School of Public Health

Indoor Environmental Risk Factors for Respiratory Symptoms and Asthma in Young Children

Krassi Rumchev

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ABSTRACT

Asthma is a common chronic disorder in Western countries and is increasing in prevalence in both children and adults. Although genetic risk for atopy is an important factor for the development of asthma, it does not explain the tremendous increase in prevalence seen in recent decades. Environmental exposures in early life that affect immune maturation appear to be the key factors for the development of asthma. The indoor environment is a likely candidate since infants spend 90% of the time indoors at a time when immune deviation usually occurs. Exposure to indoor pollutants represents a potentially modifiable cause of allergic sensitization and asthma. In this context, it becomes important to establish which environmental factors might influence the development of asthma in predisposed individuals. Allergic reactions to certain environmental allergens such as house dust mites, cats, and cockroaches, have shown a high level of association with asthma prevalence, but in the last five years increasing attention is being paid to indoor environmental factors, other than allergens, that may be involved in the development of this disorder. The potential irritants include nitrogen dioxide, environmental tobacco smoke, formaldehyde, volatile organic compounds, and particulate matter ($PM_{2.5;10}$).

The aim of the study was to examine the nature of the relationship between asthma and environmental exposure to indoor environmental irritants.

A population based case-control study had been carried out in Perth, Western Australia. The study population consisted of young children (N = 192) aged between 6 months and 3 years old. Cases (n = 88) were asthmatic children who attended the Accident and Emergency Department at Princess Margaret Hospital for Children and were discharged with asthma as a primary diagnosis. Controls (n = 104) were children in the same age group as cases who had never been diagnosed with asthma, identified from birth records accessed through the Health Department of Western

Australia. Information, regarding the respiratory conditions experienced by the study children and characteristics of the home, was collected using a standardised questionnaire. The questionnaire consists of questions about potential risk factors for asthma and these factors were grouped in three categories. The first category included information on personal and social factors such as age and gender of the child, and mother's and father's educational level. The second category was related to personal susceptibility factors such as child's allergy, parental and sibling's asthma, eczema and hay fever. The last category included environmental exposure in the house such as parental and visitors smoking inside the house, exposure to gas heating and cooking, kerosene space heaters, open fireplaces, and pets. Other questions related to environmental exposure were the presence of air conditioning, humidifiers, and type of floor covering in the child's bedroom and the living room. Measurements of indoor nitrogen dioxide (NO_2), formaldehyde (HCHO), volatile organic compounds (VOCs), particulate matter (PM_{10}), and house dust mite exposure were made on two occasions over one year, winter (middle June through September 1998) and summer (December 1998 through March 1999). Indoor temperature and relative humidity were also measured. The atopic status of the children was assessed by skin prick tests to common allergens.

The study results indicated that age, gender, family history of asthma, atopy and domestic exposure to indoor environmental factors were significant predictors of asthma early in life. The study found that indoor exposure to formaldehyde, volatile organic compounds and house dust mite significantly increased the risk of having asthma. Presence of air conditioning appeared to be a protective factor for asthma.

In conclusion, the study results confirmed the role of susceptibility factors in asthma and show that indoor environmental factors contribute as risk factors for asthma in early stage of life. The observation that exposure to indoor air pollutants in early childhood is associated with asthma suggests the possibility that irritants in indoor air might be involved in the initiation phase of asthma. Since the quality of the

indoor environment is potentially modifiable there might be opportunities for intervention to reduce asthma symptoms. In order to counteract the increasing prevalence in asthma, the significance of the indoor environment where children grow and spend most of their time need to be given greater attention.

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INTRODUCTION

1.1 Indoor air pollution

Indoor air pollution is recognised as a significant public health problem in Western countries. One of the characteristic features of these societies is that the majority of people, especially young children, elderly and sick people spend most of their time indoors – up to 90%. Studies have found that exposure to indoor air contaminants is associated with adverse health effects.

The health concern of exposure to airborne pollutants is not new. As early as 1500 BC, the Egyptians realised that silica dust produced by cutting of stones caused respiratory disease. In 460-374 BC, Hippocrates of Cos found that air in mines can produce adverse health effects in humans (Brooks, 1992). By the 13th century, air pollution due to coal combustion emissions was reported as a source of illness and death (Brimblecombe, 1978). It was not until the 17th century that serious discussion of the association between poor air quality and adverse health effects emerged (Tedeschi, 1970). After dramatic episodes of illness and death due to air pollution in Belgium, 1930 and London in 1952, concerted efforts to improve air quality began and many governments initiated programs to reduce the level of specific air pollutants (Fry, 1953; Salvaggio 1990). In the U.S., the

Clean Air Legislation of 1955 began federal air pollution regulation, followed by the 1963 Clean Air Act and The Air Quality Acts of 1967, 1970, 1977, and 1990. The U.S. Environmental Protection Agency (EPA) sponsored a significant amount of research on ambient air pollution (Brooks, 1992).

As outdoor air quality began to improve, a cognizance of potential adverse health effects due to indoor air pollution emerged (Lebowitz, 1983; Spengler, 1984). Thus, indoor air quality became an important health issue through the following events:

1) the use of synthetic building materials and furnishings after the World War II;
2) the energy conservation measures after the energy crisis in early 1970 resulted in a reduction of fresh air indoors;
3) the time people spend indoors – up to 90% (Chapin, 1974); and
4) the final major event, which significantly affected indoor air quality, was the development of new technologies including the computer revolution, colour reproduction equipment, and high performing printers. These new technologies installed at home without adequate ventilation can modify indoor air quality and may adversely affect human health.

Concern over indoor air has now risen to such an extent that the United States Centre for Disease Control has classified indoor air pollution as a factor of high environmental risk (CDC, 1994). Domestic air pollution is now seen as a major public health issue and if the asthma problem is to be successfully tackled, it seems that a good understanding of the risks it poses may be vital (Cohen, 1995). The causal role of indoor air pollution in producing adverse human health effects is certainly more complex and less well understood than outdoors (Burge, 1988). Assessment of human exposure to indoor air pollution is difficult to quantify because of the many environmental characteristics involved. The level of contaminants in one building may be quite different from those in another, depending on several factors such as the presence and usage of sources of pollutants and air movement. Also, individuals in the indoor environment are

usually exposed to complex mixtures of contaminants rather than a single pollutant.

People are exposed to indoor air in a number of different settings. These include industry, offices, public buildings, schools, sports centres, and homes. The focus of this study is on indoor air quality in domestic premises.

Air quality is of particular importance to infants and children because they are more vulnerable and susceptible to pollutants due to their immature and developing systems. Children may be exposed to a wide array of environmental agents at home, in day care centres and schools. A number of epidemiological studies have reported that indoor environmental pollutants exacerbate childhood asthma and other respiratory illness. Since indoor air pollution has been identified as a critical problem affecting children's health worldwide there is a need for further information on adverse health effects from indoor air contaminants and the implementation of remedial measures.

The evaluation and resolution of indoor air quality problems require an understanding of emission sources, ventilation rate and processes affecting the transport of contaminants.

1.2 Sources of indoor air pollution

The primary causes of indoor air quality problems in homes are indoor pollution sources that release gases or particles into the air, which include:

- combustion sources such as gas, oil, kerosene, wood, coal, and tobacco products;
- building materials and furnishings;
- products for household cleaning and maintenance;
- personal care or hobbies; and
- central heating, cooling systems and humidification devices.

Outdoor sources such as radon, pesticides, and outdoor air pollutants also contribute to indoor air quality problems.

1.3 Health effects associated with exposure to indoor air pollutants

The entrance of air pollutants into the body is mainly through the respiratory tract and humans have only limited ability to select the materials they inhale, when compared to what they eat or drink. Air pollutants are capable of acute and chronic health effects within the respiratory tract itself and they are also absorbed from the respiratory tract into the bloodstream and distributed to other organs (Brooks, 1992).

Many epidemiological studies have investigated health effects related to exposure to some indoor air pollutants and evidence points to pollutants such as nitrogen oxide, nitrogen dioxide, carbon monoxide, carbon dioxide, formaldehyde, volatile organic compounds, and respirable particulate matter ($PM_{2.5}$; PM_{10}) being related to adverse health effects in people and especially in children. It has been acknowledged that children face significant threats to health from an array of environmental hazards. Due to differences in children's immune response compared to adults they are particularly vulnerable to pollution and may become more easily sensitized. Among the most important environmental health threats to children worldwide are microbiological and chemical contaminants.

The main health effects associated with exposure to indoor air pollution are listed below (Maroni, 1995):

- effects on respiratory system
- allergic and hypersensitivity effects
- hypersensitivity pneumonitis (HP)
- humidifier fever
- irritative effects
- sensory effects

- cancer and effects on reproduction
- toxic effects on the nervous system
- cardiovascular effects

1.4 Statement of the problem

Asthma is a growing medical concern and there is evidence that asthma prevalence may be increasing in young children (Magnus, 1997). In 1991, a study by Robertson and colleagues, demonstrates an increase in asthma prevalence in Australian children of 141% over the 26 years period from 1964 to 1990 (Robertson, 1991). According to Peat, the prevalence of current asthma in Australia in children is estimated of 24% (Peat, 1995). It has been reported that asthma affects approximately one in five Australian children and one in ten adults (NHMRC, 1988). A study in Western Australia (1998) estimates that the prevalence of current asthma in Western Australia is 18% of the total population while the prevalence of doctor-diagnosed asthma is between 31% and 41% of children with at least one positive skin prick test.

Although epidemiological studies have contributed to the understanding of the risk factors that may be associated with increased incidence of asthma, the aetiology of asthma remains unclear. While genetic factors are clearly important in determing the risk of development of asthma, interactions between genetic and environmental factors are likely to explain differences in prevalence.

Consequently, research is needed in order to enable identification, first of, those features of the descriptive epidemiology that are artifacts arising from differences in children's exposure to indoor environment and, secondly, those features within the individual and the indoor environment that have a significant influence on the likelihood of the development of asthma.

1.5 Objectives of the study

An analytical epidemiological study was conducted in order to determine the indoor environmental risk factors contributing to childhood asthma.

The overall aims of this study were:

- to determine the extent to which differences in the amount of exposure to indoor environmental factors can explain the risk of the development of asthma;

- to determine the extent to which other characteristics of the child, his or her parents/guardians and siblings, modify the relationship between indoor air pollutants and childhood asthma. Factors considered included family history of asthma, personal susceptibility factors, and parents educational level;

- to determine the influence of certain house characteristics on the risk of asthma in early childhood. Exposure to gas appliances, kerosene space heaters, maternal and paternal smoking, presence of air conditioning, pets, type of floor covering, indoor temperature and relative humidity were assessed;

- to determine the extent to which the house characteristics, mentioned above, influence the concentrations of indoor air pollutants (nitrogen dioxide, formaldehyde, volatile organic compounds, particulate matter, and house dust mites);

- to use the study results to identify and quantify modifiable risk factors for asthma, and

- to propose recommendations for creating a healthy indoor environment, based on the study results, in order to reduce asthma prevalence among

children in Australia.

1.6 Prevention of further increase in asthma prevalence – significance of the study

Asthma is a particularly important disease to consider in the context of environmental hazards to which children are exposed, due to their immature and developing systems.

Thus, the approach to setting priorities for the prevention of childhood asthma has been examined in the present study, using an analytical epidemiological study that assesses risk factors contributing to asthma and respiratory symptoms in a series of cases of asthmatic children and in representative controls. The information will assist in making decisions on the appropriate approach to reduce the incidence and prevalence of asthma, and in assigning priorities to identify preventive strategies.

Such a study should make a direct contribution to the reduction of asthma prevalence in Western Australia. Moreover, the identification of potential causal factors in childhood asthma and clarification of the way in which each of these factors contributes to the asthma problem would be of value both nationally and internationally.

Recommendations to enhance indoor environment in order to prevent air quality-related health problems and create a healthy home environment for Australian children will be proposed.

1.7 Structure of the thesis

The thesis provides a comprehensive overview of childhood asthma worldwide and in Australia. It begins with a review of asthma epidemiology and also identifies the limitations of previous research (Chapter two). Chapter three

reviews the existing literature related to the main features of the indoor environment. It highlights the potential indoor environmental risk factors for adverse health effects and their occurrence and source. Separately, an extensive review of the existing risk factors for asthma including predisposing, causal, and contributing factors as well as the asthma triggers, is presented in Chapter four. Taken together, these four Chapters identify the unanswered questions, which are examined in the case-control study described in Chapters five to eight.

CHAPTER TWO

EPIDEMIOLOGY OF CHILDHOOD ASTHMA:
A LITERATURE REVIEW

2.1 Introduction

Epidemiology is defined as the scientific method used to study disease occurrence in human populations (Tinkelman, 1993). A key feature of epidemiology is the measurement of disease outcomes in relation to a population at risk. The population at risk is a group of people who would be counted as cases if they had the disease being studied. *Incidence, mortality,* and *prevalence* rates describe the occurrence of disease in a study population (Lilienfeld, 1980). The incidence rate of a disease is the rate of the number of new cases to the population at risk during a specified period. *Mortality* is a similar ratio, with the number of deaths as the numerator. *Point Prevalence* rate of a disease is the proportion of a population that is cases at a particular time. Diseases with a longer duration have a higher prevalence.

In epidemiological studies *cross-sectional surveys* are used to measure disease prevalence. *Case-control* and *cohort* studies are designed to identify risk factors for disease. In a *cohort study*, subjects are classified on the basis of the presence

or absence of exposure to a particular factor and then followed for a specified period of time to determine the development of disease in each exposure group. The occurrence of the possible cause is compared between cases (people with disease) and controls (people without disease). A *case-control* design involves the identification of a case series, such as persons with asthma, and an appropriate control group, followed by comparison of the proportions of cases and controls exposed to the risk factor of interest.

These epidemiological approaches provide important information about the occurrence and causes of asthma.

2.2 Methodological features of asthma epidemiology

Clinical, physiological tests, and questionnaires are used to identify subjects in the context of an epidemiological investigation. In studies of childhood asthma, symptom questionnaires are widely used to classify subjects as affected due to the difficulties with young children cooperating adequately in physiological and clinical tests (Tinkelman, 1993). However, even a comprehensive questionnaire may not detect all cases of asthma, because of the imperfect sensitivity of questionnaires (Woolcock, 1997). Depending on the definition used for asthma in questionnaires, it may underestimate or overestimate the prevalence of the disorder. Furthermore, epidemiological studies are observational and comparative and therefore dependent on the type of measurements made. If the measurements are not well standardized then the results may be misleading.

Although epidemiological studies have contributed to the understanding of asthma as a disease, they are not consistent or systematic about their findings. One of the reasons is due to the lack of any clear definition of asthma and the historical lack of any standardised instrument for the descriptive epidemiology of the condition. It is impossible to compare studies that use different methods and questionnaires. The American Thoracic Society has developed a standardised respiratory symptoms questionnaire for children (1978) but it is still not

comprehensive in covering the symptoms of this complex disease. Recently the International Study of Asthma and Allergy in Childhood (ISAAC) has developed a standardised methodology, which contributes significantly to describing the prevalence and severity of asthma, rhinitis and eczema in children throughout the world (ISAAC, 1998).

Also, asthma epidemiology faces difficulties in measuring asthma *incidence* in *population*-based studies due to the fact that it is difficult to determine the date on which a particular person become "asthmatic" (Pearce, 1998). There are similar problems with measuring asthma *morbidity* studies. The reason is the uncertainty related to the health services and asthma management policies, which reflect real asthma morbidity.

Although there are fewer problems with studying asthma *mortality*, asthma deaths are rare and mortality studies are only suitable for studies of large populations rather than small patient groups.

All these distinctive characteristics of asthma epidemiology have provided the basis for the development of methods in asthma studies.

2.3 Definition and recognition of asthma

The word asthma is derived from the ancient Greek for panting, and even the ancient world recognized that asthma could cause death by suffocation (Boushey, 1987). The Hippocratic writings of the fourth and fifth centuries B.C. recognised the relationship between prevailing winds and asthma (Lloyd, 1978). In the second century AD, a Greek physician provided the first accurate written description of an asthma attack, which is as follows (Unger, 1974):

" The precursory symptoms of this disorder are weight at the chest, an unwillingness to attend to one's ordinary vocation, or to business altogether, an uneasiness of respiration in running, or going uphill... . Under increasing

disorder the cheeks flush, the eyes are prominent as in cases of strangulation, a snoring is heard while they are awake and the evil is much augmented during the sleep..."

Thus, many important asthma signs and symptoms were recognized about 1800 years ago.

The understanding of asthma was progressively increased by the observations of Moses Maimonides in the 12th century. He recorded that deaths from asthma could occur "should the rules of management go unheeded and one's desires and habits be followed indiscriminately" and even more, he recognised that viral respiratory infections are important in the exacerbation of severe asthma (Boushey, 1987).

Later, in the seventeenth century, Van Helmont observed that asthma involved "a drawing together of the smallest terminal bronchi" (Ellul-Micallef, 1976) and identified exposure to dust and eating fish as triggers of asthma (Stolkind, 1933).

Despite several carefully worded statements during the past decade (Scadding, 1983; Godfrey, 1985; Sears, 1997), there is still no definition of asthma that is applicable to all asthma cases. The reason is not only due to the lack of a single biological marker or clinical test for asthma but also difficulties as a consequence of the variable expression of symptoms, aetiological factors, heterogeneous responses to treatment and different outcomes.

In 1959 a Ciba Foundation Symposium defined asthma as:
"... the condition of subjects with widespread narrowing of the bronchial airways which changes its severity over short periods of time either spontaneously or under treatment"

This definition had a strong and lasting influence and was difficult to improve until the American Thoracic Society tried to reinforce the physiological nature of

this definition by introducing the concept of bronchial hyper-responsiveness to the definition.

The most frequently used definition of asthma emerges from the National Institute of Health, 1997 Guidelines for the Diagnosis and Management of asthma (National Heart, Lung, and Blood Institute, 1995), and it is as follows:

"*Asthma is a chronic inflammatory disease of the airways in which many cells and cellular elements play a role, in particular mast cells, eosinophils, T lymphocytes, macrophages, neutrophilis, and epithelial cells. In susceptible individuals, this inflammation causes recurrent episodes of wheezing, breathlessness, chest tightness, and coughing, particularly at night or in the early morning*".

The major features of asthma in the definition above are airway obstruction, bronchial hyperresponsivenes, and airway inflammation.

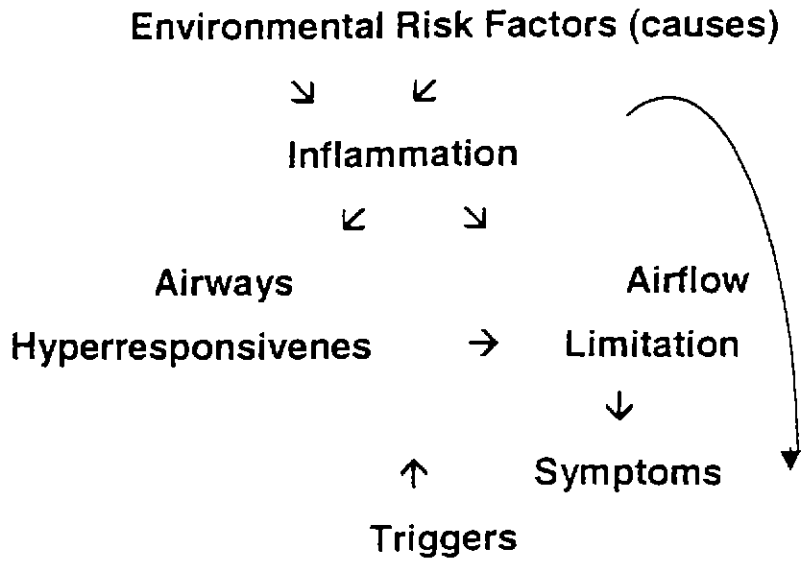


Fig 1. Mechanisms underlying the definition of asthma

The mechanisms underlying the definition of asthma are demonstrated in Fig 1 (NHLB/WHO Workshop, 1995). Inflammation causes recurrent episodes of wheezing, breathlessness, chest tightness, and cough that characterise typical asthma symptoms. These episodes are associated with airflow obstruction. Allergens may also cause the onset of asthma by continuously stimulating allergic inflammation of the airways.

Inflammation seems to be a major feature of asthma, the importance of which was first suggested in the late 19th century by Sir Andrew Clark (Clark, 1886). The inflammation also causes associated increase in the existing bronchial hyperresponsiveness to a variety of stimuli (National Hearth, Lung, and Blood Institute, 1995). Subjects with asthma were known to have extreme sensitivity of the airways, and this led the American Thoracic Society Committee to use bronchial hyperresponsiveness as a diagnostic criterion (ATS Committee, 1962). Although many factors have been incriminated in causing bronchial hyperresponsiveness, the principal focus is now directed toward those that cause and regulate airway inflammation.

2.4 Measuring asthma risk factors in epidemiological studies

Asthma epidemiological studies involve measuring the effect of an exposure on a particular outcome in a population. The term ***exposure*** refers to the presence of a substance in the environment (e.g., indoor air pollutant), whereas the term ***dose*** refers to the amount of substance that reaches susceptible target organ within the body (Pearce, 1998). Exposure levels can be assessed with regard to the ***concentration*** of the substance in the environment and the ***duration*** of time in which exposure occurs.

According to Armstrong (1992) the methods of exposure measurement in epidemiology include personal *interviews* or *self-administered questionnaires* (completed either by the study participant or by a proxy respondent), *diaries*, *observation*, *routine records*, *physical* or *chemical measurements* on the

environment, or on the person. Measurements on the person can relate either to exogenous exposure (e.g., airborne dust) or internal dose.

- ***Questionnaires***

Self-administered or interviewer-administered questionnaires have been successfully used in epidemiolgy to measure exposure to most non-biological risk factors. The validity of questionnaire data depends on the structure, format, content, and wording of questionnaires, as well as methods of administration and selection and training of interviewers (Armstrong 1992).

