03-1.52)*	1.24 (1.01-1.52)*	1.22 (1.00-1.50)	1.19 (0.97-1.45)
Ever had asthma symptoms						
Use of heating fuels						
Electric	331 (8.5)	91 (27.5)	1.00	1.00	1.00	1.00
Gas	584 (15.1)	187 (32.0)	1.24 (0.92-1.68)	1.17 (0.85-1.62)	1.10 (0.79-1.53)	1.07 (0.77-1.49)
Kerosene	2835 (73.2)	883 (31.2)	1.19 (0.93-1.54)	1.20 (0.92-1.58)	1.12 (0.85-1.48)	1.08 (0.82-1.44)
Other	124 (3.2)	36 (29.0)	1.08 (0.68-1.69)	1.09 (0.67-1.75)	1.03 (0.63-1.67)	1.00 (0.61-1.62)
Heater flue (except electric						
Flued heaters	2775 (78.3)	850 (30.6)	1.00	1.00	1.00	1.00
Unflued heaters	768 (21.7)	256 (33.3)	1.13 (0.95-1.34)	1.09 (0.91-1.30)	1.06 (0.88-1.26)	1.05 (0.88-1.26)
Ventilation						
Present	2533 (65.4)	755 (29.8)	1.00	1.00	1.00	1.00
Absent	1341 (34.6)	442 (33.0)	1.16 (1.00-1.33)*	1.15 (0.99-1.34)	1.14 (0.98-1.33)	1.13 (0.97-1.32)

Values are expressed as numbers (percentage). OR, odds ratio; CI, confidence interval

*P < 0.05

[a]Adjusted for sex, school grade, parental history of allergies, and schools

[b]Adjusted for sex, school grade, parental history of allergies, schools, residence <200 meters from a main road, presence of wall-to-wall carpeting in the house, and presence of smoker in the house

[c]Adjusted for sex, school grade, parental history of allergies, schools, residence <200 meters from a main road, presence of wall-to-wall carpeting in the house, presence of a smoker in the house, and presence of indoor dampness.

Table 2–5. Multivariate analyses for the association between combination heating systems and mechanical ventilation (ventilation) and asthma symptoms

Variable	n (%)	Asthma symptoms n(%)	Crude OR (95% CI)	Model 1 OR[a] (95% CI)	Model 2 OR[b] (95% CI)	Model 3 OR[c] (95% CI)
Current asthma symptoms						
Electric heaters	331 (8.6)	27 (8.2)	1.00	1.00	1.00	1.00
Flued heaters with ventilation	1782 (46.0)	207 (11.6)	1.48 (0.99-2.30)	1.66 (1.09-2.63)*	1.53 (0.99-2.43)	1.41 (0.91-2.25)
Flued heaters without ventilation	993 (25.6)	136 (13.7)	1.79 (1.18-2.81)*	2.00 (1.28-3.21)*	1.80 (1.15-2.91)*	1.62 (1.03-2.64)*
Unflued heaters with ventilation	501 (12.9)	76 (15.2)	2.01 (1.28-3.25)*	2.24 (1.40-3.69)*	1.96 (1.22-3.25)*	1.77 (1.09-2.95)*
Unflued heaters without ventilation	267 (6.9)	50 (18.7)	2.59 (1.59-4.32)*	2.79 (1.66-4.76)*	2.48 (1.47-4.26)*	2.23 (1.31-3.85)*
Ever had asthma symptoms						
Electric heaters	331 (8.6)	91 (27.5)	1.00	1.00	1.00	1.00
Flued heaters with ventilation	1782 (46.0)	536 (30.1)	1.13 (0.88-1.48)	1.14 (0.86-1.51)	1.09 (0.83-1.46)	1.06 (0.80-1.42)
Flued heaters without ventilation	993 (25.6)	314 (31.6)	1.22 (0.93-1.61)	1.23 (0.91-1.65)	1.17 (0.87-1.59)	1.13 (0.83-1.54)
Unflued heaters with ventilation	501 (12.9)	151 (30.1)	1.14 (0.84-1.55)	1.11 (0.80-1.54)	1.06 (0.76-1.47)	1.02 (0.73-1.43)
Unflued heaters without ventilation	267 (6.9)	105 (39.3)	1.71 (1.21-2.42)*	1.61 (1.12-2.34)*	1.53 (1.05-2.21)*	1.47 (1.01-2.14)*

Values are expressed as numbers (percentage). OR, odds ratio; CI, confidence interval

*$P < 0.05$

[a]Adjusted for sex, school grade, parental history of allergies, and schools

[b]Adjusted for sex, school grade, parental history of allergies, schools, residence <200 meters from a main road, presence of wall-to-wall carpeting in the house, and presence of smoker in the house

[c]Adjusted for sex, school grade, parental history of allergies, schools, residence <200 meters from a main road, presence of wall-to-wall carpeting in the house, presence of a smoker in the house, and presence of indoor dampness.

Table 2-6. The association of house environment and indoor dampness

Variable	Indoor dampness		P value
	Absent n (%)	Present n (%)	
Electric heaters			
Yes	355 (55.1)	289 (44.9)	<0.001
No	1204 (37.3)	2026 (62.7)	
Kerosene heaters			
Yes	1021 (36.0)	1814 (64.0)	<0.001
No	538 (51.8)	501 (48.2)	
Gas heaters			
Yes	245 (37.6)	406 (62.4)	0.136
No	1314 (40.8)	1909 (59.2)	
Other			
Yes	51 (38.6)	81 (61.4)	0.701
No	1508 (40.3)	2234 (59.7)	
Flue use			
Flued heaters	1254 (41.5)	1766 (58.5)	0.002
Unflued heaters	305 (35.7)	549 (64.3)	
Ventilation			
Presence	1105 (43.6)	1428 (56.4)	<0.001
Absence	454 (33.9)	887 (66.1)	
Residence <200 meters from a main			
Yes	1066 (36.2)	1876 (63.8)	<0.001
No	483 (53.5)	420 (46.5)	
Wall-to-wall carpeting in the house			
Yes	661 (30.0)	1542 (70.0)	<0.001
No	893 (53.9)	764 (46.1)	
Furry animals or birds in the house			
Yes	415 (42.9)	553 (57.1)	0.052
No	1142 (39.3)	1762 (60.7)	
Smoker in the house			
Yes	686 (37.2)	1159 (62.8)	<0.001
No	871 (43.0)	1154 (57.0)	

Values are expressed as numbers (percentage). *P* values were calculated using the χ^2 test

Ventilation means mechanical ventilation in the living room or bedroom

Missing data are not displayed.

Table 2-6 shows the association between house environment and indoor dampness. The presence of indoor dampness was significantly associated with no use of electric heaters, the use kerosene heaters or unflued heaters, the absence of ventilation, residence <200 meters from a main road, the presence of wall-to-wall carpeting in the house, and smoker in the house.

The results of stratified by indoor dampness are shown in table 2-7. Although not significant, the presence of dampness was associated with an increased prevalence of current asthma symptoms among households using electric heaters (OR = 1.83; 95% CI, 0.73-4.31). In houses without indoor dampness, the use of unflued heaters was associated significantly with current asthma symptoms in the presence (OR = 2.42; 95% CI, 1.22-4.85) or absence of ventilation (OR = 3.26; 95% CI, 1.46-7.18) compared with the use of electric heaters. Likewise, in houses with indoor dampness, the use of flued or unflued heaters in the presence (flued: OR = 2.02; 95% CI, 1.20-3.59; unflued: OR = 2.35; 95% CI, 1.31-4.35) or absence (flued: OR = 2.47; 95% CI, 1.45-4.42; unflued: OR = 2.89; 95% CI, 1.55-5.57) of mechanical ventilation was significantly associated with current asthma symptoms. Only the use of unflued heaters without ventilation in the presence of dampness was significantly associated with ever had asthma symptoms (OR = 1.79; 95% CI, 1.16-2.27).

Table 2-7. Multivariate analyses for the association between combination heating systems and mechanical ventilation (ventilation) and asthma, stratified by the presence or absence of indoor dampness