- ***Routine health care records***

In most cases, information on demographic factors can be obtained in a straightforward manner from routine health care records or with questionnaires (Armstrong, 1992). There are a variety of demographic factors that are associated with asthma such as gender and age (Anderson, 1992), birth order (Shaw, 1994), season of birth (Aberget, 1989), country (ECRHS, 1996), and ethnicity (Cunningham, 1996a). Liberatos (1988) suggests that socioeconomic status is also related to asthma, although it may pose significant measurement problems in some demographic groups. Socioeconomic status can be measured in different ways, including occupation, income, and education or a combination of these.

- **Serum IgE and skin testing**

Atopy is characterized by the production of circulating (Immunoglobin E) IgE in response to environmental allergens (Pearce, 1998). Martinez and colleagues (1995) show that high levels of serum IgE predict the development of asthma in childhood. Furthermore, Croner and colleagues (1982) found that 70% of newborn infants with elevated cord IgE levels develop probable atopic disease

such as asthma, rhinoconjunctivitis, dermatitis, allergic urticaria, before the age of 18 months compared with 4.9% of other infants.

Skin prick testing is also a convenient test for atopy in epidemiological studies (Burrows, 1976). It has been used to assess clinical allergic diseases since the nineteenth century and prevalence of asthma is shown to be closely related to the severity of skin test reactions to common inhaled allergens. The development of skin-test reactivity to a particular antigen depends on previous levels of allergen exposure and according to Sporic and Platts-Mills (1992) reactivity to dust mite allergen is strongly related to the level of exposure early in life.

A variety of standardised skin testing protocols are used in epidemiological studies. The ECRHS protocol uses lancets precoated with standardized allergen extracts (Burney, 1994). The ISAAC skin testing protocol uses the ALK lancet, which has good precision, safety and reproducibility (Strachan, 1995).

- ***Direct physical and chemical measurements on the environment***

Investigators use a variety of exposure measurement techniques, including questionnaires regarding home conditions such as heating and ventilation, damp patches, visible mold growth and home pets. Although questionnaires are a good source of information, systematic reporting bias can give inaccuracies in responses to some questions. Questionnaires can be combined with measures of environmental exposures to obtain a quantitative estimate of individual exposures, which give good validity with regard to current exposures (Armstrong, 1992). Direct measurements of indoor and outdoor pollutants, allergens, temperature and humidity can be performed using a variety of methods and techniques.

2.5 Prevalence of asthma in children worldwide

Most of the information concerning the occurrence of asthma is prevalence data has been collected in cross-sectional surveys. There is a substantial variation in the prevalence rates between countries, ranging from less than 1% in areas of India and Africa to 20-30% in Australia (Wjst, 1996).

Analysis of all published data suggests that increase in asthma prevalence began in the mid-to-late 1970s. The earliest reports of an increasing prevalence of asthma comes from surveys of schoolchildren in Birmingham in the late of 1960s (Morrison- Smith, 1971) and in New Zealand in the early 1980s (Mitchell, 1983). Since then, increases have been reported from national studies in other countries such as Sweden (Aberg, 1989), England (Burney, 1990), and Australia (Peat, 1994b).

There is a debate about whether asthma increase is real or is due to diagnostic problems, but recent studies indicate that both wheezing illness and asthma have shown a real increase. For example, U.S data from 1982 to 1992 demonstrates 42 % increase in the prevalence rate of self reported asthma. Similar dramatic increases occurred in New Zealand, Australia and the UK. Shaw (1990) reported that current asthma prevalence in New Zealand is increased by 60% and current wheezing by 50 %. A study in Aberdeen, Scotland, showed a doubling in the prevalence of wheezing from 10% to 20% for the interval from 1964 to 1989 and the prevalence of diagnosed asthma has risen from 4% to 10% for the same period in children aged 7 years. In Switzerland the prevalence is lower at about 7% (Robertson, 1993) and in Germany the prevalence rates were about 5% in 1994 (Von Mutus, 1994). There is evidence that asthma was rare in African children up to the late 1970s but recent research showed that asthma prevalence is also increasing in Kenya (Odhiambo, 1994) and in Zimbabwe (Keeley, 1991). It is not clear whether this is a real increase of asthma prevalence or it is due to improved diagnosis.

Despite the many reports on prevalence and mortality of asthma in different populations, the lack of a precise definition of asthma and of standardised methods make the comparison of reported prevalence from different parts of the world difficult. Thus, data are not easily compared and provide little information that can be used in health planning. On the other hand, most prevalence studies use questionnaire data that may underestimate or overestimate the prevalence of the disorder. Questionnaire definitions of asthma include "wheeze ever" and "diagnosed asthma". However, children in some communities have asthma that has never been diagnosed (Lee, 1983). A study in Newcastle shows under diagnosis of asthma (Spright, 1983) and reports that many practitioners are reluctant to label the young children as asthmatic, and this affects their willingness to acknowledge the presence of bronchospasm and treat it with bronchodilators.

Woolcock and Peat (1997) state that there seems little doubt that asthma and wheezing illness are increasing in children and young adults on the base of questionnaire studies. Data for "asthma ever diagnosed" or "current asthma" are shown in Table 1.1, above, which lists studies that use the same methods in the same populations on at least two occasions.

From the results given in the table, it is clear that asthma prevalence has increased worldwide in both developed and developing countries and asthma prevalence in Australia has doubled in the last ten years.

Table 1.1 Changes in prevalence of asthma in children and young adults from questionnaire studies.

Country	Study year	Number	Age	Asthma ever diagnosed (%)	References
Australia	1982	769	8-11	12.9	Britton et al, 1986
	1992	795	8-11	29.7	Peat et al, 1994
New Zealand	1975	715	12-18	26.2	Shaw et al, 1990
	1989	435	12-18	34	Shaw et al, 1990
Wales	1973	818	12	6	Burr et al, 1989
	1988	965	12	12	Barry et al, 1989
Scotland	1964	2743	8-13	4.1	Ninan&Russell, 1992
	1989	3942	8-13	10.2	Ninan&Russell, 1992
	1994	4034	8-13	19.6	Omran&Russell 1996
USA	1971-1974	4941	6-11	4.8	Cergen et al, 1988
	1976-1980	7399	3-17	7.6	Cergen et al, 1988
France	1968	8140	21	3.3	Perdrizet et al, 1987
	1982	10559	21	5.4	Perdrizet et al, 1987
Norway	1981	1772	-	3.4	Skjonsberg et al, 1995
	1993	4521	-	8	Skjonsberg et al, 1995

Modified from Woolcock, 1997

In 1998, the International Study of Asthma and Allergy in Childhood (ISSAC, 1998) surveyed 463, 801 children, aged 13-14 years to describe the prevalence and severity of asthma, rhinitis and eczema. It was a collaborative project,

including 155 centres in 56 countries, which developed a systematic, standardised methodology for international comparison of asthma and allergy prevalence. All study children completed a simple questionnaire regarding the symptoms of the three disorders: asthma, rhinitis and eczema. In 42 countries, a video asthma questionnaire was used in order to show the clinical signs and symptoms of asthma, followed by questions about whether their breathing has been like the person in the video. The terms of asthma or wheezing were not been mentioned.

The finding of the first phase of The International Study of Asthma and Allergy in Childhood (ISAAC) showed that the highest asthma prevalence rates are in Australia, New Zealand, the UK and Republic of Ireland with centres in North, Central, and South America next on the list. The lowest prevalence of asthma was reported in several Eastern European countries, Indonesia, Greece, China, Taiwan, Uzbekistan, India, and Ethiopia. So, the highest asthma prevalence was found mainly in English – speaking centres in Western countries, with the suggestion that environmental factors related to the living conditions in these countries might play an important role in the development of asthma. Also, the study reported an interesting finding that ambient air pollution is not a risk factor for the development of asthma while recognising that the forms of air pollutants may be different. Regions such as China and Eastern Europe with some of the highest levels of air pollution had low rates of asthma prevalence, whereas those such as Australia and New Zealand with the lowest levels of air pollution have the highest prevalence of asthma.

This finding of the ISSAC created considerable concern about the living environment indoors of the children in Western society and provided a framework for further aetiological research into lifestyle, genetic and environmental factors which may affect the prevalence rate of asthma and allergy. Furthermore, this study provided significant evidence that asthma prevalence is continuing to increase in most countries and presented data for prevalence rates for wheezing among 13-14 year olds. The prevalence rates of wheeze and asthma in some countries are shown in Table 1.2.

Table 1.2 Prevalence rates among 13-14 year olds of wheezing

Country	Wheeze	Wheeze more than 4 per year	Ever had asthma
Australia	29.4	10	28.2
New Zealand	28	8	24
UK	32.2	9.3	20.7
Hong Kong	12.4	4.4	11.2
Spain	10.3	2.7	10.5
Germany	13.8	3.4	5.7
Poland	8.1	1.9	2.4
China	4.2	0.9	6.1

Modified from ISAAC, 1998

According to Ahmad von Schlegell (1999), "while studies such as the International Study of Asthma and Allergies in Childhood (ISAAC) and the European Community Respiratory Health Survey (ECRHS) are essential for the understanding the global burden of asthma, studies of variations in the prevalence of asthma and morbidity in small areas within communities are more likely to elucidate some of the key interrelations between host, agent, and environment for this disease". In this context further research should increase the understanding of this multi-factorial disease under local conditions.

2.6 Prevalence of asthma in Australian children

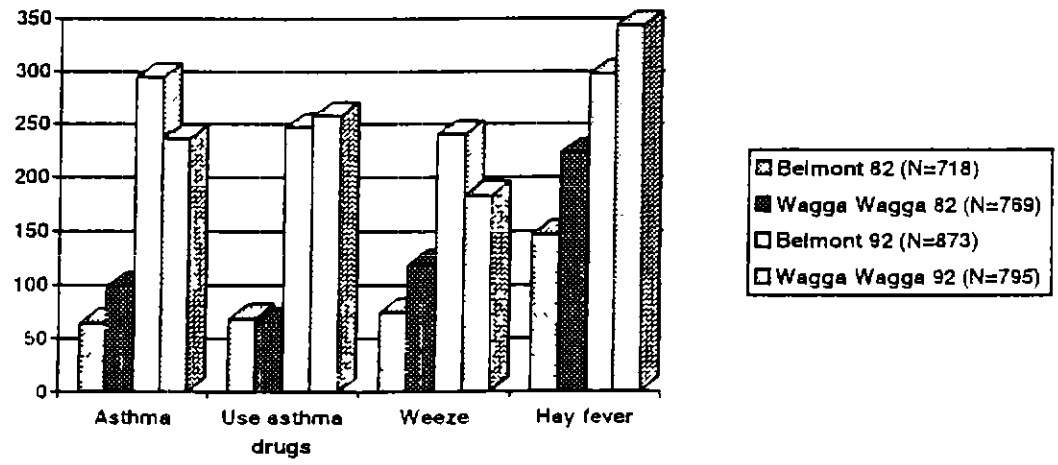
Asthma is a major health problem and one of the most common chronic childhood diseases in Australia (Landau, 1993). The National Health and Medical Research Council of Australia, reports that asthma affects approximately one in five Australian children (NHRMC, 1988). Also, Australia has the second highest asthma mortality rate (12.8%) in the world after New Zealand at 13.3% (Jackson, 1988). It has been estimated, that more than a fifth of Australian children with asthma report weekly wheeze and cough, two-thirds report school absences, and one-third report frequent sleep disturbances due to asthma (Bauman, 1992).

Of major concern is the fact that the prevalence of childhood asthma in Australia is rising. A study in Melbourne (Robertson, 1991) shows an increase in the

prevalence of wheeze or asthma of 141% over the 26 years from 1964 to 1990 (from 19.1% in 1964 to 46% in 1990). Peat and colleagues (1994) investigates whether the prevalence of asthma in children aged 8-10 had increased in two regions in NSW, Belmont and Wagga Wagga over a period of ten years. The study results demonstrate that the prevalence of asthma, recent use of drugs, and episodes of wheeze had increased significantly in both regions for the study period (see Figure 2).

Figure 2. Changes in prevalence of respiratory symptoms, hay fever, and use of asthma drugs in children aged 8-10 in two towns between 1982 and 1992.

"N" -number of the studied children



A study, as part of phase one of the International Study of Asthma and Allergy in Children (ISAAC), has been conducted in Australia (Robertson, 1998). The aim of the study is to determine the prevalence of asthma and other atopic diseases in Australian schoolchildren using the protocol of ISAAC. The study subjects are children, aged 6-7 years and 13-14 years, randomly selected from primary and secondary schools from Melbourne, Sydney, Adelaide, and Perth. A five-page questionnaire has been completed by parents of the 6-7 year olds, and by the 13-14 year olds. The results are presented in Table 1.3 and Table 1.4, which

compare the prevalence of atopic diseases between the four cities. The study found that the prevalence of current wheeze is similar to that reported in recent epidemiological studies in Australia (Peat, 1994). Furthermore, the study demonstrates a significant difference in the prevalence of current wheeze and current rhinitis between eastern and western states. According to Robertson (1998) the possible explanation is the difference in patterns of immigration. More children in the eastern cities are born outside Australia, than in the west.

Table 1.3 Prevalence (%) of atopic diseases among Australian schoolchildren, aged 6-7 years old.

	Melbourne	Sydney	Adelaide	Perth	Total
	N=2843	N=2807	N=3071	N=2193	N=10 914
Current wheeze	27.2	22.3	26.2	22.1	24.6
Wheeze ever	40.7	35.2	41.2	36.9	38.6
Asthma ever	28.6	24.4	27.4	28.4	27.1
Current eczema	11.1	10.1	11.0	11.4	10.9
Eczema ever	22.6	18.8	24.9	25.1	22.8
Current rhinitis	9.8	9.4	14.5	14.9	12.0
Hayfever ever	15.4	12.2	23.4	20.6	17.9

Table 1.4 Prevalence (%) of atopic diseases among Australian schoolchildren, aged 13-14 years old

	Melbourne	Sydney	Adelaide	Perth	Total
	N=2759	N=2841	N=3030	N=3650	N=12280
Current wheeze	27.3	24.5	33.5	31.4	29.4
Wheeze ever	38.5	35.6	46.1	48.5	42.7
Asthma ever	26.6	24.9	30.4	30.2	28.2
Current eczema	10.3	8.6	9.8	10.1	9.7
Eczema ever	16.7	9.9	19.8	17.4	15.8
Current rhinitis	16.6	15.4	22.6	22.6	19.6
Hayfever ever	42.3	24.8	54.4	49.2	43.4

Modified from Robertson, 1998

An interesting finding of this study is that children born in Australia are more likely to report current wheeze than those born elsewhere. Also, the study provides evidence that asthma prevalence in Australian schoolchildren is continuing to increase and is higher among Australian – born children than among those born elsewhere.

The overall international findings of the ISAAC shows that Australia ranks third highest in the prevalence of current wheeze for 13-14 year olds and second highest for 6-7 year olds (Beasley, 1998). A comparison of available data from 11 developed countries shows Australia to have the highest mortality rate due to asthma in 1990 (Robertson, 1995). Morbidity due to asthma also remains significant, with high levels of symptoms, emergency department attendances and hospital admissions. The Department of Human Services in Victoria estimates that asthma is the second most common reason for admission to a pediatric hospital bed in Victoria, with a rate for children of 738 per 100,000 of the total population in 1994-1995 (Information Analysis Unit, 1997).

Apparently the prevalence of childhood asthma in Australia is amongst the highest rates in the world. The reasons for that are not known. According to Peat and colleagues (1994) the research is concentrated mainly on treating asthma, and little attention is given to prevention. There are not enough studies to quantify the strength of association between asthma and its aetiological factors. Woolcock (1996) recommends to find out why asthma prevalence is still increasing and she points out that more attention should be paid to changes in lifestyle leading to a loss of protective factors and a concomitant increase in risk factors such as exposure to allergens and to domestic air pollution. There is a need to continue genetic research in parallel with environmental research to help in the understanding of the aetiological factors for this complex disease.

If the increase in asthma prevalence among children continues into adult life this will create substantial health problems and may have important economic

consequences through time off work, and the cost of treatment, as well as a decrease in the quality of life.

CHAPTER THREE

INDOOR ENVIRONMENT
A LITERATURE REVIEW

3.1 Introduction

Indoor air is defined as the air inside buildings in non-industrial areas, hospitals, and offices (Brown, 1994). In the last 20 years, the indoor environment has changed considerably with the introduction of soft furnishings, carpets, and central heating. The indoor relative humidity has increased, indoor ventilation has decreased, and the concentrations of indoor pollutants and airborne allergens have increased significantly. Monitoring studies have shown indoor air as a mixture of biological, chemical and physical contaminants. Also, it has been found that overall pollutant concentrations can be significantly higher in indoor air compared to outdoor air and exposure to indoor air pollutants has been associated with a wide variety of adverse health effects in humans (Maroni. 1995). The American Thoracic Society (1985) and U.S. Environmental Protection Authority (U.S.EPA, 1994) have published guidelines on toxicological effects and degrees of effect that might form a basis for limiting or lowering levels of air pollutants. According to U.S. Environmental Protection Authority (EPA) policy, air pollution limits must be set on the basis of a clinically significant adverse effect.

The American Thoracic Society (ATS) defines adverse respiratory health effects as medically significant physiologic or pathologic changes. The American Thoracic Society (ATS) states that *"the eyes, nose, and throat irritation associated with urban smog or photochemical oxidant air pollution is not medically important and it is therefore, not considered as an adverse health effect"* in relation to the Clean Air Act.

The impact of indoor air on human health is determined by the following components of the indoor environment (Maroni, 1995): indoor air quality and indoor climate, which might be causally linked

Indoor air quality includes physical, chemical, and biological pollutants, and their relationship to *human health.*

Indoor climate, which deals with temperature, relative humidity, and air velocity. It determines *human comfort.*

3.2 . Indoor air quality

According the American Society of Heating, Refrigeration and Air Conditioning Engineers (ASHRAE) standards (1987), acceptable indoor air quality is defined as *"Air in which there are no known contaminants at harmful concentrations and with which a substantial majority of the people exposed do not express dissatisfaction".*

A growing body of scientific evidence indicates that the air within homes and other buildings can be more seriously polluted than the outdoor air even in the largest and most industrialized cities (Brooks, 1992). Because of the time people spend indoors (approximately 90%) the risks to health may be greater due to exposure to air pollution indoors than outdoors. In addition, people who are exposed to indoor air pollution for a longer time are often those most susceptible to the effects of indoor air pollutants and such groups include the young, the

elderly and chronically ill, especially those suffering from respiratory or cardiovascular disease.

The pollutant levels from individual sources may not cause a significant health risk by themselves but most homes have more than one source that can contribute to indoor air pollution, which include:

- combustion sources such as oil, gas, kerosene, coal, wood, and tobacco products;
- building materials and furnishings, wet or damp carpet, cabinetry or furniture made of certain pressed wood products;
- products for household cleaning and maintenance, personal care or hobbies;
- central heating, cooling systems and humidification devices, and
- sources such as pesticides, radon and outdoor air pollutants, which also contribute to the indoor contamination.

Thus, the combined effects of these sources could significantly increase the concentrations of indoor air pollutants, which may cause adverse health effects in exposed people. Also, it must be taken into account that inadequate ventilation allows various pollutants to reach concentrations that are considered harmful.

The quality of indoor air is influenced both by the quality of outdoor air and emission from indoor sources.

A Indoor sources of chemical pollutants

There are many indoor sources of air pollutants and they can be grouped as follows:

- combustion processes for heating and cooking;
- building materials and furnishings;
- human activities;
- products for household cleaning and maintenance, and

- central heating and cooling systems;

The importance of any source depends on how much of a given pollutant is emitted and how hazardous those emissions are. Factors such as age of the source and whether it is properly maintained are of great importance. For example, improperly adjusted gas stoves can emit significantly more carbon monoxide and nitrogen dioxide than those that are properly adjusted.

Some sources can release pollutants more or less continuously such as building materials, furnishings, and household products. Other sources release pollutants irregularly. These include cigarette smoking inside, use of unvented stoves, space heaters and the use of cleaning products. After some of these activities high pollutant concentrations can remain in the air for a long time.

Contaminants associated with wood-burning stoves and fireplaces include carbon monoxide, nitrogen oxides, sulphur oxides, aldehydes and aromatic hydrocarbons. Emissions from gas-fired stoves or kerosene heaters can contribute to indoor levels of carbon monoxide, nitrogen oxides and formaldehyde.

B Outdoor sources of chemical pollutants

Outdoor air enters and leaves a house by infiltration, natural ventilation, and mechanical ventilation. Infiltration is a process when outdoor air flows into the house through openings, joints and cracks in walls, floors and ceilings. In natural ventilation, air moves through open windows and doors. There are a number of mechanical ventilation devices, from outdoor vented fans to systems that use fans and duct work to continuously remove indoor air and distribute filtered and conditioned outdoor air throughout the building. The rate at which outdoor air replaces indoor air is described as the "air exchange rate". When the infiltration, natural ventilation or mechanical ventilation is not sufficient, the air exchange rate is low and pollutant levels can increase (Maroni, 1995).

Because of the continuous exchange of indoor air with the outside air, all outdoor contaminants are likely to be present indoors. This includes carbon monoxide, oxides of nitrogen, oxides of sulphur, particulate matter, ozone and lead. The outdoor contamination originates from automobiles, factory emissions and other sources.

C *Health effects associated with exposure to indoor air pollutants*

Many studies have reported an association between exposure to indoor pollutants and adverse health impacts on humans. The occurrence of the health effects may be experienced soon after exposure, or possibly, years later (Woods, 1989; EPA, 1989).

The acceptable *short-term exposure* range is *"That concentration range to which it is believed from existing information that a person may be exposed over the specified time period without undue risk to health"* (Maroni, 1995).

Acute health effects may show up after a single exposure or repeated exposures and these include:

- irritation of the eyes, nose and throat;
- headaches;
- dizziness;
- fatigue;
- asthma;
- hypersensitivity pneumonitis, and
- humidifier fever.