Heating systems and ventilation	n (%)	Asthma symptoms n (%)	OR[a] (95%CI)
Current asthma symptoms			
Absence of indoor dampness			
Electric heaters	258 (16.5)	18 (7.0)	1.00
Flued heaters with ventilation	744 (47.7)	74 (10.0)	1.57 (0.91-2.83)
Flued heaters without ventilation	318 (20.4)	29 (9.1)	1.51 (0.80-2.92)
Unflued heaters with ventilation	160 (10.3)	23 (14.4)	2.42 (1.22-4.85)*
Unflued heaters without ventilation	79 (5.1)	14 (17.7)	3.26 (1.46-7.18)*
Presence of indoor dampness			
Electric heaters	73 (3.2)	9 (12.3)	1.83 (0.73-4.31)
Flued heaters with ventilation	1038 (44.8)	133 (12.8)	2.02 (1.20-3.59)*
Flued heaters without ventilation	675 (29.2)	107 (15.8)	2.47 (1.45-4.42)*
Unflued heaters with ventilation	341 (14.7)	53 (15.5)	2.35 (1.31-4.35)*
Unflued heaters without ventilation	188 (8.1)	36 (19.2)	2.89 (1.55-5.57)*
Ever had asthma symptoms			
Absence of indoor dampness			
Electric heaters	258 (16.5)	68 (26.4)	1.00
Flued heaters with ventilation	744 (47.7)	220 (29.6)	1.16 (0.82-1.64)
Flued heaters without ventilation	318 (20.4)	78 (24.5)	0.92 (0.61-1.37)
Unflued heaters with ventilation	160 (10.3)	52 (32.5)	1.41 (0.89-2.24)
Unflued heaters without ventilation	79 (5.1)	25 (31.6)	1.24 (0.68-2.21)
Presence of indoor dampness			
Electric heaters	73 (3.2)	23 (31.5)	1.22 (0.67-2.20)
Flued heaters with ventilation	1038 (44.8)	316 (30.4)	1.16 (0.83-1.63)
Flued heaters without ventilation	675 (29.2)	236 (35.0)	1.40 (0.99-2.01)
Unflued heaters with ventilation	341 (14.7)	99 (29.0)	1.01 (0.68-1.50)
Unflued heaters without ventilation	188 (8.1)	80 (42.6)	1.79 (1.16-2.27)*

Values are expressed as numbers (percentage). OR, odds ratio; CI, confidence interval

*$P < 0.05$

[a]Adjusted for sex, school grade, parental history of allergies, schools, residence <200 meters from a main road, presence of wall-to-wall carpeting in the house, and presence of a smoker in the house.

2.4. Discussion

In this study, the use of unflued heaters and fume-emitting heaters without ventilation were associated with current asthma symptoms in children compared with the use of electric heaters. This association was stronger in households without ventilation than in those with ventilation. In addition, the association between unflued heaters and current asthma symptoms in the absence of ventilation persisted, regardless of indoor dampness. On the other hand, these associations were not found in children who had ever had asthma symptoms. The home environment may have changed as the child grew up, or asthma symptom may have occurred in their early years of life. It is therefore possible that current asthma symptoms are associated with the current home environment.

This study was conducted in public primary schools located in Sapporo. Questionnaires were distributed to all children in these schools, and a response rate of 69.5% was achieved. In total, 3874 children (60.6%) were examined after excluding questionnaires with incomplete data. However, compared with the data for the 4445 children who responded, the data for sex, school grade, and parental history of allergies were not different between the children with and without asthma symptoms among 3874 children analyzed. Therefore, my results could be generalized to elementary school children living in northern Japan.

From earlier data, I know that 88.3% of households were using kerosene and gas heaters and that houses in Sapporo city are typically airtight[55]. Because my results suggest that there may be a serious adverse impact of heating without adequate ventilation on asthma symptoms, my results are important for the prevention of asthma symptoms in other areas of the world with similar airtight house as Sapporo.

The World Health Organization has reported that dampness and mold are the most important factors in the indoor environment that increase the prevalence of respiratory symptoms, allergies, and asthma[47]. These symptoms could be due to indoor pollutions including the growth of mold, fungi, and bacteria; the release of volatile organic compounds; the breakdown of building materials caused by dampness problems; and mite[47,54]. Mold may be the most important risk factors for asthma. Many previous

epidemiologic studies provide evidence that asthma symptoms in children are associated with dampness and mold problems in home building[22-24]. In this study, I found consistent result that indoor dampness was associated with current asthma symptoms in children.

In this study, dampness was associated with lower ventilation, the use of fume emitting (gas, kerosene) heaters and the use of unflued heaters in the house. It is consistent with previous studies, and which reported that indoor dampness is associated with some home environmental factors such as existing building construction[47], low home ventilation rate[47,60], and using unflued gas heaters[16]. Therefore, it is possible that the association between unflued heaters or the absence of ventilation and asthma symptoms is mediated by dampness. To confirm whether this is the case, I conducted a stratified analysis with dampness. In this study I found that, among those households using electric heaters, compared with the absence of dampness, the presence of dampness was associated with increased current asthma symptoms although not statistically significant. I also found that, regardless of indoor dampness, unflued heaters with or without ventilation were associated with current asthma symptoms. Thus, while there may be a pathway through dampness, it is possible that air pollution from fume-emitting heaters also can explain the association between the use of unflued heaters with or without ventilation and current asthma symptoms.

Several cross-sectional studies have shown that the use of gas[42,61] and kerosene[46] heating were risk factors for asthma in children. One study reported no significant association between the use of such heaters and asthma[17]. Although my study supported this to a degree, the impact of gas heaters became no significant after adjusting for potential confounding factors. Because unflued heaters can play an important role in asthma, I combined heating fuel with flue status to assess the effects on asthma. Compared with the use of electric heaters, the use of unflued heaters increased the risk of asthma. Two randomized controlled trials reported that the replacement of unflued gas heaters with flued gas heaters decreased asthma symptoms in children[31,32]. In this study, it was consistently found that unflued heaters were

associated with current asthma.

Gas and kerosene fuel stoves are known to emit nitrogen dioxide (NO_2), sulfur dioxide (SO_2), and particulate matter (PM),[52,62] which are associated with asthma symptoms in children[63]. NO_2 is a by-product of high-temperature combustion from stoves and has been found to exacerbate wheezing in children with asthma[64]. Inhaled NO_2 was found to increase the likelihood of initial sensitization to house-dust mites and play a role in the development of atopic asthma[65]. In another study, it was found to increase lung resistance, respiratory rate, and minute ventilation[66]. Furthermore, NO_2 and SO_2 can cause wheezing and breathlessness[67] and enhance the airway response to inhaled allergens[68]. Increased indoor PM concentrations have been associated with asthma exacerbation in children[69]. In mice, PM exposure increased the pathophysiological features of asthma by activating lymphocyte-dependent pathways[70]. The biological effects of PM from gas stoves are thought to be exerted by oxidative stress resulting in cell signaling, transcription factor activation, and mediator release in the respiratory tract, eventually culminating in inflammation[71]. Therefore, the use of unflued fume-emitting heaters may be associated with current asthma symptoms.

In this study, I also assessed the combined effect of heating systems and ventilation on asthma symptoms. The use of unflued heaters in the absence of ventilation increased the risk for asthma symptoms compared with the use of unflued heaters in the presence of ventilation. Previous studies have demonstrated that inadequate ventilation in houses that use unflued heaters increased the risk for asthma symptoms [51,52,57]. Improved ventilation can decrease the mean indoor NO_2 levels produced by gas stoves[51,52] and can be a useful way to decrease indoor air pollution[57]. Therefore, ventilation is recommended in houses that use unflued fume-emitting heaters to decrease asthma symptoms in children.

Limitations

This study had several limitations.

First, a causal relationship could not be ascertained due to the cross-sectional nature

of the study. Furthermore, it is also possible that before this investigation, parents changed their heating system or ventilation status due to their child's asthma symptoms. However, such actions would diminish the association between use of unflued heaters without ventilation and asthma symptoms. Indeed, for ever had asthma symptoms, a weak (but significant) association was only found with the use of unflued heaters without ventilation.

Second, asthma symptoms were not physician-diagnosed; however, I evaluated patients using the ISAAC questionnaire, which is used worldwide[48]. Therefore, the results can be considered reliable.

Third, I did not measure other major risk factors for asthma symptoms, such as socioeconomic status[72] and the presence of house-dust mite allergens[65,73]; these factors may have been confounders. However, I controlled extensively for other potential confounders and found a strong association of the use of unflued heaters and the absence of mechanical ventilation with current asthma symptoms. Moreover, the risk factors for asthma symptoms, such as the use of carpeting[20] and the presence of tobacco smoke[19] and indoor dampness and mold[22-24] were consistent with those reported previously, and these factors have been controlled in this study. Therefore, it is likely that my results are representative and that the associations are valid.

Forth, information about heating system and ventilation was obtained solely from parents, thus misclassification might have occurred. However, it would have been quite simple for parents to identify the type of heating system they had and whether they had (mechanical) ventilation. Furthermore, they would have been able to recognize flued or unflued heaters by the presence or absence of vent pipes to the outside.

Fifth, children spend a lot of time in elementary school. However, I did not have any detailed information about the schools. The prevalence of asthma symptoms in the 12 schools was different; however, the results of this study did not change after adjusting for "schools" in the multivariate analyses.

Sixth, I did not have any information on how long the children spent in the home and how they used the heater during the daytime and/or nighttime. It is possible that

some children did not spend a long time at home, or used heaters for a short time only. If I had assessed the duration and frequency of heater use in the home, the results might have been even clearer. I am planning to assess the duration and frequency of heater use in the home and the duration of time spent at home in a further study.