Other health effects may show up years after exposure has occurred, or only after long or repeated periods of exposure. The acceptable *long-term exposure* range is *"That concentration range to which it is believed from existing information*

that a person may be exposed over a lifetime without undue risk to health" (Maroni, 1995).

The health effects associated with long-term exposure include:

- respiratory disease;
- heart disease, and
- cancer.

There is uncertainty about what concentrations or periods of exposure are necessary to produce specific health problems. There is a need for further research to increase the understanding about which health effects occur after exposure to average pollutant concentrations found in the house, and which result from exposure to higher concentrations for short periods of time.

3.2.1 Biological pollutants

A Occurrence and sources

Louis Pasteur first recognise biological agents as indoor pollutants in the 19th century by demonstrating that infectious disease can be transmitted through indoor air (Brooks, 1992). The first actual evidence that patients could be specifically sensitised to house dust comes in the 1920s when Kern (1921) reports that responses produced by skin testing with extracts of dust come from homes of sensitised individuals. Experiments to identify the house dust allergen continue until 1964 when Voorhorst and his colleagues in Holland demonstrate the importance of house dust mites (Voorhorst, 1967, 1969).

The US EPA (1993) has specified the major categories of biological agents, which may affect indoor air:

- dust mites and their faeces;
- dander from pets and other furred animals;
- fungi, including molds and yeast;

- bacteria, including actenomycetes;
- mycotoxins;
- cockroaches, and
- pollen.

- *Dust mite allergen*

Dust mites are sightless, eight-legged arachnids that are up to 0.3 mm long. They are related to ticks, spiders and scabies mites. House mites live in the dust that accumulates in bedding, carpets, fabrics, and soft furnishings (Platt-Mills, 1997). Human skin scales are mite's major food source and the bedding is the primary site of dust mite infestation. The highest number of mites may vary from 10 to 1000 mites/g of house dust (Pollart, 1988).

Table 1.5 indicates recently reported values of the house dust mite allergen (Der p I) obtained with immuno-chemical assays (Verhoeff, 1994).

Table 1.5 Der p I concentrations in house dust (µg/gm of fine dust)

Sample type	Geometric mean	Range	N (Number of samples)
Living room, Uncarpeted	0.37	0.10 – 31.08	112
Living room, carpeted	3.98	0.09 – 150.52	400
Bedroom, uncarpeted	0.64	0.09 – 14.10	144
Bedroom, carpeted	3.56	0.10 – 103.56	370
Mattress	5.07	0.10 – 280.88	512

(From Verhoeff, 1994)

As can be seen from the table above, the highest concentration of house dust mites is located in carpeted rooms and mattresses.

House dust mites have been identified in most parts of the world. They require particular conditions of temperature and humidity in order to grow. The optimum conditions are 25^0C and relative humidity of 70-80%.

Three methods are commonly used to estimate exposure to dust mites: mite "counts" assays of mite allergens, and measurements of guanine. Determination of mite counts does permit the identification of live and dead mites, but it requires expertise, and it is time-consuming. Direct measurement of mite allergens in dust samples is possible with an enzyme-linked immunosorbent assay (ELISA). The measurement of guanine, which is an end product of purine digestion/extraction that is excreted in mite faeces, can also be measured to estimate dust mite exposure.

It has become of great importance for future research to establish which environmental factors lead to an increase the amount of house dust mites.

- *Animal allergens*

Studies suggest that cat's skin is the primary and most abundant source of allergens. Unlike mite allergens, the cat allergen (Fel d 1) is carried on small particles and can be detected in the air of undisturbed rooms as well as on wall surfaces (Bollinger, 1996; de Blay, 1991). Cat allergen is "sticky" and adheres to walls, furniture, carpet and clothing (Luczynska, 1990). Soft furnishings, carpets, and mattresses are reservoirs for the cat allergen. Also, Fel d 1 has been detected in carpet dust of houses where cats have never been present, suggesting it can be carried on the clothing of people exposed to cats (Bollinger, 1996). There is also concern that children with cats at home may carry cat allergen to school on their clothes. In a recent study from Sweden, cat allergen is found to be higher in classrooms than in some houses with a cat (Munir, 1993)

Dogs are also a common source of indoor allergen. Dog saliva and dog dander appear to be the main sources of dog allergen, Can f 1. Dog allergen, like the cat allergen, has been detected in public places, including schools (Munir, 1993).

- *Cockroach allergen*

The cockroach allergen is recognised in the 1960s and since then, it has been identified as an underlying cause of asthma morbidity (Rosenstreich, 1997). Socioeconomic status and race are independent risk factors for cockroach allergen exposure (Sarpong, 1996).

Water and food sources may be the key to population growth of cockroaches as the highest concentration of cockroach allergen is found in the kitchen, and dust from bedrooms is usually the best indicator of cockroach allergen exposure (Sarpong, 1996).

Cockroach allergens are similar in size to dust mite allergens and can be detected only when they are disturbed and fall within 10 minutes (Sarpong, 1995).

Two methods are used to estimate exposure to cockroach allergen: visual evidence of infestation and assays of cockroach allergen. Allergens derived mainly from faecal pellets and body parts. The major cockroaches allergens include Bla g 1 and Bla g 2. Direct measurement of Bla g 1 and Bla g 2 allergens in dust samples is possible with an ELISA (Pollart, 1991).

- *Molds*

Molds or fungi are found as well indoors as outdoors and are able to adapt to most climates. Fungi exist in two forms. yeast and mycelia. They often grow on shower curtains in damp basements and on indoor plants. The most common species of indoor molds are *Aspergillus. Penicillium* and *Rhizopus* (Solomon, 1976).

Hypersensitivity to molds is well demonstrated with positive skin test results and elevated serum IgE antibodies.

B Health effects

Some biological contaminants trigger allergic reactions, including:

- hypersensitivity pneumonitis;
- allergic rhinitis; and
- asthma.

Infectious illnesses, such as influenza measles, and chicken pox are transmitted through the air. Other symptoms of health problems caused by biological pollutants include:

- sneezing;
- watery eyes;
- coughing;
- shortness of breath;
- dizziness;
- lethargy;
- fever; and
- digestive problems.

Molds and mildews release disease-causing toxins. Fungi can be the cause of individual cases of rhinits, asthma, and atopic allergic dermatitis. A number of cases of respiratory problems are primarily associated with exposure to higher concentrations of pollen outdoors.

However, allergens produced by house dust mites and dander of furred domestic animals are generally the most important causes of disease episodes in atopic individuals.

3.2.2 Inorganic pollutants- nitrogen dioxide (NO_2)

A Physico-chemical nature

There are a number of different nitrogen oxides (NOx) of which nitrogen dioxide (NO_2) is the most widely considered in indoor air pollution studies. Nitrogen dioxide is a water-soluble red to brown, colorless gas with an acrid odor.

B Sources and occurrence

Nitrogen dioxide is emitted from indoor combustion sources - tobacco smoke, gas appliances, kerosene space heaters, wood burning stoves, and fireplaces. Outdoor air can also contribute to indoor concentrations of NO_2.

Indoor sources such as gas cooking or cigarette smoking may be the main contributors to individual exposure.

C Health effects

In humans, 80-90% of NO_2 can be absorbed upon inhalation. It has been a long-standing concern that nitrogen dioxide produced by unflued gas heating and cooking appliances contributes to respiratory morbidity in both children and adults. Also nitrogen dioxide exposure has been associated with increased airway reactivity, harmed pulmonary function, acute respiratory illness and respiratory symptoms (Samet, 1990). The weight of evidence is that nitrogen dioxide can adversely affect the respiratory health of children (Hasselbad, 1992). The underlying mechanism for these adverse respiratory effects is unclear, although it has been shown that NO_2 can harm the lung's immune defense mechanisms (Frampton 1991). Devalia and colleagues (1994) suggested that indoor exposure to nitrogen dioxide might increase the permeability of the bronchial mucous to allergens. Although more evidence suggests that nitrogen dioxide exposure contributes to respiratory morbidity, the levels of nitrogen

dioxide that are harmful have been widely debated because of the inconsistency of findings from laboratory, clinical and epidemiological studies (Samet, 1990). While some studies have reported an association between exposure to nitrogen dioxide and respiratory symptoms in children (Melia, 1979), others have found no such association (Keller, 1979). Speizer (1980) and Dekker (1991) have reported a significant association between gas cooking appliances and the prevalence of asthma in children, while Ware (1984) and Weiss (1980) have not found such a relationship. Samet and Utell (1990) have explained these inconsistent results due to misclassification of exposure and outcome and also to small study sizes.

Recently, Pilotto (1997) suggests that NO_2 exposure may be considered as a determinant of respiratory illness but still further research is needed.

Even though the results are inconclusive, many monitoring studies have found that nitrogen dioxide concentrations that do not cause any harm could range from 0.005 ppm to about 0.3 ppm (56.4 $\mu g/m^3$). Most studies show that substantial changes in pulmonary function can happen at levels above of 2 ppm (376 $\mu g/m^3$). Asthmatics appear to be responsive at about 0.5 ppm (94 $\mu g/m^3$), and subjective complaints have been reported at that level also (US EPA, 1982b; WHO, 1987).

3.2.3 Organic pollutants – formaldehyde and volatile organic compounds

In contrast to inorganic pollutants, organic compounds in indoor air occur in a much larger number of forms (Maroni, 1995). Hundreds of such chemicals have been identified but the main concern is that many of the compounds are genotoxic. Even more, monitoring studies found that the concentrations of many organic compounds in indoor air exceed that those outdoors.

A World Health Organisation Working Group categorises the range of organic indoor pollutants into four groups (WHO, 1989):

1. Very volatile organic compounds (VVOC) with boiling - point range: <0 to 50^0-100^0C.
2. Volatile organic compounds (VOC) with boiling - point range: 50^0-100^0C to 240^0-260^0C.
3. Semivolatile organic compounds (SVOC) with boiling - point range: 240^0 - 260^0C to 380^0 - 400^0C.
4. Organic compounds associated with particulate matter or particulate organic matter (POM) with boiling-point range > 380^0C.

For analytical reasons, some organic compounds cannot be include in the classification scheme, e.g. formaldehyde.

- **Formaldehyde**

A Physico-chemical nature

Formaldehyde (HCHO) is a colourless, strong-smelling gas and the most common aldehyde found in the indoor and outdoor environment. Although formaldehyde is a volatile compound it is not detected by the gas chromatographical methods applied to VOC analysis. For the detection of formaldehyde, the 2,4- dinitrophenylhydrazine (2,4-DNPH) method is used and analysed by liquid chromatography.

B Occurrence and sources

Formaldehyde is present in substantial concentrations indoors and outdoors, although the sources of formaldehyde affecting human beings are mostly found indoors (Maroni, 1995). The major sources of formaldehyde inside include:

- urea-formaldehyde foam insulation;
- durable-press fabrics, draperies and coated paper products;

- cosmetics, paints, coatings;
- pressed wood products, and
- combustion sources.

The most significant sources of formaldehyde inside are more likely to be pressed wood products made using adhesives that contain urea formaldehyde (UF) resins.

Formaldehyde levels indoors depend mainly on the source of the released formaldehyde, temperature, relative humidity and air exchange.

Increasing the airflow of outdoor air inside decreases the concentration of formaldehyde but when the temperature or relative humidity rises, more formaldehyde is released from the products. Thus, indoor formaldehyde levels change with the season and may change from day-to-day and day-to-night. Levels may be high on a hot and humid day and low on a cool and dry day (U.S. EPA, 1990).

C Health effects

Formaldehyde can affect people differently. Some people are very sensitive to formaldehyde exposure while others may not have any noticeable reaction to the same level.

Formaldehyde may cause watery eyes, burning sensations in the eyes and throat, nausea, and difficulty in breathing in some humans exposed to levels above 0.1 ppm (Maroni, 1995). While some people may develop allergic reactions to formaldehyde through skin contact with solutions of formaldehyde or durable-press clothing containing formaldehyde, others may develop asthmatic reactions and skin rashes. A number of studies point to formaldehyde as a potential risk factor for children to respiratory tract infections and exposure to the indoor environment may cause asthma-like symptoms (Helwig, 1977). Formaldehyde is a reactive indoor air pollutant that may also induce airway irritation at low

concentrations (Norbäck, 1995; Samet, 1990). Higher concentrations may trigger attacks in people with asthma and Norbäck and colleagues (1995) have reported a relationship between attacks of nocturnal breathlessness and indoor concentrations of formaldehyde and VOCs. In addition, the emissions of formaldehyde or other VOCs from wood paint, can be a contributory cause of bronchial hyperresponsiveness (BHR) and symptoms related to asthma (Weislander, 1997)

Table 1.6 summarises the human health effects of formaldehyde exposure. It shows that the adverse health effects start at 0.1 mg/m^3, progressing to eye irritation at 0.5 mg/m^3 and the irritation and discomfort increases between 1 and 20 mg/m^3.

Table 1.6 Effects of formaldehyde on humans after short-term exposure

Effects	Formaldehyde concentration (mg/m^3)	
	Estimated median	reported range
Odour detection threshold	0.1	0.06 - 1.2
Eye irritation	0.5	0.01 - 1.9
Throat irritation threshold	0.6	0.1 - 3.1
Biting sensation in nose, eye	3.1	2.5 - 3.7

Modified from Maroni, 1995

- **Volatile organic compounds (VOCs)**

A Physico-chemical nature

The Volatile Organic Compound (VOC) category has been defined by a boiling-point range with a lower limit of between 50°C and 100°C and an upper limit of between 240°C and 260°C. It exists mainly in the gas phase in a temperature and humidity range encountered indoors.

B Occurrence and sources

Volatile Organic Compounds are ubiquitous in indoor air. Compilations of 307 VOCs have been identified indoors by authors from different countries (Berglund, 1986), and by 1989 over 900 compounds had been identified (U.S. EPA, 1989). The sources of VOCs consist of a broad range of products and appliances. The main are listed below:

- consumer and commercial products;
- paints and associated supplies;
- pesticides;
- adhesives;
- cosmetic/personal care products;
- automotive products;
- hobby supplies;
- furnishings and clothing;
- building materials;
- heating, ventilating, and air-conditioning systems;
- garage attached to the house;
- combustion appliances;
- tobacco smoke;
- pets and indoor plants;
- outdoor air;
- potable water, and
- contaminated groundwater and soil.

C Health effects

Exposure to VOCs results in both acute and chronic effects. VOCs can cause irritation of the eyes and respiratory tract and sensitisation reactions, which involve eyes, skin, and the respiratory tract. Also, they could affect the liver and

kidney, central nervous system, and result in depression of the central nervous system. Two experimental studies show that VOCs may affect the airways, as to induce inflammation (Koren, 1992) and airway obstruction (Harving, 1991) even at low concentrations of 25 mg/m^3. In one population study the presence of newly painted surfaces indoors is associated with an increased prevalence of asthma related symptoms (Norbäck, 1994). More recently, Norbäck and colleagues (1995) report a relationship between nocturnal attacks of breathlessness and indoor concentrations of VOCs.

The health symptoms related to VOCs exposure may include:

- fatigue;
- headache;
- dizziness;
- weakness;
- skin irritation;
- eyes irritation, and
- respiratory tract irritation.

Table 1.7 summarises the health effects associated with exposure to selected volatile organic compounds according to Maroni and colleagues (1995).

Table 1.7. Volatile organic compounds and associated health effects

Compound	Health effects
Benzene	Respiratory tract irritant, carconogen
Ethyl benzene	Severe irritation to eyes and respiratory tract;
1,4-Dichlorobenzene	eye and respiratory tract irritant;
Benzyl chloride	eye and respiratory tract irritant;
Xylenes	Irritant, narcotic
Toluene	Irritant, narcotic
Styrene	Irritant, possible human carcinogen

Modified from Maroni, 1995

Many of the VOCs such as benzene and which have been measured indoors are known human carcinogens and according to U.S. EPA (1989), exposure to VOCs is likely to pose a significant risk of cancer.

3.2.4 Particulate matter (PM)

A Physico-chemical nature

Airborne particulate matter (PM) represents a complex mixture of organic and inorganic substances. The majority of particles are in the submicron fraction, and numerous distinctions exist between fine (under 2.5 micrometer) and course (over 2.5 micrometer) particulates. These distinctions are significant in terms of health effects. Most important is that fine particulates contain a disproportionate amount of toxic substances, such as arsenic and lead. Even when inert, they can serve as carriers of harmful or carcinogenic vapors (Kane, 1985). Organic substances constitute 30-40% of all fine particulates (Perera, 1979).

B Occurrence and sources

Combustion appliances and tobacco smoke are probably the chief indoor source of fine particles although sprays and cooking aerosols may also contribute to the occurrence of particulates.

Biological contaminants such as viruses, bacteria, fungal spores and fragments, house dust mites faeces and animal dander may also be found primarily in the fine-mode fraction.

U.S. Department of Energy (1985) have published the emission rates for particulate matter from indoor combustion sources, which are presented in Table 1.8 (Maroni, 1995)

As can be seen from the table, wood heaters and kerosene space heaters have the highest and the lowest emission rates, respectively.

Table 1.8 Emission rates for particulate matter and particulate-build materials (mg/h),

Source	Appliance type	Emission rate (mg/hr) Particles	Benzopyrene
Kerosene space heaters	a. Radiant	0.13 - 0.16	Not detected
	b. Convective	<0.03 - 0.03	Not detected
Gas space heaters		0.21 - 3.23	Not detected
Wood heaters		2.6	$1.4.\ 10^{-3}$ - $3.5.10^{-3}$
Gas appliances	Range (1burner)	1.9 - 30	Not detected
	Oven	0.118 - 0.126	

Modified from Maroni, 1995

Environmental tobacco smoke can also be a significant source of indoor particles and these particles are especially hazardous due to their chemical composition. They are inhalable and remain airborne for hours after smoking stops.

C Health effects

The most extensive data on the health effects from exposure to particles are derived from epidemiological studies. Evaluating the existing data indicates, that particulate matter can cause adverse health effects, such as:

- eyes, nose, and throat irritation;
- respiratory infections;
- bronchitis, and
- lung cancer.

The National Academy of Science in U.S. (1975), believes there is a possibility that exposure to suspended sulfates is related to an increase in lower respiratory tract infection and decreased lung function in children. Because of the small size of particulates and easy and deeper deposition in the respiratory tract, they pose a

particular threat to small children. A substantial percentage is deposited in the alveoli, the air sacs of the lung. In the pulmonary region, fine particulates can slow down or block the clearing mechanism of the lower lung, thus cause other toxic materials to remain (Kane, 1979).

3.2.5 Environmental tobacco smoke (ETS)

A Physico-chemical nature

Environmental tobacco smoke is probably the most important contaminant of indoor air where smoking exists. The inhalation of ETS is known as "involuntary smoking" or "passive smoking". ETS is a mixture of smoke that comes from burning of a cigarette pipe, or cigar, and smoke exhaled by the smoker.

ETS is a complex mix of several thousand compounds. This mix contains many known or suspected human carcinogens and toxic agents.

B Health effects

There have been a number of studies, which have examined the effect of ETS on respiratory illness and pulmonary function among young children. Several studies have confirmed the exposure and uptake of ETS in young children by assaying saliva, serum, or urine for cotinine. The National Research Council in America (1986) has reported the potential association between parental smoking and respiratory disorders in their children and these effects include:

- symptoms of respiratory irritation-cough, sputum, or wheeze;
- acute diseases of the lower respiratory tract - pneumonia, bronchitis, bronchiolitis, asthma;
- reduced lung function;
- acute upper respiratory tract infections;
- lung cancer;
- major coronary events, and

- sudden infant deaths.

The US Environmental Protection Agency (1992) has reviewed epidemiological studies of the association between parental smoking and childhood respiratory diseases in detail. A review of 26 studies about the prevalence of cough, sputum and wheezing in children show that parental smoking increases the risk, more in infants than school age children. The results of 20 studies of acute illness in infants and in older children have demonstrated a greater risk in children exposed to tobacco smoke at home. Furthermore, ten studies have reported that passive smoking increases the frequency and severity of asthma episodes in children who already have the disease and increases the incidence rate.

There is a strong evidence to support the conclusion that parental smoking increases the risk of respiratory illness in infancy and childhood. The results consistently show a stronger relationship with maternal than paternal smoking in younger than older children, and demonstrate reduced lung function in children of parents who smoke (NHMRC, 1986).

3.3 Indoor air climate

Environmental conditions existing inside a building at any given moment are a product of a number of physical factors including temperature, relative humidity, air movement, ventilation, lighting, noise, vibration and a variety of electrical and magnetic phenomena. Many of these factors have been evaluated for their potential contribution to adverse health effects or comfort complaints but most attention has been paid mainly to temperature, relative humidity and air movement.

Parameters that affect the thermal balance of the body as a whole include air temperature, radiant temperature, air movement and relative humidity, which jointly comprise the thermal environment or indoor air climate (Tromp, 1974). Relative humidity affects thermal comfort by its effect on evaporative heat losses

from the body and air velocity affects heat loss by convection. Under warm conditions velocity induced convective heat losses are desirable to maintain thermal comfort. Radiant temperature is a common cause of thermal comfort complaints also, and these may occur despite the fact that air temperature is in the comfort range. When a wall is warm, it radiates heat toward an individual who absorbs it. When a wall is cold, heat will be lost from the portion of the body facing it, and the person may experience a chilling effect (Tromp, 1974).

The majority of people, especially the elderly, sick people and young children, spend a greater part of their time indoors and consequently in an artificial climate. Whatever artificial climate is created for human occupation, the thermal environment has to be adapted, so that each individual is in a thermal comfort. Fanger (1984) defined the thermal comfort as *"That condition which expresses satisfaction with the thermal environment"* .

The thermal comfort requirements for winter and summertime conditions recommended by Fanger are summarised in the Table 1.9

Table 1.9 Thermal comfort requirements during summertime and wintertime conditions

Summertime	Wintertime
Air temperature - 23°C - 26°C.	Air temperature - 20°C - 24°C
Vertical air temperature difference between 1.1 and 0.1 m above floor less than 3°C.	Surface temperature of floor between 19°C and 26°C.
	Vertical air temperature Difference between 1.1 and 0.1 m (head and ankle level), less than 3°C.
Mean air velocity less than 0.25m/s. m/s.	Mean air velocity less than 0.15

From Fanger, 1984. Proceedings, Third International Conference on Indoor Air Quality and Climate, vol. 1, Stockholm.

Studies have found that thermal environmental factors have the potential to affect humans either directly or indirectly. Serious attention has been given to both temperature and relative humidity. A significant linear relationship has been reported between the temperature range of 21^0C -25^0C and allergic or asthmatic symptoms (Reinkainen, 1993). In a study, Green (1984) shows a significant association between indoor humidity levels and increased prevalence of acute respiratory infections.

There is evidence to suggest that airway cooling through inhalation of cold and dry air, and large changes in air temperature over short periods of time can induce bronchoconstriction. The combination of high humidity and low temperature might contribute to susceptibility of respiratory illness in children (Tromp, 1974).

Particular conditions of temperature and relative humidity could be a good source for increasing house dust mites population and indoor mold. Furthermore, a study has shown that temperature above the thermal comfort range (23^0C-26^0C) may increase the level of volatile organic compounds (American Society of Heating, 1981). According to Godish (1986) humidity levels can significantly affect the concentrations of formaldehyde, as a one percent rise in relative humidity will result in a one percent increase in formaldehyde levels.

Relatively few studies have attempted to address the relationship between air movement and adverse health effects and the uncertainties are too great to make any inferences (Godish, 1994).

Because of the lack of enough evidence there is a need for further research, which could give insight into the understanding of the potential contribution of the parameters of the thermal environment to childhood respiratory diseases.

CHAPTER FOUR

RISK FACTORS FOR ASTHMA
A LITERATURE REVIEW

Risk factors are determinants of the risk of developing disease (Tinkelman, 1993). Risk factors may increase the probability of disease, and are applied by epidemiologists to personal characteristics, and to environmental characteristics.

Asthma is a chronic inflammatory disorder of the airways. This chronic inflammation is considered responsible for increased airway hyper responsiveness to a variety of stimuli and airflow limitation characteristic of asthma.

This chapter reviews the risk factors involved in the development or onset of asthma and then the risk factors (triggers) involved in the development of exacerbations.

4.1 Risk factors involved in the development of asthma

4.1.1 Predisposing factors

Predisposing factors are the factors that give an individual susceptibility to asthma. These include atopy, gender and genetic factors.

A Atopy

Atopy is defined as the "*susceptibility for developing immunoglobulin IgE directed to epitopes expressed on common environmental allergens such as domestic mites, animal proteins, pollens, and fungi*" (Cookson, 1993). As a consequence, the mast cell is sensitised, and when activated leads to the inflammatory response.

In the context of an epidemiological investigation, atopic status may be assessed by (Zimmerman, 1988):

- measuring skin test reactivity to common antigens;
- measuring serum levels of IgE;
- questionnaire evaluation of diseases, associated with atopy (eczema, allergic rhinitis), and
- assessment of parental history of atopy as marker of genetic predisposition.

Several investigators have examined whether evidence of eczema, allergic rhinitis, and skin test reactivity to antigens is associated with asthma in children. Buffum (1966) find that 11.4% of the study children with eczema have severe asthma compared with 2.4% of those without. Similarly, 15.4% of those with positive skin test reaction to whole-egg extract have had severe disease after 10 years of follow up compared with only 3.5% of nonreactors. Blair (1977) has reported that persistence of infantile eczema is associated with chronic or recurrent asthma in 88% of subjects. He has not found an association between skin test reactivity and prognosis of asthma. Later, Sears (1991) reports that the prevalence of asthma is more strongly associated with levels of IgE than a skin reactivity test. Another study demonstrates that the prevalence of asthma increases with increasing levels of IgE (Burrows, 1989).

A large percentage of asthmatic patients are atopic to allergens such as house dust mite, mold and pollen. In this case, asthma results from an immunological

response to the inhalation of airborne allergens, which are primarily of biological origin. Studies report that the dominant allergens associated with asthma are found indoors, i.e., dust mites, mold, cats, dogs and cockroaches (Platts-Mills, 1993).

Although, asthma in childhood (less then six years old) is frequently associated with atopy, in cases atopy occurs in the absence of asthma. However, when it becomes expressed in the lower airways, atopy is one of the strongest predisposing factors for the development of asthma.

B Gender

Gender is also considered as an important predisposing factor for asthma, although investigators to date have not provided consistent results concerning child's gender as a predictor of asthma. In 1952, Rackemann and Edwards have followed 688 asthmatic children over 20 years and found that boys and girls do not differ in the severity of asthma. Blair's (1977) findings in a study of 244 children evaluated over 20 years were similar. In contrast to these reports in 1964, Williams and McNicol have studied sample of 30,000 Australian schoolchildren and report that at age of 14 years, a higher proportion of boys had severe asthma. Likewise, Weiss (1980) has demonstrated that M:F ratio for asthma was 1.8:1 and for "recurrent wheeze most days or nights" was 1:1. In 1984, Verity suggests that male predominance of asthma relates to a greater degree of bronchial liability and not to a greater prevalence of atopy. Similar results in a study of Peat (1992), no difference in asthma prevalence among boys and girls, after correcting for atopy, has been found. In 1993, Sears has suggested that gender differences in diagnosed asthma in children can be explained by gender differences in allergen sensitivities.

C Genetic factors

Asthma is a complex genetic disorder with a high population prevalence compared with other genetic pulmonary disorders. In an intensive search for the "asthma gene" researchers have used atopy and airway responsiveness as markers of the phenotype of asthma rather than using asthma symptoms.

It is clear that asthma has a genetic component, i.e., there is a greater risk of an individual to develop asthma, if asthma, allergic rhinits, or eczema already exists in a family member. The prevalence of asthma, hay fever, and eczema is significantly higher among relatives of patients with atopic asthma than among relatives of non-atopic asthmatics (Sibbald, 1980). Higgins and Keller (1975) have found that the prevalence of asthma increases among children younger than 16 years when one or both parents had asthma. The prevalence increase in boys from 7.4% when neither parent had asthma, to 18.3% when one or both parents had asthma. Among girls the prevalence increase from 4.1% to 11.7%. In 1976, Leeder and colleagues have investigated the influence of family factors on asthma and wheezing during the first five years of life and find that asthma incidence increases from 2.5% if neither parent had asthma to 5.4% if one parent had asthma. In addition, Foucard and Sjoberg (1984) report that infants and children with wheezy, bronchitis and a family history of asthma or allergy have twice the risk of developing persistent asthma compared to those without such a family history. Studies in twins have shown a genetic effect on serum IgE levels in adults and children (Bazaral, 1974).

Genetic factors are clearly important in determing the risk of the development of asthma, but the increase in prevalence over the past decade is much too great to be attributed only to genetic variations. Studies in migrating populations who have developed more airway responsiveness and more atopy when changing environments, for example, differences in asthma between urban and rural populations, indicate the important role of environmental factors (Crane, 1989). Peat and colleagues (1992) have suggested that the increase responsiveness in

atopic children may be due to a change in the degree of exposure to allergens in a child's environment. Further evidence of important environmental influences comes from a study, which investigates the relation between asthma and atopy in genetically similar children living in East and West Germany (von Mutius, 1994). The results show that sensitisation to common aeroallergens is more frequent in West Germany which can be explained by the difference in the lifestyle between western and eastern countries in Europe. Consequently, environmental factors are likely to be one of the primary determinants of expression of that disorder.

4.1.2 Causal factors

Causal risk factors are these factors that cause the onset of asthma. Allergens sensitise atopic subjects by stimulating the production of specific IgE antibodies. Once a subject is sensitised, she or he is predisposed to develop allergic inflammation and asthma exacerbations upon re-exposure (Pope, 1993). Population studies have demonstrated a correlation between prevalence of asthma and long-term allergen exposure (Platts-Mills, 1991), and the improvement of asthma after cessation of exposure (Platts-Mills, 1982) There is also a suggestion that allergen exposure may cause the onset of asthma by continuously stimulating chronic allergic inflammation of the airways. In contrast to these findings, Pearce (2000) states that no longitudinal studies have been identified in which allergen expoosure during infancy in a random population sample has been related to asthma risk after the age of six years. Evenmore, many of the identified prevalence studies in children showed negative assossiations between allergen exposure and current asthma so currently available evidencce does not indicate that allergen exposure is a major risk factor for the primary causation of asthma in children.

The most common allergens, indoors and outdoors, suspected to cause the onset of asthma, are explained below.

A Indoor allergens

Indoor allergens include house-dust mites, animal allergens (cat and dog), cockroach allergen, and fungi.

- *House-dust mites*

House dust mite allergy has been first documented in 1920s when Cooke and Kern find that dust from vacuum cleaner bags caused positive skin reactions in asthmatics (Kern, 1921; Cooke, 1922). Later, it has been found that mites are implicated in the development of dust allergy (Voorhorst, 1964) and furthermore that house dust mites are a major source of allergens for asthma and allergic rhinitis (Voorhorst, 1967). The two most important species are *Dematophagoides pteronyssinus* (*Der* p I) and *Dermatophagoides farinae* (*Der* f I).

The relationship between symptoms and dust-mite allergen exposure has been well studied but the results have been controversial In 1991, Velvloef observed a dose-response relationship between the mite allergen concentration in dust and the severity of asthma symptoms among individuals with mite allergy. Sporik (1990) finds that exposure to domestic mites in the first years of life correlates with the subsequent development of asthma. Furthermore, studies suggest that continuing exposure to allergens plays an important role in most cases of chronic asthma, as reductions in allergen exposure could reduce symptoms, bronchial reactivity, and signs of inflammation (Boner 1985; Charpin, 1991).

In contrast to these findings, several research groups have failed to find a clear dose-response relationship between symptoms of asthma and exposure to indoor allergens. Recently, Ingram and colleagues (1995) reported that among schoolchildren who are allergic to cats or dogs, no clear relationship has been found between sensitisation or symptoms and the current level of allergens in an individual house (Ingram, 1995). Furthermore, Marks and colleagues (1995) have

demonstrated that the concentration of mite allergens is no higher in the houses of asthmatic patients with mite allergy than in other houses in the study town Sydney, Australia. The concentrations of mite and cockroach allergens, found in the dust from apartments of asthmatic and nonasthmatic children in Atlanta, USA, have also been very similar (Call, 1992) There is still little evidence on the effects of allergen exposure at different ages on the development of asthma. Exposure of infants, younger than 6 months, to dust mites is usually low, because their mattresses are commonly covered with impervious material and because their bedding is washed frequently.

Although there are still many uncertainties about the causal relationship between allergen exposure and asthma, some studies have provided consistent results that have led to the proposal that exposure to more than 2 μg/gm of fine dust of *Dermatophagoides pteronyssinus* allergen, *Der* p 1, is a significant risk factor for the development of sensitisation in at-risk individuals, and exposure to more than 10 μg/gm of fine dust has been associated with acute asthma symptoms and hospital admission (Platts-Mills, 1992).

Though asthma and exposure to dust mites have been studied widely there are still many areas that need to be clarified. There are still insufficient data about the relationship of exposure to mites and severe or fatal asthma. Also, there is still not enough evidence to state the concentration of allergen exposure at which the risk of asthma in sensitised individuals increases.

- *Animal allergens*

Cats

Cats and dogs are likely to be the most common animal species with which humans have close domestic contacts. The allergens produced by pets are mostly associated with dander, hair, saliva and urine (Lowenstein 1986). The most important source of cat allergens is dander. The major allergen of the cat, Fel d I,

is found in cat pelt. The allergen becomes airborne as particles 1-10 μm in diameter, presumably after it dries and flakes off the fur (Reed, 1986). A study suggests (Lopes da Mata, 1990) that cats are the most important pets causing allergy in the home. The threshold risk levels of Fel d 1 exposure for sensitisation and asthma have not been as well defined as they have for the mite allergen. The current tentative proposal as the threshold level for both sensitisation and asthma is > 8 μg Fel d 1/g of fine dust (Platts-Mills, 1997).

Dogs

Allergic sensitivity to dogs is not as common as to cats. Nevertheless, up to 30% of allergic individuals have positive skin tests to dog extracts. A dog allergen has been purified from dog hair and dander. This antigen, Ca d I, is present in large concentrations in saliva and can be measured in house dust (Ford, 1989).

- *Cockroach*

In some locations and among some ethnic groups, sensitisation to cockroach allergen may be even more common than to the domestic dust mite. Most species of cockroaches live in tropical climates. The main cockroach species are German, American, and Oriental. The cockroach allergy was first recognized in the 1960s and identified as an underlying cause of asthma morbidity in many inner city children (Pollart, 1989).

- *Fungi*

Fungi grow in dark, humid, poorly ventilated places, both indoors and outdoors. They also grow well within the systems used for cooling, heating, and humidification.

A large number of species can be found in indoor air but those of prime interest in indoor environments are molds and yeasts. Among these is Alternaria, which is an established risk factor of asthma in different populations and has been

associated with the risk of asthma death in the United States (Holaren, 1991). The prevalence of fungi shows wide seasonal differences (Gravesen, 1972) with highest numbers in outdoor air found during summer and autumn. During these seasons the outdoor air is the main source of fungi indoors.

The most common indoor fungi are *Penicillium*, *Aspergillus*, *Alternaria*, *Cladosporium*, and *Candida* (Salvaggio, 1981).

4.1.3 Contributing factors

The contributing factors either enhance the likelihood of asthma developing or may increase susceptibility to asthma. These include tobacco smoke, air pollution, viral infections, small size at birth, and diet (Tinkelman, 1993).

Studies are necessary to clarify the potential role of the contributing factors.

A Environmental tobacco smoke

Tobacco smoke produces a large and complex mixture of gases, vapors, and particulate matter. More than 4500 compounds and contaminants have been identified in tobacco smoke, including respirable particles, carbon monoxide, carbon dioxide, nitrogen dioxide, and nicotine. Exposure to tobacco smoke has been associated with increased lower respiratory symptoms in children (cough and wheeze) and an increased risk for the development and exacerbation of asthma (Chilmonczyk, 1993; Weitzman, 1990). Several studies have reported that the risk of asthma appears to increase in children exposed to passive smoking by parents who smoke, especially in those with mothers who smoke (Sherill, 1992; Magnusson, 1986). In contrast, some other studies failed to confirm these findings (Peat, 1992b).

B Air pollution

Both indoor and outdoor irritants contribute to air pollution.

- *Outdoor pollutants*

Environmental pollutants such as sulfur dioxide, ozone, and nitrogen oxide can, at concentrations found in heavily polluted cities, trigger bronchoconstruction, may increase airway responsiveness, and enhance allergic responses. Although asthma seems to be more frequent in industrialised countries, there is little evidence that air pollution is directly responsible for the increased prevalence of asthma in these countries (Pierson, 1992). The association between air pollution and the development of asthma has been studied by comparing the prevalence of asthma in school children living in two German cities: Leipzig with heavy industrial pollution and Munich with its heavy automobile traffic. The results show that asthma is more prevalent in Munich, while bronchitis is more prevalent in Leipzig (von Mutius, 1994).

According to Woolcock (1996) "it is time to stop blaming air pollution and examine other possibilities"

- *Indoor pollutants*

The relationship between human health and indoor air pollutants is an area of growing interest. Some data suggest that indoor air pollutants may contribute to the development of asthma, but due to lack of enough evidence is difficult to make any clear inferences.

- *Viral respiratory infections*

There is no evidence that viral respiratory infections directly cause the development of asthma, although it is well established that the viral respiratory

infections can exacerbate asthma, acting as a trigger (Busse, 1993). Also, a study (Pullan, 1982) has suggested that there is an association between viral infections, particularly bronchiolitis, in early life and the later development of asthma. According to Busse (1993), the viral respiratory infections should be considered as one of the risk factors that may contribute to the development of asthma.

Woolcock (1996) has stated that with the hygienic western lifestyle, infants have few bacterial infections, multiple immunisations, frequent courses of antibiotics, which lead to a loss of protective factors and the potential for the development of asthma.

C Diet

The influence of diet on asthma is not well examined. Controversial results have been reported about the protective effect of breast-feeding for the development of asthma (Chandra, 1985; Arshad, 1992a). A study has suggested that the elimination of eggs from the diet of mother and child in the first year of life appears to reduce the incidence of atopic diseases (Arshad, 1992b).

Although the relationship between diet and the development of asthma is still unclear there is some evidence of the association between food allergy in infancy and asthma.

Woolcock (1996) points out that possible change to the diet, including shorter periods of breastfeeding, lower antioxidant intake, and higher salt intake could prevent late development of asthma.

4.2 Risk factors that cause asthma exacerbations – asthma triggers

Triggers cannot cause asthma development but can exacerbate asthma once it is present. Triggers vary from person to person and from time to time. They

include exposure to cold air, irritant gases, weather changes, emotional expression, and exercise.

4.2.1 Air pollutants and allergens

Once the subject is sensitised, exposure to indoor and outdoor air pollutants and allergens can cause asthma exacerbations. Some recent studies have shown that even small amounts of airborne allergens are able to cause asthma exacerbations. Sulfur dioxide is an irritant that can trigger asthmatic patients at concentrations as low as 1 ppm, although it has no effect on the airways of normal subjects at higher concentrations (Hackney, 1993).

Other irritants such as volatile organic compounds, formaldehyde and wood smoke may also exacerbate asthma but because of lack of evidence no clear conclusions can be made.

4.2.2 Respiratory infections

While there is a need for more evidence to prove the role of viral infections for the development of asthma, it is well established that viral respiratory infections can exacerbate asthma in children under age of 10 (Busse, 1993). Respiratory virus, rhinovirus, and influenza virus have been noticed in the majority of the exacerbations of childhood asthma.

4.2.3 Weather change

Published reports have related asthma exacerbations to various environmental factors such as low atmospheric temperature, high humidity, thunderstorms, and episodes of acute pollution (Khot, 1988; Ayres, 1994). A recent study reports a significant association between asthma and lightning strikes, increase in humidity or sulphur dioxide concentration, a drop in temperature or high rainfall the

previous day. Also a decrease in maximum air pressure or changes in grass pollen counts have been related to asthma (Celenza, 1996).

4.2.4 Exercise

Exercise is probably one of the most common triggers of asthma as it incites airflow limitations in most children. The mechanisms of exercise-induced asthma are mainly related to changes in the airway mucous induced by the associated hyperventilation, either cooling or rewarming (Blackie, 1990).

4.2.5 Emotion

Emotional stress itself (anxiety, frustration, anger) can trigger asthma, because extreme expressions of laughing, crying, anger, or fear can lead to hyperventilation that can cause airway narrowing (Lehrer, 1993). These normal emotional responses involve deep rapid breathing, which in turn can trigger asthma.

CHAPTER FIVE

RESEARCH METHODOLOGY

5.1 Study design

A population based case - control study was chosen as appropriate to achieve the aims of the study and there were a number of reasons for choosing this study design. First, case-control studies are relatively quick and inexpensive compared with other analytical designs. Secondly, considering the multifactorial nature of asthma, this study design allowed multiple aetiological factors to be examined. Third, in order to explore the variables age and gender as risk factors for asthma and incorporate them in a multivariate analysis, a population case-control study was appropriate to conduct, which would not be possible to accomplish in a matched case-control study. Thus, the case and control subjects were not mached by age or any other variables but the age group was restricted for cases and controls by defining an eligible age range within which childhood asthma genesis was believed to occur.

5.2 Study samples

The study was carried out in the Perth Metropolitan area from December 1997 through to March 1999. The participants (N = 192) were children, aged between 6 months and 3 years old. This young age group of children was chosen in order to identify risk factors for asthma that might be important early in life or early in the natural history of the disease. The age group was restricted for cases and controls by defining an eligible age range and hence they were not matched by age. The cases were (n=88) children who attended the Accident and Emergency Department at Princess Margaret Hospital and were discharged with asthma as the primary diagnosis. The size of the case group was determined by the availability of case subjects from the above source over a period of 8 months. Controls (n = 104) were children in the same age group as cases who had never been diagnosed with asthma, and identified from birth records accessed through the Midwife's Notification System at the Health Department of Western Australia.

Information on health and house characteristics was collected by using a questionnaire, completed by each child's parents or guardians. In order to assess atopy, skin prick tests for common allergens were performed on each child. Assessment of exposure to indoor environmental factors was conducted twice, winter and summer to detect seasonal variation in indoor pollutants. Each household was monitored for the following pollutants and physical factors: nitrogen dioxide (NO_2), formaldehyde (HCHO), volatile organic compounds (VOCs), allergen levels of house dust mite, particulate matter with size less than 10 microns (PM_{10}), temperature (T^0C) and relative humidity (RH %).

5.3 Study population

5.3.1 Definition and selection of cases

Cases were defined as children, who attended the Accident and Emergency Department at Princess Margaret Hospital for children and were discharged with asthma as the primary diagnosis. The choice of the age range between 6 to 36 months was made in order to measure potential risk factors in early periods in life, from birth to the time of diagnosis. Due to time constraints, asthmatic children were recruited only for a limited period of time, between January and August 1998.

Cases were identified from a computerised roster which was kept at the hospital that included, date of birth, age of the child, home address, the discharge diagnosis, and child's medical record number. From this roster, children, between 6 months and 3 years old, who were discharged with asthma diagnosis, and reside in the Perth Metropolitan area, were contacted. Parents or guardians were contacted by a letter, explaining the nature of the study. Parents who agreed to participate in the study were asked to sign a consent form, complete a questionnaire and return them to the researcher in a reply-prepaid envelope.

5.3.2 Definition and selection of controls

As cases were selected to represent childhood asthma in a defined population - the Perth metropolitan area, community-based controls were selected from the same area to ensure that the results of the study could be generalised to the population (Miettinen, 1985; Schlesselman, 1982).

Controls were children of the same age group as the cases, aged between 6 months and 3 yers old, who had had no diagnosis of asthma made by a physician. Parents who had children aged between 6 months and 3 years old were randomly approached by mail through the Midwife's Notification System in the Health

Informational Centre at the Health Department of Western Australia and invited to participate in the study. Parents were asked to notify their willingness by completing a consent form and a questionnaire and to return them in a reply-prepaid envelope to the researcher. The control group was recruited in the period between December 1997 and July 1998.