2.5. Conclusion

Compared with the use of electric heaters, the use of kerosene heaters was significantly associated with current asthma symptoms in children, and the use of gas or other heaters was not significant. However, when I factored in the use of flues and the presence of ventilation, significant differences emerged in use of fume-emitting heaters such as kerosene or gas heaters. Compared with the use of electric heaters, the use of unflued fume-emitting kerosene or gas heaters was associated with current asthma symptoms, and this association was stronger among participants who lived in houses using unflued kerosene or gas heaters in the absence of ventilation. In addition, this association of unflued heaters in the absence of ventilation persisted, regardless of indoor dampness. Ever had asthma symptoms were also associated with the use of unflued heaters without ventilation. Therefore, in northern cities like Sapporo, particular attention needs to be paid to the use of fuel heaters, especially those that have no flue or ventilation, since there might be an association with asthma symptoms in children.

vii. Summary and further studies

I reviewed studies that investigated the association between heater use and asthma symptoms in children. There is enough evidence to show an adverse impact of the use of fume emitting gas, wood, or coal heaters on asthma symptoms in children. However, the effect of kerosene heaters on asthma in children remains unknown. According to the results of this survey in Sapporo, the use of kerosene heaters was significantly associated with asthma symptoms in children, compared with the use of electric heaters.

I found that the use of unflued fume emitting fuel heaters was associated with current asthma symptoms, compared with the use of electric heaters. In particular, the absence of ventilation was associated with a higher prevalence of asthma symptoms than the presence of ventilation. According to data from this study, I knew that 88.3% households were using kerosene and gas heaters in Sapporo city, and that houses in Sapporo city are typically airtight. Because my results suggest that there may be a serious adverse impact of heating without adequate ventilation on asthma symptoms, my results should be important for the prevention of asthma symptoms in other areas of the world with similar airtight houses as Sapporo.

I also found that, regardless of indoor dampness, unflued heaters with or without ventilation were associated with current asthma symptoms. Thus, while there may be a pathway through dampness, it is possible that air pollution from fume-emitting heaters can also explain the association between the use of unflued heaters with or without ventilation and asthma symptoms.

Therefore, I recommended that in northern cities like Sapporo, particular attention needs to be paid to the use of fuel heaters, especially those that have no flue or ventilation, since there might be an association with asthma symptoms in children.

In a further study, I plan to assess the duration and frequency of heater use in the home and the duration of time spent at home for children. It is possible that some children did not spend a long time at home, or used heaters for a short time only. If I had assessed the duration and frequency of heater use in the home, the results might have been even clearer. Furthermore, schoolchildren also spent a lot of time in their

school. Previous studies reported that the prevalence of children's asthma and allergic symptoms were associated with traffic-related pollution in schools[74,75]. Air quality in school is very important to schoolchildren. Thus, I also plan to collect detailed environmental information on schools.

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ix. References

1 WHO. Asthma. Vol. Fact sheet No 307 (World Health Organization, Geneva, 2011).

2 WHO. *Asthma*. Data accessed http://www.who.int/respiratory/asthma/en/ (World Health Organization, 2013).

3 Singh, B. B. *et al.* Herbal treatments of asthma: a systematic review. *J Asthma* **44**, 685-698 (2007).

4 Taras, H. & Potts-Datema, W. Childhood asthma and student performance at school. *J Sch Health* **75**, 296-312 (2005).

5 Bousquet, J. & Khaltaev, N. *Global surveillance, prevention and control of chronic respiratory diseases: a comprehensive approach*. (World Health Organization, 2007).

6 Nieto, A. *et al.* Pediatric allergy and immunology in Spain. *Pediatr Allergy Immunol* **22**, 742-750 (2011).

7 Fedortsiv, O. *et al.* Prevalence of childhood asthma, rhinitis, and eczema in the Ternopil region of Ukraine--results of BUPAS study. *Adv Med Sci* **57**, 282-289 (2012).

8 Duggan, E. M., Sturley, J., Fitzgerald, A. P., Perry, I. J. & Hourihane, J. O. The 2002-2007 trends of prevalence of asthma, allergic rhinitis and eczema in Irish schoolchildren. *Pediatr Allergy Immunol* **23**, 464-471 (2012).

9 Nishima, S. *et al.* Surveys on the prevalence of pediatric bronchial asthma in Japan: a comparison between the 1982, 1992, and 2002 surveys conducted in the same region using the same methodology. *Allergol Int* **58**, 37-53 (2009).

10 Tanihara, S., Nakamura, Y., Oki, I., Ojima, T. & Yanagawa, H. Trends in asthma morbidity and mortality in Japan between 1984 and 1996. *J Epidemiol* **12**, 217-222 (2002).