5.4 Sample size

Selecting enough participants for studies that investigate disease-exposure relationships is a fundamental consideration in planning of studies.

When the frequency of exposure between cases and controls is compared by means of a statistical test, the probability of making a Type I error is called the *level of significance*, and it is denoted by alpha-error (α). The probability of making a Type II error is represented by "β" and the quantity $(1-\beta)$ is called the *power* of the study. This is the ability of the study to demonstrate an association, given that an association exists. The power of a study is strongly influenced by the sample size.

To select adequate subjects for a case-control study, the calculation of sample size considers the following factors:

a) the relative frequency of exposure among controls in the target population, denoted by p_o;
b) a hypothesized relative risk associated with exposure that would have public health importance, denoted by R;
c) desired level of significance, α; and
d) desired study power, $1-\beta$.

In the present unmatched case-control study, it was assumed that there is no need to have equal numbers of cases and controls. The desired values for α and β were specified as $\alpha = 0.05$ and $\beta = 0.10$.

The required sample size for each group ("n" per group) was calculated, using the following formula:

$$n = [z_\alpha \sqrt{2\bar{p}\bar{q}} + z_\beta \sqrt{(p_i q_i + p_o q_o)}]^2 / (p_i - p_o)^2, \qquad (1)$$

where

$$p_i = p_o R / [1 + p_o (R - 1)]$$

and

$$\bar{p} = \tfrac{1}{2}(p_i + p_o)$$
$$\bar{q} = 1 - \bar{p}$$
$$q_i = 1 - p_i$$
$$q_o = 1 - p_o$$

For practical purposes the formula (1) is given in the following way:

$$n = 2\bar{p}\bar{q}(z_\alpha + z_\beta)^2 / (p_i - p_o)^2 \qquad (2)$$

Corresponding to $\alpha = 0.05$ (two-sided) and $\beta = 0.10$, one has $z_\alpha = 1.96$ and $z_\beta = 1.28$, equation (2) reduces to the following simple formula:

$$n = 21\bar{p}\bar{q} / (p_i - p_o)^2$$

In the present study it was supposed that the expected rate of exposure among controls is $p_o = 0.40$. Furthermore, with the significance level of $\alpha = 0.05$ (two sided), power of 90% ($\beta = 0.10$), and hypothesized relative risk $R = 2.5$, the calculations of the sample size proceed as follows:

$$n = 21*0.51*0.49/(0.625-0.4)^2 = 104$$

Thus, the desired sample size was 208.

An essential part of the study was finding participants willing to have a detailed air sampling of their home, which can be considered as an intrusion into their private life. Also, all participants were required to complete aspects of the study such as skin prick tests. Thus, the recruitment of the study participants was a

greater challenge than expected. Although an encouraging letter was sent to all parents, which had a good response, a good deal of time was spent contacting people to remined them of the study and explaining certain aspects that were of concern. The limited number of asthmatic children in the required age group presenting at the hospital was also a contributing factor to the difficulties experienced.

Assumptions for sample size calculations were based on odds ratio of 2.0, which applies to dichotomous risk factors. However, due to time and other resource constraints the odds ratio of 2.5 was chosen. This corresponds to a smaller sample size of 208 study subjects and consequently resulted in a study with lower statistical power, which is acknowledged as a limitation of the study. Consequently this will result in increased the probability of a Type II error for non-significant risk factors.

Because of the limitations explained above, 194 children were selected and that sample size allowed the study to have sufficient power to detect odds ratio of 2.5 with high precision. Out of 194, 106 were controls and 88 were cases.

5.5 Data collection

5.5.1 Procedure for admission to study

As highlighted earlier, once an asthmatic child was identified through the Accident and Emergency Department at Princess Margaret Hospital, the researcher sent a letter to the parent or guardian of the child informing him or her of the nature of the study and inviting participation in it. After receiving the completed consent form and the questionnaire, a telephone call was made by the researcher to answer any questions of concern and to arrange a time for indoor monitoring in the house.

As previously alluded to, controls were randomly drawn from the community within the Perth Metropolitan area. In order to maximise their participation, a personal letter of encouragement from the Health Department of Western Australia was sent to children's parent or guardian. After receiving the completed consent form and questionnaire, a telephone call was made by the researcher to answer any questions and make an appointment for house monitoring.

5.5.2 Sources of data

There were three sources of collecting the data for this study:

- The first included a comprehensive health and dwelling questionnaire;
- The second entailed winter and summer indoor monitoring of the household of each participant, and
- Finally, atopy assessment was performed on each child by conducting skin prick tests to common air-borne allergens.

i) Questionnaire survey data

The questionnaire used in the present study was based upon the American Thoracic Society (ATS) (Ferris, 1978) questionnaire for respiratory symptoms. The questionnaire (See Appendix C) was administered to the parent or guardian of all participants in the study before the winter monitoring commenced. It comprised two parts: the first part asked mainly about the child's health and the second part was a dwelling questionnaire, related to the child's home environment.

The aim of the questionnaire survey was to measure the severity of asthma and to assess the potential effects of the house characteristics on respiratory symptoms in children.

In the first part of the questionnaire, standard questions about information on personal and social factors such as age and gender of the child, mother's and father's educational level (elementary school, high school, collage, and university) were included. Also, the questionnaire asked if the child had ever had asthma diagnosed by a physician had ever had wheeze or an attack of wheezing that had caused him/her shortness of breath. Some further questions, related to personal susceptibility factors such as child's hay fever, trouble breathing, allergy reactions, or runny nose, were also asked. Questions assessing family history of asthma, such as parental or sibling's asthma, eczema, and hay fever were also included.

The second part of the questionnaire survey was mainly related to the child's home environment. This included maternal and paternal smoking, exposure to gas appliances, kerosene space heaters, fireplaces or wood fires. Environmental factors of a physical nature such as presence of air conditioning, humidifier in the child's room and ventilation in the house were covered. Questions on the presence of family pets, type of floor coverings, age of the house, garage attached to the house, and occupant density per room were also asked.

During the second visit in summer, all parents were asked to complete a short questionnaire in order to test for any changes in child's health conditions and his/her home environment (See Appendix D). Parents were asked to report whether their child had a cough, wheeze, hay fever, eczema, allergies, runny nose, and watery eyes in the month before the summer monitoring commence. Questions related to any changes inside the house such as current smoking, new carpeting, new furniture, newly painted walls, and use of gas or electricity for cooking were included.

ii) Atopy Assessment

In order to determine the atopic status of the study children, skin prick tests were performed on all study children using a lancet technique. Subjects were tested to

extracts of: cows milk, egg white, rye grass, grass mix, house dust mites *Dermatophagoides farinae (Der p I)* and *Dermatophagoides pteronyssinus (Der f I)*, cat hair, dog hair, fungi (*Alternaria* and *Aspergillus)*.

A saline solution was used as a negative control, and histamine was used as a positive control. The tests were performed between July and September 1998, during the winter monitoring. Largest wheal diameters were measured 20 minutes after pricking. The ratio of allergen wheal size divided by the histamine wheal size was calculated, and tests were considered positive if the ratio was equal to or exceeded 0.5 (Meinert, 1994). Children with at least one positive skin test were defined as atopic.

iii) Indoor Air Monitoring - methods and instruments

In the present study indoor monitoring of formaldehyde (HCHO), VOCs (volatile organic compounds), particulate matter with size less than 10 microns (PM_{10}) and nitrogen dioxide (NO_2) was performed in each household. Samples of house dust were also collected for dust mite assessment.

Indoor concentrations of the air pollutants were measured in the living room, winter and summer. Additional measurements of formaldehyde and nitrogen dioxide were performed in the child's bedroom. Samples of dust mites were collected winter and summer from the child's bedroom floor and child's bedding. Indoor temperature (T^0C) and relative humidity (H%) were also measured.

The methods and instruments used in the monitoring of the indoor environmental factors are described below.

A. *Nitrogen Dioxide (NO_2)*

Nitrogen dioxide sampling was performed using a passive sampler with triethanolamine used as an absorbing reagent. The method used follows that described by Palmes and colleagues (Palmes, 1976).

The passive sampler consists of a tube of seven cm length and ten mm internal diameter, containing triethanolamine, which was used as an absorbing reagent. The sampling procedure was based on the measurement of the quantity of the gas transferred through a tube to the absorbent by molecular diffusion during a given exposure period. The sampling period was eight hours for the child's bedroom and the living area. After exposure, the nitrite formed was eluted with water and determined spectrophotometrically. The concentration of nitrogen dioxide was evaluated from a prepared calibration curve.

A 1 Procedure for use of sampler

Commercial acrylic tubing was used in the study. The tubes were washed with detergent, rinsed with distilled water and air-dried. Stainless steel grids were cut, as each screen was with 0.3 mm diameter. The screens were cleaned and coated with triethanolamine (TEA). Three screens were stacked at the bottom of the tube and a "fixed cup" was used to hold the triethanolamine coated screens in position. For protection during storage, the other end of the tube was closed with the same type of cap, the so-called "removable cap". Finally, the fixed cap was secured with a plastic tape and the tube was ready for sampling.

During the sampling the protective cap was removed and the tube was exposed to the atmosphere. The sampling period for nitrogen dioxide in the study was eight. After the exposure the protective cap was replaced and the samples were kept at room temperature until analysis.

A 2 Analysis

The analyses were performed using a spectrophotometer at 540 nm. After removing the protective cap, 2.1 ml of a combined reagent was added directly into the sampler, mixed well and read after ten to thirty minutes from the spectrophotometer.

After the analysis the stainless steel screens were cleaned by dipping them in chromic acid, then rinsed thoroughly with distilled water, dried in an oven at 125^{0}C, cooled and dipped into solution of triethanolamine (TEA) in acetone. The screens were left on paper for 10-15 minutes to allow the acetone to evaporate. After finishing this procedure the sample was ready for a new sampling.

B. Formaldehyde

Measurements of the indoor concentrations of formaldehyde were conducted using the passive sampling method described by Levin (1985). This method utilizes passive diffusers containing acidified 2,4-dinitrophenylhydrazine (DNPH), which reacts with atmospheric formaldehyde to form stable and non-volatile hydrazine. The hydrazine was desorbed into a suitable solvent and its concentration determined by high-performance liquid chromatography (HPLC). The air sampling rate was 77 ml/min for 8 hours.

B 1 Filters used in the passive sampling

In the present study 37-mm diameter dinitrophenyl-coated filters were used. The filters were mounted with a support pad in a standard 37 mm three section filter cassette.

B 2 Diffusive sampler preparation

To prepare the 2,4-dinitrophenylhydrazine (DNPH) solution, double recrystallized 2,4-dinitrophenylhydrazine was dissolved in a solution of 85% orthophosphoric acid (1.7 ml) and 20:80 glycerol/ethanol in 90 ml of HPLC grade acetonitrile. To prepare the filters for sampling, 0.5 ml of 2,4-dinitrophenylhydrazine solution was dispensed onto the glass fiber filter positioned on a sheet of glass and dried in an oven (40^0-50^0C). Then the filter containing 2,4-dinitrophenylhydrazine was mounted between the middle and the third sections of the cassette so the cassette remained sealed until use in the sampling procedure. The first section of the cassette was removed during the sampling.

The sampling rate for the sampler was calculated from Flick's law:

$$\textbf{Sampling rate (ml/min) = D (A/L) * 60,}$$

where **D** is the diffusion coefficient of formaldehyde	0.16 cm^2s^{-1}
A is the crossectional area of the sampler	8.04 cm^2
L is the diffusion path length	1.0 cm

B 3 Preparing the samples for analysis

The first step was to remove the filter from the cassette and place it in a 5 ml plastic screw cap test tube. Then, 3.0 ml of HPLC grade acentonrile was added to the tube and shaken for about 1 minute before the solution was injected into the liquid chromatography for analyses. The concentration of formaldehyde was determined in ppb and $\mu g/m^3$.

B 4 Liquid Chromatography

In the present study, high-performance liquid chromatography (HPLC), model Hewlett Packard, series 1100 performed the formaldehyde analysis with Variatle Wavelength Detector. Data acquisition was done using a HP ChemStation A.06.01. The column was Merck LiChrosper RP-18.

C. *Volatile organic compounds (VOCs)*

The indoor concentration of volatile organic compounds in the study was measured using active sorbent sampling method. For this purpose a relatively small and lightweight battery driven pump with an adjustable constant sample flow was used. The sorbent used in the study was charcoal. The duration of the sampling period was eight hours with sample flow rate of 1 l/min.

C 1 Gas Chromatograph

A Perkin Elmer Autosystem XL gas chromatograph, equipped with a detector (FID at 250^{0}C) and injector at 200^{0}C, was used in this study. The injection volume was 1 µl. Data acquisition was handled by Turbochrom 6.1.02:607.

The oven temperature was programmed with:

1) Initial temperature at 35^{0}C for 6 minutes;
2) Ramp 1 at 20^{0}C/min to 100^{0}C holds for 0 min, and
3) Ramp 2 at 8^{0}C/min to 200^{0}C holds for 5 min.

C 2 Preparing the charcoal tubes for analysis

The charcoal tubes were desorbed with 1 ml of carbon disulfide, followed by transferring the solvent into a vial and then analyzed by gas chromatograph (GC).

Table 2.0 Volatile organic compounds and the corresponding retention time

Component Name	Retention Time (min)	Area (μV.s)
Benzene	6.645	104190.73
Toluene	9.040	125202.85
Chlorobenzene	10.261	96810.6
Ethylbenzene	10.560	132715.15
o,p – xylene	10.704	256958.90
Styrene	11.003	146338.12
m – xylene	11.093	145561.91
1,3– dichlorobenzene	12.997	84102.42
1,4– dichlorobenzene	13.083	88992.39
1,2 – dichlorobenzene	13.509	89194.50

Ten components, related to respiratory symptoms, were identified and quantified by the external standard technique, by comparing the retention time (Table 2.0). The concentration of VOCs is presented in $\mu g/m^3$

D. Allergen levels of dust mites

Dust samples were collected from two sites: 1) the child's bedroom floor and 2) child's bedding. A portable vacuum cleaner (Hoover Dustette), with disposable bags, was used in the study. The dust was collected by vacuuming a 1-m^2 surface area of each sampling site for two minutes, which was followed by taking the bag to the laboratory, emptied into a sealable plastic container and stored at -20^0C until analyses.

E 2 Maintenance of the DustTrak

- Each day zero checking and cleaning the 1.0 μm and 2.5 μm inlet conditioners were performed.
- The sample flow rate was adjusted regularly to 1.7 L/min.
- The internal filters were replaced when it was needed.

F. Temperature and air humidity

Tinytalk II Data Loggers measured temperature and relative humidity.

F1 Tinytalk II Data Loggers.

Tinytalk II is a battery-operated device. This unit is small and easy to use. The logger may be programmed to delay the start of the logging cycle by up to 45 days. It can store 1800 data readings. Data may be exported from the host software in text formats suitable for importation into spreadsheet programs.

- Tinytalk II – Temperature Loggers: all loggers use 10K NTC Thermistors. The available ranges of temperature measurements are from -40^0C to 75^0C.
- Tinytalk II – Relative Humidity Logger: the operating range is from 0 to 95% relative humidity (RH%). The relative humidity sensor has to be exposed and hence care must be taken not to cause damage.

F.2 Temperature and relative humidity measurements

The temperature and relative humidity were measured in each household twice per year, winter and summer in the living room. The sampling period was 8 hours.

5.6 Statistical analysis

The analysis involved preliminary assessment of both the case and control subjects datasets to ensure that coding of the data had been performed correctly. This involved assessing the frequencies, mean, mode and median for each variable, as well as cross tabulations of variables. This procedure was undertaken twice during the data collection phase. The first time was midway through the data collection phase and the second at the completion of data collection. Data found to be incorrectly coded were corrected.

The next stage involved assessment of the missing variables and outliers, and determining the distributions of the variables. The latter were assessed for continuous variables via *stem and leaf plots.*

A single missing value of continuous variable was replaced by the mean for all cases.

Variations in proportions between cases and controls were initially assessed using the *Pearson Chi-square test.* Systematic trends in the proportion of cases and controls across the levels of an ordered categorical variable were assessed using the Pearson Chi-square test for trend whilst differences between paired proportions of cases and controls across levels of a categorical variable, were assessed using the *McNemar test* and the *Spearman Rank correlation coefficient.* Differences in the means between case and control subjects were examined using *unpaired t-tests.* A Levene F Test of similarity of variance preceded each t-test. The critical level of significance adopted for each statistical test was 0.05.

Multiple regression analyses were used to analyze the relationship between one continuous dependent variable and set of independent or predictor variables. These analyses were performed to identify those house characteristics that affected the indoor concentrations of nitrogen dioxide (NO_2), formaldehyde

(HCHO), volatile organic compounds (VOCs), particulate matter (PM_{10}), and house dust mite.

The process of constructing a multivariate regression model started with a full model including all relevant house characteristics and all possible two way interactions. The modeling process then continued with the removal of variables from this full model using the forward logistic regression So, only the variables that made a significant contribution to the levels of indoor air pollutants were left in the model

The independent contributions to the overall risk of asthma and respiratory symptoms in children of variables shown to be significant in the univariate analyses were assessed using multiple logistic regression analysis. Logistic regression was used to establish a relationship between one dependent dichotomous variable, such as asthma, and the respiratory symptoms including wheeze, cough, runny nose, and hayfever with values of 0 and 1, and one or more independent variables. Instead of producing regression coefficients, as in the multiple regression models, the logistic regression generates an *odds ratio*. An odds ratio is defined as the probability or the risk of developing a disease under given exposure conditions related to the probability of not developing the disease. In every case, the process of constructing a logistic regression model started with a full model including all relevant main effects and all possible two way interactions. The next step in the modeling process was the removal of variables from this full model using Backward Logistic Regression, Forward Logistic Regression and finally Enter selection method. Variables that only had significant ($p \leq 0.05$) or marginally significant effect ($p \leq 0.09$) on childhood asthma and respiratory symptoms were included in the final regression model.

Odds ratios and 95 percent confidence intervals were derived from the logistic model. The parameters of the model were estimated using the maximum-likelihood method.

Statistical analyses were performed using SPSS for Windows, version 9.

Finally, in order to assess the potential impact of the exposure to the significant risk factors for asthma a population attributable risk proportion (**PARP**) was calculated using the formula described by Fleiss (1979). The population attributable risk (**PAR**) is defined as the fraction of all cases of a disease in a population, which can be attributed to exposure to a given risk factor. If Pe denotes the proportion of the population exposed to the risk factor and **R** the relative risk, **PAR** may be defined as:

$$PAR = P_e(R - 1) / P_e(R - 1) + 1$$

Some authors (Cole and MacMahon, 1971; Walter, 1975) have considered **PAR** estimation from case-control studies, when it was assumed that the odds ratio closely approximates **R** and that the rate of exposure in the control group closely approximates $\mathbf{P_e}$. So, the formula, which corresponds to a case-control study, may be defined as:

$$PARP = P_e (OR - 1) / 1 + P_e (OR - 1) \qquad (1)$$

In the present study, the population attributable risk proportions (**PARP**) were calculated using the odds ratios from the multivariate model. The population attributable fraction is defined as the fraction of the total number of causes of the disease that would not have occurred in the population if the causally related factor had been absent. Thus, this is an estimate of the fraction of the cases of the disease that might be prevented by eliminating exposure to a risk factor.

Finally, a number of measures of reliability and validity were built into the study design. Proportion of agreement, Kappa statistic and McNemar test for significance of change were used to assess the reliability of the questionnaire (Altman, 1995).

5.7 Ethical considerations

It was acknowledged that all participants had to spend some time on the study and the major consideration was to minimise participant inconvenience. All parents or guardians of the study children were invited in writing to participate in the study. Those parents willing to participate responded by signing a "consent to participate" form and completing a respiratory questionnaire. Each child was given an identification number and names were not used. All the study data remained strictly confidential and it is stored in locked archives at Curtin University. All research data was aggregated and the research findings will be published in a form that will not allow identification of any individual. Throughout the study the privacy of the participants was protected at all times.

The Human Research Ethics Committee at Curtin University, the Princess Margaret Hospital Ethics Committee and the Confidentiality of Health Information Committee at the Health Department of Western Australia approved the study and the questionnaire.

CHAPTER SIX

RESULTS

6.1 Introduction

This chapter describes the results of univariate and multivariate analyses. The initial part of the Chapter describes the demographic features of the case and control subjects, their health status, child's family factors and house characteristics.

This is followed by multivariate models of asthma and respiratory symptoms.

The remainder of the Chapter includes multivariate models of the studied indoor air pollutants including nitrogen dioxide, formaldehyde, volatile organic compounds, allergen levels of house dust mite, and particulate matter. These analyses examine potential house characteristics that might influence the indoor levels of air pollutants such as ventilation, gas appliances, presence of air conditioning, humidifier and etc. Multivariate models of indoor temperature and relative humidity are also included.

There are two separate models for winter and summer. These analyses address the aims and objectives of the study.

Finally, the public health impact of the exposure variables, that were significantly predictive of the likelihood of childhood asthma, is examined by population attributable risk proportion (PARP).

6.2 Study population

One hundred and ninety two children participated in the study. Eighty eight children were diagnosed with asthma and 104 children were controls.

6.2.1 Demographic features of the sample

1) Age

Children aged between 6 months and 3 years old, participated in the study. The summary statistics for age of the study subject are reported in Table 2.1

Table 2.1 Summary statistics for age (months) in winter

Asthma Status	N	Minimum	Maximum	Mean	Std. Deviation	95% CI
No	104	6	36	19.59	7.54	18.12-21.05
Yes	88	6	36	24.50	7.46	22.92-26.08

From Table 2.1 is evident that the mean age of case subjects was higher than controls and the difference was significant ($t = -4.52$; $df = 190$; $p = 0.000$).

During summer 12 participants were lost to follow up due to moving interstate or overseas but the distribution of the age was similar as those in winter (Table 2.2). The difference in mean age between case subjects and controls ($t = -4.52$; $df = 178$; $p = 0.000$) remained significant.

Table 2.2 Summary statistics for age (months) in summer

Asthma child	N	Minimum	Maximum	Mean	Std. Deviation	95% CI
No	96	6	36	19.51	7.63	17.95-21.05
Yes	84	6	36	24.74	7.64	23.04-26.38

2) Gender of the study subjects

Of the 192 children in the study, 124 (65%) were boys and 68 (35%) were girls. Table 2.3 and Table 2.4 report the distribution of gender according to asthma status.

Although there were significantly more boys (69.3%) as girls (30.7%) diagnosed with asthma, the difference in gender between case and control subjects was not significant in winter ($\chi^2 = 1.58$; df = 1; p = 0.20).

Though twelve children were lost to follow up during the summer monitoring, more boys 116 (64%) than girls 64 (36%) continued to participate in the study. The difference in gender between asthmatic and non-asthmatic children was not significant ($\chi^2 = 1.45$; df = 1; p = 0.23).

Table 2.3 Distribution of gender according to asthma status of the children in winter

Asthma child	Gender	Percent (%)	95% CI (%)
No	Girls	39.4	29.99-49.48
	Boys	60.6	50.51-70.02
Yes	Girls	30.7	21.29-41.42
	Boys	69.3	58.58-78.71

Table 2.4 Distribution of gender according to asthma status of the children in summer

Asthma child	Gender	Percent (%)	95% CI (%)
No	Girls	40.6	30.71-51.13
	Boys	59.4	48.87-69.28
Yes	Girls	31.0	21.31-41.98
	Boys	69.0	58.02-78.68

6.2.2 Day care attendance

In order to collect information on whether the study subjects were exposed to indoor environment, different from those at home, the health questionnaire asked questions pertaining to a day care attendance and if so, for how many hours on a daily basis. The study results are reported in Table 2.5 and in Table 2.6.

It is evident from the Table 2.5 that more asthmatic (48%) than non-asthmatic children (31%) have attended a day care and the difference was significant (χ^2 = 5.78; df = 1; p = 0.016).

Table 2.5 Attendance of day care according to asthma status of the study subjects

Asthma child	Attendance of day care	Percent (%)	95% CI (%)
No	No	69.2	59.42-77.91
	Yes	30.8	22.09-40.58
Yes	No	52.3	41.35-63.04
Yes	No	52.3	41.35-63.04
	Yes	47.7	36.96-58.65
	Yes	47.7	36.96-58.65

According to Table 2.6, children diagnosed with asthma spend more hours at day care than the non-asthmatic children. The difference is significant (p=0.02) and the value of the Spearman's rank correlation is r = 0.165.

Table 2.6 Attendance a day care per week among case and control subjects

Time	Asthma Status			
	Asthmatic	95% CI	Non-asthmatic	95% CI
No attendance	45	34.80-56.42	71	61.44-79.62
1-5 hrs	9	4.0-17.13	6	2.1-12.13
6-10 hrs	11	15.58-19.90	6	2.1-12.14
11 – 20 hrs	6	2.10-12.13	10	4.70-18.97
21 hrs or more	17	9.87-26.55	11	15.58-19.90

6.3 Characteristics of the child's family

Each parent or guardian has answered a schedule of questions pertaining to the family characteristics of the study subjects such as asthma status of the child's parents and siblings, presence of eczema and hayfever. Questions regarding the educational level of the parents and smoking habits inside the house have also been included.

6.3.1 Health characteristics of child's parents and siblings

Among the mothers of the case subjects 36% had asthma compared to 20% of those in controls and the difference was significant (χ^2 = 6.2; df = 1; p = 0.01) (Table 2.7). Within the case group, 26% of the fathers reported to have asthma, whilst in the control group 21% had asthma but the difference was not significant (χ^2 = 0.55; df = 1; p = 0.45). More than a double the number of siblings of the asthmatic had asthma compared to those of non-asthmatic children and the difference was significant (χ^2= 10.78; df = 1; p = 0.001).

Table 2.7 Prevalence of asthma among child's parents and siblings

	Cases (%)	95% CI	Controls (%)	95% CI	P-value
Asthma mother	36.4	26.37-47.31	20.2	12.95-29.19	0.012
Asthma father	26.1	17.35-36.59	22.1	14.56-31.31	0.45
Asthma brother/sister	36.4	26.37-47.31	15.4	9.05-23.77	0.001

According to the results presented in Table 2.8 both parents of the case subjects suffered from eczema more than those of the control subjects but the difference was not significant for the mothers ($\chi^2 = 0.80$; df = 1; p = 0.37) or for the fathers ($\chi^2 = 1.32$; df = 1; p = 0.22). Although more siblings of the case subjects were reported to have eczema, the difference between cases and controls was also not significant ($\chi^2 = 0.56$; df = 1; p = 0.45).

Table 2.8 Prevalence of hay fever and eczema among child's parents and siblings

	Cases (%)	95% CI	Controls (%)	95% CI	P-value
Eczema mother	30.7	21.29-41 42	25	17.03-34.44	0.37
Eczema father	18.2	10.76-27.84	12.5	6.83-20.44	0.25
Eczema brother/sister	26.1	17.35-36.59	21.2	13.75-30.25	0.45
Hayfever mother	54.5	43.57-65.2	49	39.10-59.03	0.35
Hayfever father	38.6	28.44-49.62	37.5	28.19-47.53	0.67
Hayfever brother/sister	22.7	14.47-32.90	12.5	6.82-20.42	0.06

The number of siblings reported to have symptoms of hayfever was marginally different for the case and control subjects ($\chi^2 = 3.3$; df = 1; p = 0.06). The difference of having hayfever between asthmatic and non-asthmatic children was not significant for mothers ($\chi^2 = 0.86$; df = 1; p = 0.35) or for fathers ($\chi^2 = 0.17$; df = 1; p = 0.67).

6.3.2 Educational level of the parents

In order to investigate the relationship between parent's education and childhood asthma, all parents or guardians were asked to give information on the level of education they attained.

Table 2.9 and Table 3.0 illustrate the level of education attained by the parents according to the asthma status of the study subjects. The educational level was classified as lower secondary school (years 8 to 10), upper secondary school (years 11 and 12), Technical and Further Education (TAFE), and tertiary (university) education. Most of the parents of the case and control subjects completed upper secondary school education.

The Kruskal Wallis test showed that there was no significant difference in the level of maternal education (χ^2 = 0.00; df = 1; p = 0.99) and paternal education (χ^2 = 1.50; df =1; p = 0.22) between cases and controls.

Table 2.9 Distribution of case and control subjects by mother's educational level

Asthma Child	Level of Education	Percent (%)	95% CI (%)
No	Year 10 and below	23.1	14.56-31.31
	Year 11 and 12	2.0	12.95-29.19
	TAFE	15.4	9.05-23.78
	University	36.5	27.31-46.55
Yes	Year 10 and below	30.7	21.29-41.42
	Year 12	12.5	6.40-21.26
	TAFE	14.8	8.11-23.93
	University	39.8	29.49-50.77

Table 3.0 Distribution of case and control subjects by father's educational level

Asthma child	Level of Education	Percent (%)	95% CI (%)
No	Year 10 and below	26.0	17.85-35.48
	Year 11 and 12	16.3	9.82-24.87
	TAFE	27.9	19.53-37.53
	University	28.8	20.38-38.55
Yes	Year 10 and below	19.3	11.67-29.12
	Year 11 and 12	19.3	11.67-29.12
	TAFE	18.2	10.76-27.84
	University	38.6	28.44-49.62

6.4 Health status of the study subjects

The data related to child's health status covered the following topics:

1. Asthma status of the children
2. Respiratory symptoms, including cough, wheeze, shortness of breath; runny nose, trouble breathing, hayfever in cases and controls;
3. Atopic status of the case and control subjects.

All parents or guardians were asked to report any of the following symptoms experienced from their child 3 months before the monitoring commenced:

- Asthma status;
- Wheeze;
- Breathlessness;
- Cough;
- Runny nose and hayfever, and
- Atopic status.

6.4.1 Asthma status of the study subjects

Due to family reasons twelve children pulled out of the study so out of 180, 84 were cases and 96 were control subjects.

6.4.2 Wheeze

As wheezing is one of the classic sign of asthma (the definition is referred to the description given by the International Study of Allergy and Asthma in Children, ISAAC, 1998) the health questionnaire asked whether the child had ever experienced wheezing and if so how often this symptom occurred:

- with a cold;
- apart from a cold; and
- most of the day and night.

The frequency of wheeze according to asthma status of the children is reported in Table 3.1.

Table 3.1 Frequency of wheeze among case and control subjects in winter

Asthma child	Wheeze	Frequency (%)	95% CI (%)
Yes	No	3.4	0.71 – 9.64
	With a cold	28.4	19.30 – 39.02
	Apart from a cold	8.0	3.26 – 15.71
	Most of the time	60.2	49.23 – 70.51
No	No	56.7	46.65-66.41
	With a cold	24.0	16.20-33.41
	Apart from a cold	9.6	4.71-16.97
	Most of the time	9.7	4.61-16.97

It is evident from the table that asthmatic children had six times more wheezing most of the time than non-asthmatic children. As an overall estimation, 96.6% of the case subjects had wheeze compared to 43.3% of the control subjects and the difference was significant with (χ^2 = 72.86; df = 1; p = 0.000).

The frequency of wheeze appeared to be fewer in summer (Table 3.2) compared to winter, and the test for significance of change, showed that the difference in the frequency of wheeze between both seasons, winter and summer, was significant (χ^2= 16.26; df =1; p = 0.000).

Table 3.2 Frequency of wheeze in summer

Asthma status	Wheeze			
	Yes (%)	95% CI (%)	No (%)	95% CI (%)
Cases	51.2	40.03 –62.25	48.8	37.74 – 59.56
Controls	3.1	0.65 – 8.86	96.9	91.14 – 99.35

6.4.3 Breathlessness

The study investigated whether the study subjects had experienced shortness of breath (the definition is referred to ISAAC, 1998) and if so, how often it occurred. The results are reported in Table 3.3.

Table 3.3 Frequency of shortness of breath in cases and controls

Asthma child	Shortness of breath	Frequency (%)	95% CI (%)
No	No	86.5	78.44-92.44
	1-3 episodes per week	1.0	0.02-5.24
	>3 episodes per week	12.5	6.83-20.43
Yes	No	18.2	10.76-27.84
	1-3 episodes per week	25.0	16.38-35.37
	>3 episodes per week	56,8	45.82-67.34

The majority of asthma free children (86.5%) did not report such symptoms, while 82% among the asthmatic children had three or more episodes per week. The Chi Square test of significance showed that the difference in the frequency of breathlessness between cases and controls was significant (χ^2 = 101.21; df = 1; p = 0.000).

6.4.4 Cough

As part of the health questionnaire, all parents were asked to provide information if their child had experienced a cough in the last 6 months before the monitoring commenced:

- with a cold;
- apart from a cold; and
- most of the day and night;

The study results for winter months are reported in the Table 3.4.

The table above shows that two and a half times more asthmatic children had a cough most of the time, compared with non-asthmatic children and the Chi-Square test was significant (χ^2= 38.26; df = 1; p = 0.000).

Table 3.4 Frequency of cough in cases and controls in winter

Cough	Cases (%)	95% CI (%)	Controls (%)	95% CI (%)
No	3.4	0.71-9.64	26.9	18.69-36.51
With cold	28.4	19.30-39.02	38.5	29.09-48.51
Apart from cold	8	3.26-15.70	10.6	5.40-18.13
Most days and nights	60.2	49.23-70.51	24.0	16.20-33.41

Table 3.5 reports the frequency of cough among the case and control subjects during summer and the study findings showed that the asthmatic children experienced cough twice as often as non-asthmatic children and the difference was significant (χ^2 = 21.19; df = 1; p = 0.000).

The McNemar test for the significance of change, showed a significant change in the frequency of cough between winter and summer, for cases (p= 0.000) and controls (p= 0.000). In winter 97% of the case subjects reported having a cough while in summer they were only 67%.

Table 3.5 Frequency of cough in cases and controls in summer

Asthma status	Cough			
	Yes (%)	95% CI (%)	No (%)	95% CI (%)
Cases	66.7	55.54-76.58	33.3	23.42-44.46
Controls	32.3	23.10-42.61	62.7	52.03-72.18

6.4.5 Runny nose and hay fever

As part of the study, each parent or guardian answered questions related to presence of symptoms of hayfever and runny nose in their child. The results (Table 3.6) showed that 94% of the case subjects reported to have a runny nose compared with 69% of the control subjects and the difference was significant (χ^2 = 27.55; df = 1, p = 0.000).

Table 3.6 Frequency of runny nose in study children in winter

Runny nose (Occurrence)	Case subjects		Control subjects	
	%	95% CI (%)	%	95% CI (%)
No	5.7	1.87 – 12.76	30.8	22.09 – 40.58
Occasionally	60	49.23 – 70.51	58.7	48.58 – 68.22
Frequently	34.1	24.31 – 44.97	10.6	5.4 – 18.14

With regard to hay fever, 28% of the asthmatic children had this symptom compared with 6.8% to non-asthmatic children and the difference was significant (χ^2 = 17.34; df = 1; p = 0.000) (Table 3.7).

Table 3.7 Frequency of hay fever in study children in winter

Hay fever	Case subjects		Control subjects	
(Occurrence)	%	95% CI (%)	%	95% CI (%)
No	65.9	55.03 – 75.68	93.3	86.62 – 97.25
Occasionally	27.3	18.32 – 37.80	5.8	2.14 – 12.13
Frequently	1.1	0.03 – 6.17	1.0	0.02 – 5.24

In order to determine whether there is a change in the frequency of runny nose and hay fever between summer and winter months, all parents were asked to report if their child had runny nose and hay fever in the month before the summer visit. The results are shown in Table 3.8 and Table 3.9.

The Chi-square test of significance showed that there was a significant difference in the frequency of runny nose and hay fever during summer between the case and (χ^2 = 10.23; df = 1; p=0.0014) and control subjects (χ^2 = 14.32; df: p=0.0002). With regard to runny nose, 71% asthmatic children complained having runny nose compared with 48% in control subjects.

Table 3.8 Frequency of runny nose among cases and controls in summer

Runny nose	Case subjects		Control subjects	
(Occurrence)	%	95% CI (%)	%	95% CI (%)
No	28.6	19.24 – 39.47	52.1	41.64 – 62.39
Yes	71.4	60.53 – 80.76	47.9	37.61 – 58.35

The McNemar test shows that there was a significant change in the frequency of having runny nose and hay fever between winter and summer, for the case and control subjects with p=0.0000 and p=0.0000, respectively.

Table 3.9 Frequency of hay fever among cases and controls in summer

Hay fever	Case subjects		Control subjects	
(Occurrence)	%	95% CI (%)	%	95% CI (%)
No	1	70.92 – 88.70	97.9	92.67 – 99.74
Yes	19	11.30 – 29.08	2.1	0.25 – 7.32

6.4.6 Atopic status of the study subjects

In order to determine the atopic status of the study children, skin prick tests were performed on all children for common allergens (See Chapter 5.1). The results are reported in the Table 4.0.

Sixty three percent of all children were found to be atopic, but more cases (72%) than controls (50%) were defined as atopic and the difference was significant with (χ^2 = 10.6; df = 1; p = 0.001).

Table 4.0 Atopic status of cases and controls

Atopy	Cases (%)	95% CI (%)	Controls (%)	95% CI (%)
Yes	71.6	60.98-80.70	50.0	40.03-59.97
No	22.7	14.46-32.89	45.2	35.41-55.25
Missing data	5.7		4.8	

6.5 House characteristics

As part of the study all parents or guardians completed a dwelling questionnaire to gather information on the living environment of the residents to ascertain if this affected the indoor air quality and child's respiratory symptoms. Each parent or guardian answered a schedule of questions related to their house such as type of heating and cooking; air conditioning and ventilation in the child's bedroom and the living room; smoking inside the house; use of humidifier and kerosene for heating. Questions such as family pets, type of floor coverings, age of the house, and occupant density per room were also included. Table 4.1 summarises the results of the study with regard to the following house characteristics: presence of gas and electric appliances; presence of closed and open fire places; smoking status in the house; presence of air conditioning; presence of humidifier; attached garage to the house, and age of the house.

Fifty five percent of all study families reported to use gas heaters, as more controls (55%) than cases (51%) were exposed to them but the difference was not significant (χ^2 = 0.49; df = 1; p = 0.48). Thirty nine percent of cases were exposed to unflued gas heaters compared to 36% of control subjects and the difference was also not significant (χ^2 = 1.06; df = 1; p = 0.3).

Table 4.1 Comparison in some house characteristics between case and control subjects

House appliances	Cases (%)	Controls (%)	P-value
Gas heaters	51	55	0.48
Gas cooking appliances	69	85	0.47
Electric appliances	61.4	55.8	0.48
Closed wood fire	19.3	28.8	0.13
Open fireplace	4.5	9.6	0.18
Kerosene space heater	0	6.7	0.01
Smoking inside:			
- visitiors	6.7	6.8	0.51
- parents	4.5	6.7	0.99
Air conditioning:			
- in child' bedroom	27.3	36.5	0.17
- central	33	51.9	0.008
Humidifier	17	10.6	0.19
Attached garage	36.4	44.2	0.27
Age of the house			
- < 5 years old	22.7	18.3	0.71
- 5-10 years	13.6	16.3	
- 10 years old	65.6	64.4	

Eighty percent of the families used gas for cooking as 85% of controls and 69% of cases but the difference was also not significant (χ^2 = 0.51, df = 1; p = 0.47). Furthermore, no case subjects reported to have kerosene space heaters inside the house while among the controls they were 7%. Within the case group, 24% had fireplaces whilst in the control group there were 38% but the difference was not

significant (χ^2 = 1.81; df = 1; p =0.18). The study showed that the frequency of using closed wood fire and fireplaces is higher among controls compared to cases but the difference was not significant for wood fire (χ^2 = 2.34; df =1; p = 0.12) or fire place (χ^2 = 1.81; df = 1; p = 0.18).

The study results demonstrated that 90% of the families avoided smoking inside and within the control group only 13.4% of the families reported to smoke inside whilst in the case group they were 11.3%.

Forty three percent of the families indicated of having central air conditioning in the house as 52% were controls compared to 33% of cases and the difference was significant (χ^2 = 5.12; df = 1; p = 0.008).

Only 13% of the study residences had a humidifier. The frequency was greater in the case than in the control group but the difference was not significant (χ^2 = 1.70; df =1; p=0.193). There was also no significant difference in having a garage attached to the house between case and control subjects (χ^2 = 1.22; df; p = 0.26).

According to the study results, 20% of all families live in a new house, aged less then 5 years as cases were more (23%) than controls (18%) but the difference was not significant (χ^2 = 0.14; df = 1; p = 0.71).

The present study found that 34% among the case subjects kept family pets inside the house compared to 44% in controls but the Chi – square test showed no significant difference between case and control subjects (χ^2 = 2.05; df = 1; p = 0.15).

6.5.1 Ventilation in the house

Table 4.2 shows the results with regard to the type of ventilation in the house.

The Chi-square test for significance showed that there is no significant difference with regard to the subjective perception of the adequacy of ventilation in the house between case and control subjects for the child's bedroom (χ^2 = 0.00; df =1; p =0.98) and the living room (χ^2 = 0.01; df =1; p =0.92).

Table 4.2 Parent's evaluation of ventilation in the child's bedroom and the living room in dwellings with and without asthmatic child

Ventilation	Cases (%)	95% CI (%)	Controls (%)	95% CI (%)
Living room				
very good	54.5	43.58-65.20	56.7	46.65-66.41
good	37.5	27.40-48-46	39.4	29.98-49.49
poor	2.3	0.27-7.97	2.9	0.59-8.19
Child's room				
very good	30.7	21.29-41.42	32.7	23.81-42.59
good	63.6	52.69-73.63	58.7	48.58-68.22
poor	5.7	1.87-12.76	8.7	4.03-15.79

6.5.2 Floor covering in the child's bedroom and the living room

The dwelling questionnaire investigated the type of floor covering people used most, which included carpet, slate, ceramic, floorboards or parquet, linoleum, and concrete.

Table 4.3 and Table 4.4 present the results and it becomes evident that the most commonly used floor covering is carpet.

Table 4.3 Floor coverings used in dwellings with asthmatic child

	Cases					
Floor covering	Child's room %	95% CI (%)	Living room %	95% CI (%)	Both rooms %	95% CI (%)
Carpet	31.8	22.29-42.61	1.1	0.03-6.17	43.2	32.66-54.18
Ceramic	0	-	26	17.25-36-59	1.1	0.03-6.17
Linoleum	2.3	0.27-7.97	8.0	3.26-15.70	1.1	0.03-6.17
Concrete	0	-	4.5	1.25-11.23	1.1	0.03-6.17
Slate	0	-	6.7	2.54-14.25	0	-
Parquet/ floor boards	9	4.00-17.13	12	6.41-21.27	12	6.41-21.27

Ninety one percent of the study families reported to have carpet in both rooms, in the child's bedroom and in the living area, as 49% were cases and 43% were controls but the difference was not significant ($\chi^2 = 2.50$; df = 1; p = 0.11). The second most frequently used floor covering is parquet or floor boards with 12% among cases and the same percent in controls.

Table 4.4 Floor coverings used in dwellings with non-asthmatic child

	Controls					
Floor covering	Child's Room %	95% CI (%)	Living room %	95% CI (%)	Both rooms %	95% CI (%)
Carpet	35.6	26.43-42.61	3.8	1.06-9.55	49.0	39.10-59.03
Ceramic	0	-	21.2	13.75-30.28	0	-
Linoleum	0	-	13.5	7.56-21.55	0	-
Concrete		-	1.9	0.23-6.77	0	-
Slate	0	-	9.1	4.03-15.79	0	-
Parquet/ Floor boards	3	0.60-8.20	3	6.11-19.30	12.5	6.31-20.43

6.6 Concentrations of indoor environmental irritants

During the study the following four air pollutants were monitored inside each house:

- Nitrogen dioxide (NO_2);
- Formaldehyde (HCHO);
- Volatile organic compounds (VOCs);
- Particulate matter (PM_{10}).