11 Asher, M. I. *et al.* Worldwide time trends in the prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and eczema in childhood: ISAAC

Phases One and Three repeat multicountry cross-sectional surveys. *Lancet* **368**, 733-743 (2006).

12 Futamura, M. *et al.* Age-related prevalence of allergic diseases in Tokyo schoolchildren. *Allergol Int* **60**, 509-515 (2011).

13 Brasche, S. & Bischof, W. Daily time spent indoors in German homes--baseline data for the assessment of indoor exposure of German occupants. *Int J Hyg Environ Health* **208**, 247-253 (2005).

14 Van Miert, E., Sardella, A., Nickmilder, M. & Bernard, A. Respiratory effects associated with wood fuel use: a cross-sectional biomarker study among adolescents. *Pediatr Pulmonol* **47**, 358-366 (2012).

15 Public Health and Environment (PHE): household air pollution Population using solid fuels (%), 2010, Total. Data accessed http://gamapserver.who.int/gho/interactive_charts/phe/iap_exposure/atlas.html (World Health Organization, 2012).

16 Ponsonby, A. L. *et al.* The relation between infant indoor environment and subsequent asthma. *Epidemiology* **11**, 128-135 (2000).

17 Phoa, L. L., Toelle, B. G., Ng, K. & Marks, G. B. Effects of gas and other fume emitting heaters on the development of asthma during childhood. *Thorax* **59**, 741-745 (2004).

18 Peat, J. K. The epidemiology of asthma. *Curr Opin Pulm Med* **2**, 7-15 (1996).

19 Tsai, C. H., Huang, J. H., Hwang, B. F. & Lee, Y. L. Household environmental tobacco smoke and risks of asthma, wheeze and bronchitic symptoms among children in Taiwan. *Respir Res* **11**, 11 (2010).

20 Herr, M. *et al.* Influence of host and environmental factors on wheezing severity in infants: findings from the PARIS birth cohort. *Clin Exp Allergy* **42**, 275-283 (2012).

21 Shima, M., Nitta, Y. & Adachi, M. Traffic-related air pollution and respiratory symptoms in children living a trunk roads in Chiba Prefecture, Japan. *J Epidemiol* **13**, 108-119 (2003).

22 Mendell, M. J., Mirer, A. G., Cheung, K., Tong, M. & Douwes, J. Respiratory and allergic health effects of dampness, mold, and dampness-related agents: a review of the epidemiologic evidence. *Environ Health Perspect* **119**, 748-756 (2011).

23 Reponen, T. *et al.* High environmental relative moldiness index during infancy as a predictor of asthma at 7 years of age. *Ann Allergy Asthma Immunol* **107**, 120-126 (2011).

24 Bornehag, C. G. *et al.* 'Dampness' at home and its association with airway, nose, and skin symptoms among 10,851 preschool children in Sweden: a cross-sectional study. *Indoor air* **15 Suppl 10**, 48-55 (2005).

25 Annesi-Maesano, I. *et al.* Poor air quality in classrooms related to asthma and rhinitis in primary schoolchildren of the French 6 Cities Study. *Thorax* **67**, 682-688 (2012).

26 Ma, L. *et al.* Effects of airborne particulate matter on respiratory morbidity in asthmatic children. *J Epidemiol* **18**, 97-110 (2008).

27 Yoshida, K. *et al.* Cedar and cypress pollen counts are associated with the prevalence of allergic diseases in Japanese schoolchildren. *Allergy* **68**, 757-763 (2013).

28 Desai M, M. S., Smith K. Indoor smoke from solid fuels. Assessing the environmental burden of disease at national and local levels. *World Health Organization, Protection of Human Environment* **2004**.

29 Schei, M. A. *et al.* Childhood asthma and indoor woodsmoke from cooking in Guatemala. *J Expo Anal Environ Epidemiol* **14 Suppl 1**, S110-117 (2004).

30 Padhi, B. K. & Padhy, P. K. Domestic fuels, indoor air pollution, and children's health. *Ann N Y Acad Sci* **1140**, 209-217 (2008).

31 Howden-Chapman, P. *et al.* Effects of improved home heating on asthma in community dwelling children: randomised controlled trial. *BMJ* **337**, a1411 (2008).

32 Pilotto, L. S. *et al.* Randomized controlled trial of unflued gas heater

replacement on respiratory health of asthmatic schoolchildren. *nt J Epidemiol* **33**, 208-214 (2004).

33 Somerville M, M. I., Owen P, Miles D. Housing and health: does installing heating in their homes improve the health of children with asthma? *Public Health* **114**, 434-439 (2000).