The allergen levels of house dust mites, indoor temperature and relative humidity were also measured.

In order to examine if there was a seasonal difference in the levels of indoor air pollutants, each household was monitored twice over one year in winter and summer.

6.6.1 Indoor concentrations of nitrogen dioxide (NO_2)

Recently, the Committee of the National Environmental Protection Council (statutory body established in Australia, 1995, to develop environmental protection policy) proposed a maximum one-hour exposure level of 125 ppb (235 $\mu g/m^3$) to nitrogen dioxide, which was adopted as the recommended standard level of nitrogen dioxide for Australia (NEPCC, 1997).

The levels of NO_2 during winter in the child's bedroom ranged from 7 3 ppb (13 $\mu g/m^3$) to 271 ppb (510 $\mu g/m^3$) and these levels tended to be lower than those in the living room, which ranged from 9.6 ppb (18 $\mu g/m^3$) to 296 ppb (556 $\mu g/m^3$). There was a small but statistically significant positive correlation between the levels of the two rooms ($r = 0.497$, $p = 0.000$).

The distribution of nitrogen dioxide is not normal and thus a transformation was performed to reduce the skewness. Normal logarithmic transformations were

applied and the geometric mean and geometric standard deviation were calculated as an estimate of average for the transformed data. Table 4.5 displays the summary statistics for nitrogen dioxide, winter monitoring.

The study results indicated that the mean levels of NO_2 in winter were lower then the recommended standard value. Higher levels than the standard were measured in 13 families with and among 31 families without asthmatic child.

The results from summer monitoring showed a small but statistically significant positive correlation between summer levels of nitrogen dioxide in both rooms, the child's bedroom and the living room, (r=0.350, p=0.000).

Table 4.5 Summary statistics for indoor concentrations of NO_2 (ppb) in winter and summer

	Cases		Controls		p-value
	Geometric mean	St Dev	Geometric Mean	St Dev	
Winter					
- child's room	4.15	0.65	4.40	0.63	0.008
- living room	4.11	0.74	4.26	0.86	0.22
Summer					
- child's room	8.36	2.63	8.39	2.89	0.41
- living room	8.57	2.33	8.59	2.72	0.38

The levels of NO_2 in the child's bedroom were lower than those in the living room in summer.

The Wilcoxon Signed Paired Test showed a significant difference in the concentrations of nitrogen dioxide between winter and summer for the child's bedroom (Z = -5.616; p = 0.000) but not for the living room (Z = -1.217; p=0.22).

6.6.2 Indoor concentrations of formaldehyde (HCHO)

According to the National Health and Research Medical Council, the maximum permissible level of exposure to formaldehyde within domestic premises and schools in Australia is 120 $\mu g/m^3$ (NHRMC, 1983).

There was a statistically significant positive correlation between the levels of formaldehyde in the child's bedroom and the living room (r=0.584, p=0.000) for the winter.

To reduce the extreme skewness and improve the normality, the data for formaldehyde was logarithmically transformed.

Summary statistics for formaldehyde (HCHO) for winter and summer for both rooms, the child's bedroom and in the living room are presented in the Table 4.6.

Table 4.6 Summary statistics for indoor concentrations of formaldehyde (HCHO) ($\mu g/m^3$) in winter and summer

	Cases		Controls		p-value
	Geometric mean	St Dev	Geometric mean	St Dev	
Winter					
- child's room	3.63	1.43	3.85	1.58	0.32
- living room	3.64	1.37	3.77	1.39	0.50
Summer					
- child's room	3.20	1.00	2.94	0.67	0.04
- living room	3.13	0.88	2.80	0.88	0.01

During winter monitoring the levels of formaldehyde in the bedroom ranged from 0.24 to 62.91 $\mu g/m^3$ and these levels tended to be lower than those in the living room, which ranged from 0.61 to 80.05 $\mu g/m^3$. During the winter, all children were exposed to levels lower than the recommended levels of exposure.

There was a statistically significant positive correlation between formaldehyde levels (summer) in the child's bedroom and the living room ($r = 0.565$, $p = 0.000$). The levels of formaldehyde in the child's bedroom ranged from 0.49 to 223 $\mu g/m^3$, which levels were higher than those in the living room, which varied from 0.73 to 189.72 $\mu g/m^3$.

The Wilcoxon Signed Ranked test showed statistical significance for formaldehyde levels between winter and summer for the child's' bedroom ($Z = -10.41$; $p=0.000$) and the living room and the living room ($Z = -6.61$; $p=0.000$).

6.6.3 Indoor concentrations of volatile organic compounds (VOCs)

The following ten volatile organic compounds were monitored during winter and summer, in the living room: *benzene; toluene; chlorobenzene; ethylbenzene; p-xylene; styrene; m-xylene; 1,3-dichlorobenzene; 1,4-dichlorobenzene, and 1,2-dichlorobenzene.* According to the National Health and Medical Research Council, the maximum premissible level of exposure to VOCs is 500 $\mu g/m^3$ average per hour, as a single compound should not contribute more than 50% of the total.

The evaluation of assumptions for normality led to transformation of the data for all compounds to reduce skewnes, reduce the number of outliers and improve the normality. All possible transformations were performed but normality was improved after deleting some outliers.

Summary statistic for the volatile organic compounds, winter and summer data, are shown in Table 4.7. The results demonstrate that the levels of VOCs didn't exceed the recommended threshold limit of exposure. Also, the mean values for most volatile compounds in winter appeared to be similar for the case and control subjects, with no significant difference between them, except for m-xylene.

Table 4.7 Summary statistics for selected volatile organic compounds ($\mu g/m^3$), winter and summer

Volatile Organic Compound	Cases		Controls		P-value
	Mean	St Dev	Mean	St Dev	
Winter					
- Benzene	49.26	32.94	46.49	23.64	0.5
- Toluene	16.06	19.01	19.77	14.02	0.82
- Chlorobenzene	1.49	4.13	2.75	6.64	0.06
- Ethylbenzene	1.70	3.00	1.90	3.24	0.44
- P-xylene	11.86	11.98	12.26	12.13	0.75
- Styrene	0.73	2.83	0.77	1.82	0.42
- M-xylene	1.68	3.91	2.81	5.43	0.02
- 1,3 Dichlorobenzene	12.58	9.26	17.26	26.29	0.22
- 1,4 Dichlorobenzene	5.67	14.11	3.24	6.25	0.27
- 1,2 Dichlorobenzene	16.87	31.25	28.40	35.56	0.12
Summer					
- Benzene	20.92	14.57	8.35	9.84	0.000
- Toluene	17.08	20.88	7.90	6.38	0.000
- Chlorobenzene	1.57	6.36	0.27	1.06	0.02
- Ethylbenzene	2.23	3.16	1.9	1.38	0.001
- P-xylene	9.89	15.41	4.75	4.60	0.001
- Styrene	0.46	1.25	0.13	0.65	0.01
- M-xylene	16.29	79.44	1.87	4.42	0.008
- 1,3 Dichlorobenzene	13.03	27.85	4.36	9.83	0.001
- 1,4 Dichlorobenzene	2.56	13.75	0.36	1.38	0.001
- 1,2 Dichlorobenzene	16.73	27.31	8.09	13.41	0.016

In contrast to the findings for winter, the difference in the mean values of all compounds between the case and control subjects for summer is significant as case subjects were exposed to significantly higher levels compared to control subjects.

The t-test found a statistically significant difference between summer and winter mean concentrations for all study volatile organic compounds, except for ethylbenzene ($p = 0.4$) and m-xylene ($p = 0.2$)

6.6.4 Indoor concentrations of particulate matter (PM_{10})

United States Environmental Protection Agency has established 24-hour standard of exposure to particulate mater, which is 150 $\mu g/m^3$.

The evaluation of the assumption of normality led to logarithmic transformation of the data for particulate matter (PM_{10}).

The study found that the average concentration for indoor particles in winter was 45.71$\mu g/m^3$ (St Dev: 40.09), which is slightly higher than those in summer - 39.12 $\mu g/m^3$ (St Dev: 22.20) but the difference was not significant (p = 0.26).

Summary statistics for particulate matter (PM_{10}) in winter and summer is displayed in the Table 4.8.

Table 4.8 Summary statistics for particulate matter (PM_{10}) in $\mu g/m^3$

	Cases		Controls		p-value
	Mean	St Dev	Mean	St Dev	
Winter	45.53	39.79	45.86	40.55	0.95
Summer	40.14	19.28	38.24	24.55	0.56

There was no notable difference in concentrations of the particles between cases and controls for winter and summer. Furthermore, the difference in the concentrations of particulate matter between winter and summer was also not significant (p=0.129).

6.6.5 Allergen levels of house dust mite

The evaluation of the assumption of normality led to transformation of the data for house dust mite for winter and summer. All possible transformations were used but normality was improved after deleting some outliers.

The summary statistics for house dust mites, winter and summer data, are shown in Table 4.9. The mean allergen level of house dust mites for winter was 0.63 µg/gm which was less then those in summer (1.11 µg/gm) and the difference was significant with p= 0.009. The difference in the levels of house dust mite between cases and controls was significantly different for winter (-2.73; df =190; p = 0.007) and summer (- 4.53; df = 178; p = 0.000).

Table 4.9 Summary statistics for the allergen levels of house dust mites for case and control subjects

	Cases		Controls		p-value
	Mean	St Dev	Mean	St dev	
Winter	1.15	3.50	0.19	0.56	0.007
Summer	1.99	3.39	0.34	1.05	0.000

6.6.6 Indoor temperature (T^0C) and relative humidity (RH%)

The distribution of the relative humidity and the temperature were not normal and in order to reduce the skewness, number of outliers and improve the normality a log linear transformation was used for both, the temperature and the relative humidity. Summary statistic for the indoor temperature and relative humidity is displayed in the Table 5.0.

Table 5.0 Summary statistics for the average indoor temperature (T^0C) and relative humidity (RH%), winter and summer

	Cases		Controls		p-value
	Geom. Mean	St Dev	Geom. Mean	St Dev	
Temperature (^0C)					
Winter	2.99	0.14	2.95	0.11	0.13
Summer	3.27	0.14	3.26	0.09	0.41
Relative Humidity (%)					
Winter	4.01	0.18	3.97	0.18	0.41
Summer	3.96	0.17	3.93	0.17	0.38

The study did not find a significant difference in the temperature and in the relative humidity between case and control subjects but there was a significant difference in the values for of the temperature and relative humidity between winter and summer, (t = 7.1; df = 179; p=0.000) (t = 12.98; df = 179; p=0.021), respectively.

6.6.7 Summary statistics for indoor concentrations of the environmental irritants

Table 5.1 summarises the information found in the study with regard to the concentrations of the study indoor pollutants.

Nitrogen dioxide levels were significantly different between case and control subjects in winter, as the higher concentrations were measured in houses of non-asthmatic children.

It is evident from the study findings that indoor concentrations of formaldehyde are much higher during summer compared to those in winter. Also, the concentrations of formaldehyde vary between the houses with and without asthmatic children and between the two seasons, winter and summer.

Table 5.1 Seasonal variations of the studied indoor air pollutants for the case and control subjects

Environmental	Winter			Summer		
Irritant	Cases	Controls	P-value	Cases	Controls	P-value
Nitrogen Dioxide ppb (µg/m^3)						
Mean	76.75	99.65	0.004	76.72	78.71	0.80
	(144)	(187)		(144)	(148)	
St Dev	46.08	46.08		43.82	58.67	
Formaldehyde (µg/m3)						
Mean	15.32	17.32	0.26	37.78	23.50	0.001
St Dev	11.47	13.54		37.80	16.56	
PM10 (µg/m3)						
Mean	45.53	45.86	0.95	40.14	38.24	0.57
St Dev	39.79	40.55		19.28	24.55	
Dust mite (µg/gm)						
Mean	1.15	0.194	0.007	1.99	0.34	0.000
St Dev	3.50	0.56		3.40	1.05	
Benzene (µg/m3)						
Mean	49.26	46.49	0.50	20.92	8.35	0.000
St Dev	32.94	23.64		14.57	19.84	
Toluene (µg/m3)						
Mean	16.06	19.77	0.31	17.08	7.90	0.000
St Dev	19.01	29.56		20.88	6.39	
M-xylene (µg/m3)						
Mean	1.68	2.81	0.10	16.29	1.87	0.07
St Dev	3.92	5.43		79.44	4.42	

Table 5.1 (cont.)

P-xylene (µg/m3)						
Mean	11.86	12.25	0.82	9.89	4.75	0.002
St Dev	11.98	12.13		15.14	4.60	
Styrene (µg/m3)						
Mean	0.73	0.77	0.34	0.46	0.14	0.03
St Dev	2.83	1.82		1.25	0.65	
Chlorobenzene (µg/m3)						
Mean	1.49	2.75	0.12	1.57	0.26	0.04
St Dev	4.13	6.64		6.360	1.06	
Ethylbenzene (µg/m3)						
Mean	1.70	1.90	0.65	2.23	1.10	0.002
St Dev	3.00	3.25		3.16	1.38	

There is no notable difference in the concentrations of particulate matter between cases and controls and no significant seasonal variation in the particles was measured.

Allergen levels of house dust mite are higher in summer compared to those in winter and the difference is significant.

Regarding the volatile organic compounds, there is a significant difference in summer concentrations between case and control subjects.

6.7 Predictors of asthma and respiratory symptoms

As described in section 4.5.5 in the study, logistic regression analysis was performed in order to:

- investigate the association between the respiratory symptoms and asthma and indoor environmental factors;
- estimate the factors which made a significant effect on asthma and respiratory symptoms, and
- evaluate and compare the odds ratio of the significant predictors.

Logistic regression analysis was performed using SPSS 9.0 for Windows. Several models were tested and the model was chosen by the criteria used for assessing model fit (Altman, 1991).

Logistic regression analysis was employed on the following respiratory disorders:

a. Asthma
b. Wheeze
c. Runny nose
d. Hay fever
e. Cough

Unconditional logistic regression was used to analyse the unmatched data sets. Odds ratios and their 95 percent confidence intervals were estimated. All statistical tests were two-sided. A multivariate model was developed that included all the studied variables. Logistic regression analyses were performed for winter and summer in order to determine if there is a difference in the potential risk factors for asthma between the two seasons. Variables, which made an independent contribution ($p \leq 0.5$) and those, which were marginally significant ($p \leq 0.05$) are included.

The four statistics, which are listed below for each of the variables selected into the models, have the following interpretations:

1) The odds ratio (OR)

2) Significance (p) is the alpha probability of an error if the null hypothesis is rejected. Adopting a conventional level of alpha of 0.05, all variables with a significant regression coefficient into the model were selected. However the significance alone is not enough to assess the importance of a variable in the model and the next two parameters provide this information.

3) 95% CI

4) The constant term in a logistic regression analysis is an indication of whether the regression equation requires a constant term to express the probability when all of the independents have the value zero

The model chi-square is a method of assessing goodness of fit and if the p value is highly significant it indicates that the model with all selected variables is a better predictor of asthma than a model, which includes the constant.

6.7.1 Predictors of asthma

Logistic regression analysis for asthma, winter data, is presented in the Table 5.2.

Table 5.2 Predictors of asthma, winter

Dependant Variable	Model Characteristics	Predictors	Odds Ratio	Sign (p)	95% CI
Asthma (living room)	Goodness of fit: 168.11	Age (months)	1.08	0.002	1.03 – 1.13
	Model chi-square = 69.36	Atopy (yes)	3.29	0.003	1.48 – 7.33
		Family history of asthma (yes)	2.82	0.006	1.33 – 5.96
	df = 9	Gender (m)	1.90	0.112	0.86 – 4.20
	p = 0.000	House dust mites	1.94	0.005	1.22 – 3.07
		Humidifier (yes)	2.77	0.064	0.94 – 8.15
		Air conditioning (yes)	0.28	0.002	0.12 – 0.63
		Fireplace (yes)	0.41	0.027	0.18 – 0.90
Asthma (child's bedroom)	Goodness of fit: 159.47	Age (months)	1.08	0.003	1.02- 1.01
	Model chi-square = 75.41	Atopy (yes)	3.24	0.005	1.43 – 7.36
		Family history of asthma (yes)	2.87	0.006	1.34 – 6.14
	df = 9	Gender (m)	1.81	0.149	0.80 – 4.05
	p = 0.000	House dust mites	2.02	0.005	1.24 – 3.28
		Humidifier (yes)	2.59	0.088	0.87 – 7.76
		Air conditioning (yes)	0.28	0.003	0.12 – 0.65
		Fireplace (yes)	0.35	0.014	0.15 – 0.81
		NO_2	0.99	0.009	0.98 – 0.99

It is evident from the table that the predictors of asthma for child's bedroom and the living room are similar except that exposure to nitrogen dioxide in the child's bedroom has a significant effect on asthma.

Interpretation of the study results regarding the asthma risk factors for the living room (child's bedroom) is presented below.

The first variable to enter both models is age and it is a powerful predictor of asthma. The odds ratio has been adjusted to indicate that for each one month increase in age the probability of having asthma increases by 8%.

Atopy is the next significant risk factor for asthma. This categorical variable is scored 1 for having atopy and 0 for not having atopy. This is the most powerful predictor and the odds ratio of OR = 3.29 (3 24) indicates that children who were defined as atopic resulted in a three fold increase in the odds of having asthma.

Family history of asthma is the third entered variable. This is also a categorical variable as 1 scored for having any first degree relative (mother, father or sibling) who has a history of asthma, and 0 scored for the opposite. It is also a strong predictor with an odds ratio of OR = 2.82 (2.87) indicating that children with family history of asthma are at three times higher risk of having asthma compared to those who do not have any first degree relatives diagnosed with asthma.

According to the regression model, exposure to house dust mites results in a two-fold increase, OR = 1.94, (OR = 2.02) in the odds of having asthma, which makes dust mites also a very strong predictor.

Air conditioning and fireplaces are two categorical variables as 1 scored for use and 0 for non-use of these appliances. The odds ratios indicate that the use of air conditioning and fireplaces at home decrease the probability of having asthma by 28 percent and 40 percent, respectively.

Exposure to humidifier has a marginally significant effect on asthma with p = 0.06 (0.08). The variable that was included in the model but didn't appear to be a significant factor for asthma is gender. The predictors of asthma, summer, are reported in the Table 5.3

The predictors of asthma for the child's bedroom and the living room are very similar. The first significant predictor of asthma for both models is age The odds ratio OR = 1.10 indicates that for each month increase in age the probability of having asthma increases by 10%.

Table 5.3 Predictors of asthma, summer

Dependant Variable	Model Characteristics	Predictors	Odds Ratio	Sign (p)	95% CI
Asthma (living room)	Goodness of fit: 144.80	Age (months)	1.10	0.001	1.03 – 1.17
	Model chi-square = 98.62	Gender	2.55	0.038	1.05 – 6.17
	df = 9	House dust mites	1.82	0.007	1.17 – 2.83
	P = 0.000	Formaldehyde	1.02	0.051	1.00 – 1.03
		Benzene	1.07	0.000	1.03 – 1.11
		Toluene	1.09	0.050	1.02 – 1.16
		Family history of asthma (yes)	2.35	0.050	1.00 – 5.53
		Time outdoors (>2hrs a day)	0.41	0.008	0.01 – 0.55
Asthma (child's bedroom)	Goodness of fit: 178.75	Age (months)	1.11	0.001	1.04 – 1.18
	Model chi-square = 105.53	Gender (m)	2.29	0.069	0.93 – 5.64
	df = 8	House dust mites	1.86	0.005	1.19 – 2.90
	P = 0.000	Formaldehyde	1.03	0.003	1.00 – 1.05
		Benzene	1.07	0.000	1.03 – 1.11
		Toluene	1.09	0.004	1.03 – 1.16
		Family history of asthma (yes)	2.19	0.07	0.91 – 5.25
		Time outdoors (>2hrs a day)	0.25	0.003	0.10 – 0.64

Gender appears as a significant factor for asthma for the living room and marginally significant for the child's bedroom. The odds ratio of OR = 2.55

(OR_{bed} = 2.29 for the child's bedroom) indicates that boys are at two and a half times increased risk of having asthma compared to girls.

The next variable to enter the model is house dust mites. This variable is also a very strong predictor of the probability of having asthma. The odds ratio of OR = 1.82 (OR_{bed} = 1.86), indicates that children who are exposed to house dust mites, for every one unit increase in the allergen level of dust mites results in two fold increase in odds of having asthma.

The next significant predictor of asthma is domestic exposure to formaldehyde. During hot months indoor exposure to formaldehyde is a significant risk factor for asthma as the odds ratio of OR = 1.02 indicates that for every one unit ($\mu g/m^3$) increase in the level of formaldehyde the risk of having asthma increases by 2%. Given a range of formaldehyde from 0 - 200 $\mu g/m^3$ this means that if the concentrations of formaldehyde increase by 20% (40 $\mu g/m^3$) this is associated with 80% increase in risk of having asthma.

Benzene and toluene, both volatile organic compounds, are the next variables to enter into the model. The odds ratios of OR = 1.07 for benzene and OR = 1.09 for toluene indicate that for every one unit ($\mu g/m^3$) increase in benzene and toluene, the risk of having asthma increases by 7% and 9% respectively. Similar to the explanation given above for formaldehyde, having a range of benzene and toluene from 0 - 50 $\mu g/m^3$ means that id the concentrations of benzene or toluene increase by 20% (10 $\mu g/m^3$) this is associated with 70% or 90% increase in risk of having asthma, respectively.

Children who spend at least 2 hours a day outdoors are at less risk of having asthma compared to those who do not spend such a time. Thus, spending more time outdoors has a protective effect for asthma.