34 Kasznia-Kocot, J., Kowalska, M., Gorny, R. L., Niesler, A. & Wypych-Slusarska, A. Environmental risk factors for respiratory symptoms and childhood asthma. *Agric Environ Med* **17**, 221-229 (2010).

35 Behrens, T. *et al.* Symptoms of asthma and the home environment. The ISAAC I and III cross-sectional surveys in Munster, Germany. *Int Arch Allergy Immunol* **137**, 53-61 (2005).

36 Qian, Z., Zhang, J., Korn, L. R., Wei, F. & Chapman, R. S. Factor analysis of household factors: are they associated with respiratory conditions in Chinese children? *Int J Epidemiol* **33**, 582-588 (2004).

37 Zheng, T. *et al.* Childhood asthma in Beijing, China: a population-based case-control study. *Am J Epidemiol* **156**, 977-983 (2002).

38 Nguyen, T. *et al.* The National Asthma Survey--New York State: association of the home environment with current asthma status. *Public Health Rep* **125**, 877-887 (2010).

39 Duhme, H. *et al.* Asthma and allergies among children in West and East Germany: a comparison between Munster and Greifswald using the ISAAC phase I protocol. International Study of Asthma and Allergies in Childhood. *Eur Respir J* **11**, 840-847 (1998).

40 Maier, W. C., Arrighi, H. M., Morray, B., Llewellyn, C. & Redding, G. J. Indoor risk factors for asthma and wheezing among Seattle school children. *Environ Health Perspect* **105**, 208-214 (1997).

41 Von Mutius, E., Illi, S., Nicolai, T. & Martinez, F. D. Relation of indoor heating with asthma, allergic sensitisation, and bronchial responsiveness: survey of children in south Bavaria. *BMJ* **312**, 1448-1450 (1996).

42 Belanger, K., Gent, J. F., Triche, E. W., Bracken, M. B. & Leaderer, B. P.

Association of indoor nitrogen dioxide exposure with respiratory symptoms in children with asthma. *Am J Respir Crit Care Med* **173**, 297-303 (2006).

43 Mommers, M. *et al.* Indoor environment and respiratory symptoms in children living in the Dutch-German borderland. *Int J Hyg Environ Health* **208**, 373-381 (2005).

44 Lanphear, B. P., Aligne, C. A., Auinger, P., Weitzman, M. & Byrd, R. S. Residential exposures associated with asthma in US children. *Pediatrics* **107**, 505-511 (2001).

45 Garrett, M. H., Hooper, M. A., Hooper, B. M. & Abramson, M. J. Respiratory symptoms in children and indoor exposure to nitrogen dioxide and gas stoves. *Am J Respir Crit Care Med* **158**, 891-895 (1998).

46 Venn, A. J. *et al.* Increased risk of allergy associated with the use of kerosene fuel in the home. *Am J Respir Crit Care Med* **164**, 1660-1664 (2001).

47 *WHO Guidelines for Indoor Air Quality: Dampness and Mould*. (World Health Organization. Geneva, 2009).

48 Worldwide variation in prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and atopic eczema: ISAAC. The International Study of Asthma and Allergies in Childhood (ISAAC) Steering Committee. *Lancet* **351**, 1225-1232 (1998).

49 Rehfuess, E. A., Tzala, L., Best, N., Briggs, D. J. & Joffe, M. Solid fuel use and cooking practices as a major risk factor for ALRI mortality among African children. *J Epidemiol Community Health* **63**, 887-892 (2009).

50 Akunne, A. F., Louis, V. R., Sanon, M. & Sauerborn, R. Biomass solid fuel and acute respiratory infections: the ventilation factor. *Int J Hyg Environ Health* **209**, 445-450 (2006).

51 Saintot, M. *et al.* [Nitrogen dioxide and ozone exposures in a population sample from Ile-de-France]. *Rev Epidemiol Sante Publique* **48 Suppl 2**, 2S54-61 (2000).

52 Zota, A., Adamkiewicz, G., Levy, J. I. & Spengler, J. D. Ventilation in public housing: implications for indoor nitrogen dioxide concentrations. *Indoor air* **15**, 393-401 (2005).

53 Ghosh, J. K., Wilhelm, M. & Ritz, B. Effects of residential indoor air quality and household ventilation on preterm birth and term low birth weight in Los Angeles County, California. *Am J Public Health* **103**, 686-694 (2013).

54 NIOSH Alert: Preventing Occupational Respiratory Disease from Exposures Caused by Dampness in Office Buildings, Schools, and Other Nonindustrial Buildings. (November 2012).

55 Kanazawa, A. *et al.* Nationwide study of sick house syndrome: comparison of indoor environment of newly built dwellings between Sapporo city and Southern areas including those in Honshu and Kyushu. *Nihon Eiseigaku Zasshi* **65**, 447-458 (2010).

56 Free, S., Howden-Chapman, P., Pierse, N. & Viggers, H. More effective home heating reduces school absences for children with asthma. *J Epidemiol Community Health* **64**, 379-386 (2010).

57 Rao, D. & Phipatanakul, W. Impact of environmental controls on childhood asthma. *Curr Allergy Asthma Rep* **11**, 414-420 (2011).

58 Ukawa, S., Araki, A., Kanazawa, A., Yuasa, M. & Kishi, R. The relationship between atopic dermatitis and indoor environmental factors: a cross-sectional study among Japanese elementary school children. *Int Arch Occup Environ Health* **86**, 777-787 (2013).

59 Sankei Nishima, H. O. Prevalence of childhood allergic diseases in Japan using International Study of Asthma and Allergies in Childhood (ISAAC) Phase One Protocol. *Jpn J Pediatr Allergy Clin Immunol* **16**, 207-220 (2002).

60 Hagerhed-Engman, L. *et al.* Low home ventilation rate in combination with moldy odor from the building structure increase the risk for allergic symptoms in children. *Indoor air* **19**, 184-192 (2009).

61 Ciuk, J., Volkmer, R. E. & Edwards, J. W. Domestic nitrogen oxide exposure,

urinary nitrate, and asthma prevalence in preschool children. *Arch Environ Health* **56**, 433-438 (2001).

62 Kumie, A. *et al.* Sources of variation for indoor nitrogen dioxide in rural residences of Ethiopia. *Environ Health* **8**, 51 (2009).

63 Liu, M. M. *et al.* Effects of outdoor and indoor air pollution on respiratory health of Chinese children from 50 kindergartens. *J Epidemiol* **23**, 280-287 (2013).

64 Chauhan, A. J. *et al.* Personal exposure to nitrogen dioxide (NO2) and the severity of virus-induced asthma in children. *Lancet* **361**, 1939-1944 (2003).

65 Ponsonby, A. L. *et al.* A prospective study of the association between home gas appliance use during infancy and subsequent dust mite sensitization and lung function in childhood. *Clin Exp Allergy* **31**, 1544-1552 (2001).

66 Januszkiewicz AJ, S. J., Sturgis JW, Rayburn DB, Dodd KT, Phillips YY, Ripple GR, Sharpnack DD, Coulson NM, Bley JA. Pathophysiological responses of sheep to brief high-level nitrogen dioxide exposure. *Inhal Toxicol* **4**, 359-372 (1992).

67 Zhao, Z. *et al.* Asthmatic symptoms among pupils in relation to winter indoor and outdoor air pollution in schools in Taiyuan, China. *Environ Health Perspect* **116**, 90-97 (2008).

68 Devalia, J. L. *et al.* Effect of nitrogen dioxide and sulphur dioxide on airway response of mild asthmatic patients to allergen inhalation. *Lancet* **344**, 1668-1671 (1994).

69 McCormack, M. C. *et al.* Indoor particulate matter increases asthma morbidity in children with non-atopic and atopic asthma. *Ann Allergy Asthma Immunol* **106**, 308-315 (2011).

70 Saunders, V. *et al.* Particulate matter-induced airway hyperresponsiveness is lymphocyte dependent. *Environ Health Perspect* **118**, 640-646 (2010).

71 Ghio, A. J. Mechanism of asthmatic exacerbation by ambient air pollution particles. *Expert Rev Respir Med* **2**, 109-118 (2008).

72 Schatz, M. Predictors of asthma control: what can we modify? *Curr Opin Allergy Clin Immunol* **12**, 263-268 (2012).

73 Custovic, A., Taggart, S. C., Francis, H. C., Chapman, M. D. & Woodcock, A. Exposure to house dust mite allergens and the clinical activity of asthma. *J Allergy Clin Immunol* **98**, 64-72 (1996).

74 Kim, H. H. *et al.* Analysis of the association between air pollution and allergic diseases exposure from nearby sources of ambient air pollution within elementary school zones in four Korean cities. *Environ Sci Pollut Res Int* **20**, 4831-4846 (2013).

75 McConnell, R. *et al.* Childhood incident asthma and traffic-related air pollution at home and school. *Environ Health Perspect* **118**, 1021-1026 (2010).