Family history of asthma appears to be a strong predictor of asthma with odds ratio of OR = 2.57 which explains that children with family history of asthma

results in a two-fold increase in the odds of having asthma compared to those without any first degree relatives with asthma. In the model for the child's bedroom family history of asthma appears as a marginally significant variable.

6.7.2 Predictors of wheeze

The logistic regression model of wheeze, winter data, is presented in the Table 5.4.

Because of the similarity between the models in the child's bedroom and in the living room, the logistic regression model of wheeze in the living room is not displayed.

Table 5.4 Predictors of wheeze, winter

Dependant Variable	Model Characteristics	Predictors	Odds Ratio	Sign (p)	95% CI
Wheeze (child's bedroom)	Goodness of fit: 214.47	Age (months)	1.07	0.02	1.02 – 1.12
	Model chi-square = 27.08	Gender	1.98	0.047	1.01 – 3.89
	df = 5	House dust mites	1.53	0.077	0.95 – 2.46
	P = 0.000	P-xylene	1.03	0.076	1.00 – 1.06
		Humidity (%)	1.04	0.018	0.27 – 1.07

The first variable to enter the model is age and the odds ratio of OR = 1.07 indicates that for each month increase in age the probability of wheeze increases by 7%.

Gender is the next variable to enter. The odds ratio of OR = 1.98 shows that boys are at double risk of having wheeze than girls. It should be noted that since age is already part of the model, the odds ratio for gender is age adjusted.

High humidity appears to have significant effect on wheeze with the odds ratio of OR =1.04, which indicates that for every one percent increase in the humidity, the risk of having wheeze increases by 4%.

Exposure to house dust mites and p-xylene (volatile organic compound) appeared in the model with marginally significant effect on wheeze with p = 0.077 and p = 0.076, respectively.

The factors that significantly contributed to wheeze during summer for child's bedroom and the living room are shown in the Table 5.5.

Table 5.5 Predictors of wheeze, summer

Dependant Variable	Model Characteristics	Predictors	Odds Ratio	Sign (p)	95% CI
Wheeze (living room)	Goodness of fit: 180.19 Model chi-square = 21.07 df = 2 P = 0.000	Age (months) Benzene	1.09 1.02	0.000 0.082	1.03 – 1.15 0.99 – 1.05
Wheeze (child's bedroom)	Goodness of fit: 184.82 Model chi-square = 27.42 df = 3 P = 0.000	Age (months) Benzene Formaldehyde	1.09 1.02 1.02	0.000 0.090 0.015	1.03 – 1.15 0.99 – 1.05 1.00 – 1.03

The predictors of asthma for both rooms, the child's bedroom and the living room are similar except that formaldehyde is not a significant indicator of wheeze in the model for the living room.

The first significant predictor of wheeze is age. The odds ratio of OR = 1.09 indicates that an increase with one month of age is being associated with a 9% increase in the probability of having wheeze.

Indoor exposure to formaldehyde is a significant risk factor for wheeze only in the child's bedroom with odds ratio of OR = 1.02. With each unit increase in formaldehyde level ($\mu g/m^3$) the probability of having wheeze is increasing by

2%. Formaldehyde was also a significant risk factor for asthma with similar odds ratio of OR = 1.03.

Domestic exposure has marginally significant effect on wheeze with p = 0.08.

6.7.3 Predictors of hay fever

Table 5.6 presents the significant predictors of hayfever for winter and summer data.

Table 5.6 Predictors of hayfever, child's bedroom

Dependant Variable	Model Characteristics	Predictors	Odds Ratio	Sign (p)	95% CI
Hayfever Winter	Goodness of fit: 212.35	Age (months)	1.07	0.047	1.00 – 1.13
	Model chi-square = 52.8	Carpet	5.54	0.035	1.12 – 27.3
	df = 8	Gas heaters	1.98	0.157	0.77 – 5.08
	p = 0.000	Humidity	1.06	0.032	1.0 – 1.11
		NO_2	0.98	0.039	0.97 – 0.99
		Temperature	1.36	0.004	1.10 – 1.68
		Toluene	1.02	0.047	1.00 – 1.03
		Pets allergy	23.82	0.002	3.93- 206.8
Hayfever Summer	Goodness of fit: 100.7	Benzene	1.05	0.002	1.02 – 1.08
	Model chi-square = 16.33	Temperature	1.14	0.025	1.02 – 1.29
	df = 2				
	p = 0.000				

Due to similarity of the logistic regression models of hayfever for the child's bedroom and the living room, the regression model for the living room is not presented.

The first variable to enter the model is age. The odds ratio of OR = 1.07 indicates that for each month increase in age the probability of having hayfever increases by 7%.

The next variable in the model is carpet. This categorical variable is scored 1 for presence of carpet in the house and 0 for absence. Presence of carpet is very powerful indicator of hayfever with odds ratio of OR = 5.54, which indicates that having carpet in the house results in a five and a half fold increase in the odds of having hayfever.

The most powerful predictor of the probability of hayfever appeared to be child's allergy to pets with odds ratio of OR = 23.8. Child who has allergy to pets results in a twenty-four fold increase in the odds of having hayfever.

Gas heating is a significant indicator of wheeze with odds ratio of OR = 1.98, which explains that exposure to a gas heater results in two fold increase of having hayfever.

The next variable to enter the model is the relative humidity. The odds ratio of OR = 1.06 indicates that with each percent increase in the relative humidity the probability of having hayfever increases by 6%.

Nitrogen dioxide (NO_2) is a variable also included in the regression model. The odds ratio of OR = 0.98 indicates that exposure to nitrogen dioxide has a protective effect on hayfever.

Temperature with odds ratio of OR = 1.36 explains that for each unit increase in the temperature there was an increase of 36% in risk of having hayfever.

Although toluene is not a strong predictor, it contributes significantly to the probability of having symptoms of hayfever with odds ratio of OR = 1.02. For every one unit increase in toluene ($\mu g/m^3$) there is an increase of 2% in risk of having hayfever.

During summer, out of 180 study children, only 18 reported to have hayfever, as 16 (90%) were asthmatic and 2 (11%) were controls. Since the logistic

regression models for the child's room and the living room are similar, the model for the child's bedroom is presented only, see Table 5.6.

There are two variables only, which have a significant effect on hayfever during the hot months, which are benzene and temperature.

The odds ratio of OR = 1.05 for benzene indicates that for every one unit ($\mu g/m^3$) increase in the level of benzene the probability of having hayfever increases by 5%.

Indoor temperature is also a significant predictor with odds ratio of OR = 1.14. For every one degree increase in the temperature there is an increase of 14% in the risk of having hayfever.

6.7.4 Predictors of runny nose

Runny nose is the next study respiratory symptom. This categorical variable is scored 1 for presence of runny nose and 0 for absence.

According to the study results the predictors of runny nose for winter and summer are shown in Table 5.7. Due to similarity of the models for the child's bedroom and the living room, the logistic regression analysis for the living room is not presented.

For winter data, there are three variables, which are significant predictors of runny nose among young children, which are age, dichlorobenzene and family history of asthma.
The first variable to enter the model is age and the odds ratio of OR = 1.07 indicates that for each month increase in age the probability of having runny nose increases by 7%.

Dichlorobenzene is a volatile organic compound and although it is not a strong predictor (OR = 1.02), it significantly contributes to the likelihood of having a runny nose. For every one unit ($\mu g/m^3$) increase in 1,3 Dichlorobenzene there is an increase of 2% in the risk of having asthma.

Family history of asthma is a very powerful predictor and the odds ratio of OR = 2.7 indicates that child with a family history of asthma results in three fold increase the risk of having runny nose.

Table 5.7 Predictors of runny nose

Dependant Variable	Model Characteristics	Predictors	Odds Ratio	Sign (p)	95% CI
Runny nose Winter	Goodness of fit: 168.65 Model chi-square = 15.82 df = 3 p = 0.001	Age (months) 1,3 – Dichlorobenzene Family history of asthma	1.07 1.02 2.7	0.012 0.058 0.014	1.02 – 1.09 1.0 – 1.45 2.1 – 5.9
Runny nose Summer	Goodness of fit: 177.97 Model chi-square = 23.49 df = 4 p = 0.000	Ethylbenzene Family history of asthma (1) Time outdoors (1)	1.05 3.16 0.28	0.002 0.000 0.045	1.02 – 1.08 1.87 – 6.90 0.08 – 0.97

Similar to the logistic regression model for winter, family history of asthma is the strongest predictor of runny nose for summer data with odds ratio of OR = 3.16. Ethylbenzene as a volatile organic compound, which also is a significant indicator for runny nose with odds ratio of OR = 1.20. During summer, for every one unit increase in ethylbenzene ($\mu g/m^3$) the risk of having runny nose is associated with 20% increase.

Time spend outdoors is the last variable to enter the model. This categorical variable is scored 0 for time spends outdoors of one hour or less; 1 for spending

2-3 hours a day, and 2 for spending 4 or more hours a day. The odds ratio of OR = 0.28 indicates that children who spend 2-3 hours a day is associated with 28% decrease of the probability of having runny nose.

6.7.5 Predictors of cough

The logistic regression analyses of cough, winter and summer, are presented in the Table 5.8 and the results show that there are only two variables, which have a significant association with cough for winter data.

Table 5.8 Predictors of cough

Dependant Variable	Model Characteristics	Predictors	Odds Ratio	Sign (p)	95% CI
Cough Winter	Goodness of fit: 226.69 Model chi-square = 16.59 df = 3 p = 0.009	Day care attendance House dust mites Temperature	3.35 3.10 1.11	0.021 0.056 0.243	1.20 – 9.34 0.93 – 1.33 0.97 – 9.96
Cough Summer	Goodness of fit: 171.17 Model chi-square = 21.73 df = 4 p = 0.003	Airconditioning Particulate matter Benzene Atopy	0.05 1.01 1.04 2.30	0.050 0.064 0.012 0.019	0.27 – 1.00 0.99 – 1.03 1.00 – 0.06 1.14 – 4.60

The first independent variable entered the model is attending a day care centre. This is a powerful predictor and the odds ratio of OR = 3.35 indicates that children who attend a day care centers results in a three fold increase in odds of having cough.

The second variable is allergen levels of house dust mite, which is also a very strong indicator with odds ratio of OR = 3.10. For every one unit increase in the level of dust mites ($\mu g/m^3$) results in three fold increase the risk of having cough. During the hot months the presence of air conditioning appears to be a protective factors with odds ratio OR = 0.519 which indicates that children who live in

houses with air conditioning it is associated with 52 percent reducing the probability of having cough.

Domestic exposure to benzene is a significant predictor of cough with an odds ratio of OR = 1.03 which explains that children who are exposed to benzene, for every one unit increase in the level of benzene ($\mu g/m^3$) there is an increase of 3% in the risk of having cough.

Atopy is the most powerful predictor for this respiratory symptom. The odds ratio of OR = 2.30 indicates that children who are defined as atopic are two times more likely to have a cough than nonatopic children.

Particulate matter (PM_{10}) appeared as a marginally significant factor for cough with value p = 0.06.

6.8 Factors contributing to indoor levels of the environmental irritants

In order to meet the objectives of the study to determine the extent to which certain house characteristics influence the concentrations of the indoor air pollutants multiple linear regression analysis were performed. The description of statistics given blew applies here. Only the specific model parameters will be described.

Multiple **"R"** indicates the multiple correlation coefficient of all independent variables in the model with the dependent variable. It can vary between +1 and 0 as a high value close to +1 shows a good prediction of the dependent variable by the independents.

Adjusted "$\mathbf{R^2}$" provides an indication of what proportion of the variance in the dependent variable is explained by the joint effect of the independent variables.

The "**F**" statistics is testing the null hypothesis that the model is no better at predicting the dependent variable than the constant would be alone. The significance shows that the F test is significant.

"B" is the regression coefficient and it is indicator of the strength of association between each independent variable and the dependent. One-unit increase in the independent variable is associated with one unit change in the dependent. A positive value of **B** indicates a direct linear association, and the negative indicates an inverse linear relationship.

"β" is the standardised regression coefficient and indicates the change in the dependent variable, which is associated with one standard deviation change in the dependent variable. β allows comparing the relative effect of changes in the different variables.

The "**p-value**" shows the significant effect of each independent variable, testing the null hypothesis that there is no association between that variable and the dependent, allowing for the effect of all other variables in the model.

6.8.1 Factors associated with indoor levels of formaldehyde

As discussed in Chapter 3, the major sources of formaldehyde include combustion sources, tobacco smoke, and urea-formaldehyde resins. Table 5.9 illustrates the variations in the levels of formaldehyde in houses with and without the following selected house characteristics: new furniture; cooking appliances; gas heater; cooking and heating appliances; cigarette smoking inside, and air conditioning.

Table 5.9 Concentrations of HCHO ($\mu g/m^3$) in homes with and without selected house characteristics

House characteristics	Mean levels of formaldehyde in the living room ($\mu g/m^3$)		Mean levels of formaldehyde in the child's room ($\mu g/m^3$)	
	Mean	St Dev	Mean	St Dev
All appliances	16.37	12.64	15.67	11.79
Without gas heater	14.41	10.19	12.60	7.68
Without gas cooking appliances	14.32	12.82	13.35	8.97
Without any gas appliances	12.66	12.12	12.22	7.99
Without air conditioning	15.85	12.09	15.12	11.97
Without new furniture	15.00	11.12	14.47	9.33

It is evident from the table above that the use of gas for heating and cooking made most notable effect on formaldehyde level, followed by the presence of new furniture.

Multiple linear regression analysis was performed to assess the potential relationship between formaldehyde and several important variables, which were likely to affect its levels. These include indoor temperature, relative humidity, age of the house; use of gas for heating and cooking; presence of air conditioning, kerosene, humidifier, closed wood fire, open fire place, attached garage, smoking inside the house, carpet and floor boards.

According to the study results, the factors, which made significant effect on the level of formaldehyde in the living room for winter data, are reported in the Table 6.0.

6.8.2 Factors associated with indoor levels of nitrogen dioxide (NO_2)

Table 6.1 reports the average concentrations of nitrogen dioxide in homes with and without selected house characteristics, such as gas heater, cooking appliances, any gas appliances (including heating and cooking appliances), air conditioning, and smoking inside. The table shows that the presence of gas heater has major effect on the levels of nitrogen dioxide. Smoking inside the house does not make any notable effect on the nitrogen dioxide levels.

Table 6.1 Summary statistics of NO_2 in ppb ($\mu g/m^3$) in homes with and without selected house characteristics

House characteristis	Mean levels of NO_2 in living room ppb ($\mu g/m^3$)		Mean levels of NO_2 in child's bedroom ppb ($\mu g/m^3$)	
	Mean	St Dev	Mean	St Dev
All appliances	88.61 (166)	66.83 (125)	89.16 (168)	55.62 (104)
Without gas heaters	80.61 (151)	63.34 (119)	84.16 (158)	52.05 (98)
Without gas cooking	81.64 (153)	58.43 (110)	91.59 (172)	56.79 (107)
Without air conditioning	82.94 (156)	66.12 (124)	84.08 (158)	55.18 (104)
No smoking Inside	88.30 (162)	66.28 (125)	88.77 (167)	52.05 (98)

The independent variables included in the multiple regression model for winter and summer that might have an effect on nitrogen dioxide levels were: indoor temperature and relative humidity, smoking inside, humidifier, gas heating, gas cooking, kerosene, smoking inside, air-conditioning, and ventilation in the house.

Results from the multiple linear regression analysis of nitrogen dioxide are presented in the Table 6.2.

Table 6.2 Indicators of nitrogen dioxide (NO_2)

Dependent Variable	Model characteristics	Predicted Variables	B	St Error	(p)
Winter living room	R = 0.17 R^2 = 0.03 F = 5.85	Gas heater	0.34	0.14	0.017
Summer Living room	R = 0.16 R^2 = 0.025 F = 4.4	Air conditioning	- 0.80	- 0.16	0.03 0.09

The variable that influenced significantly the levels of nitrogen dioxide in winter is the use of gas for heating which is associated with increase of the level of nitrogen dioxide with $e^{0.36}$ = 1.4 ppb (2.5 $\mu g/m^3$).

According to the model for summer data, only presence of air conditioning in the house is a significant indicator of nitrogen dioxide which is associated with $e^{-0.806}$ = 0.45 ppb (0.8 $\mu g/m^3$) decrease in the level of nitrogen dioxide.

6.8.3 Factors associated with indoor levels of volatile organic compounds (VOCs)

Since the correlation analysis (see Appendix) indicated significant but week correlation between the different volatile compounds, separate multiple regression models for each compound were needed.

Multiple linear regression analysis was performed to assess the relationship between the studied volatile organic compounds and several important variables, which were likely to affect their levels. These variables include age of the house, combustion appliances, attached garage, new furniture, floor boards or parquet, presence of kerosene and humidifier, fire places, air conditioning, ventilation in the house, new furniture, new painting, and new carpet in the house.

B. *Indicators of benzene*

Benzene is an aromatic hydrocarbon and its main sources are automotive products (motor oils, automotive cleaners), vehicular exhaust, paints, solvents and cigarette smoking.

In order to reduce the skewness of benzene, some outliers were deleted which improved its normal distribution.

The results of the multiple linear regression analysis of benzene, in winter, are displayed in the Table 6.3.

Table 6.3 Indicators of benzene

Dependent Variable	Model characteristics	Predicted Variables	B	St Error	Sign (p)
Winter Benzene	R = 0.72 R^2 = 0.02 F = 1.02	Ventilation	- 0.021	0.02	0.03

The only variable that has a significant effect on benzene is the adequacy of the ventilation in the house. Since the relationship between benzene and ventilation is a positive, it shows that better ventilation in the house is associated with $e^{-0.02}$ = 1 $\mu g/m^3$ decreases of the level of benzene.

According to the study finding, there was no variable, which had a significant influence on benzene concentrations in summer.

C. *Indicators of ethyl benzene*

Ethyl benzene is also an aromatic hydrocarbon and the main sources are solvents, plastics, paints, synthetic rubber and resins.

In order to find any seasonal differences in the variables that might have influenced the concentrations of ethyl benzene, multiple linear regression models for winter and summer were performed (Table 6.4).

The distribution of ethyl benzene for the winter and summer data were very skewed. All possible transformations were used but the normality was improved after deleting 10 outliers and then performing a square root transformation.

From the Table 6.4 is evident that for winter, tobacco smoke is a significant indicator for ethyl benzene with a positive relationship with it. If people smoke inside the house the level of ethyl benzene is associated with an increases of $e^{0.61}$ = 1.8 $\mu g/m^3$.

Table 6.4 Indicators of ethylbenzene

Dependent Variable	Model characteristics	Predicted Variables	B	St Error	Significance (p)
Winter		Smoke inside	0.61	0.24	0.006
Ethylbenzene	R = 0.36	New carpet	0.51	0.24	0.015
	R^2 = 0.11	Humidity	- 0.01	0.007	0.015
	F = 6.24				
Summer					
Ethylbenzene	R = 0.33	Smoking			
	R^2 = 0.06	inside	0.79	0.25	0.05
	F = 2.06	New furniture	0.57	0.12	0.004

New carpet is also a strong indicator of ethyl benzene with a positive relationship with it. The presence of a new carpet in the house is associated with an increase of the concentrations of ethyl benzene with $e^{0.51}$ = 1.6 $\mu g/m^3$.

The last variable entered the model is the average humidity. For every one percent increase in the humidity, the level of ethyl benzene decreases with $e^{-0.010}$ = 1.0 $\mu g/m^3$.

Similarly with the multiple linear regression model for winter data, tobacco smoke is a significant indicator with a positive relationship with ethylbenzene. Smoking inside is associated with an increase the level of ethylbenzene with $e^{0.79}$ = 2.2 $\mu g/m^3$.

The second variable, significantly associated with ethylbenzene is the new furniture, which is associated with an increase of the concentrations of ethylbenzene with $e^{0.78}$ = 2.2 $\mu g/m^3$.

D. *Indicators of toluene*

Toluene also belongs to aromatic hydrocarbons but its presence is more common indoors than the other hydrocarbons. The sources include quite large range as solvents, adhesives, paint, combustion appliances, including tobacco smoke, vinyl floor covering, and chipboards.

Table 6.5 displays the predictors of toluene.

Table 6.5 Indicators of toluene

Dependent Variable	Model characteristics	Predicted Variables	B	St Error	Sign. (p)
Winter Toluene	R = 0.227 R^2 = 0.07 F = 3.7	New carpet	0.29	0.014	0.01

According to the study results, only presence of a new carpet has a significant relationship with toluene for winter data and it is associated with $e^{0.29}$ = 1.3 $\mu g/m^3$ increase of the level of toluene.

E. Indicators of xylenes: m-xylene and o,p-xylene

Xylenes as o,p-xylene and m-xylene are aromatic hydrocarbons The main sources are adhesives, floor covering, dyes, tobacco smoke, kerosene, solvents, and wallpaper.

The multiple regression analysis of o,p-xylene and m-xylene are presented in the Table 6.6.

Table 6.6 Indicators of o,p-xylene and m-xylene

Dependent Variable	Model characteristics	Predicted Variables	B	St Error	Sign. (p)
Winter	R = 0.28				
p-xylene	R^2 = 0.07	Attached garage	0.207	0.106	0.05
	F = 1.35				
m-xylene	R = 0.40	Kerosene			
	R^2 = 0.16	New carpet	0.8	0.4	0.048
	F = 3.07	Smoking inside	0.71	0.36	0.05
		Age of the	0.72	0.26	0.006
		house	0.20	0.098	0.035
Summer	R = 0.26				
p-xylene	R^2 = 0.07	New furniture	0.48	0.22	0.035
	F = 2.12	New painting	0.42	0.19	0.027
m-xylene	R = 0.42				
	R^2 = 0.18	New furniture	0.99	0.39	0.01
	F = 6.3	New painting	1.52	0.33	0.000

There is only one significant indicator of o,p-xylene for winter data which is a garage attached to the house. House with an attached garage is associated with $e^{2.07}$ = 1.2 $\mu g/m^3$ increase of the level of o,p-xylene.

There are four significant predictors of m-xylene for winter data. The first variable is kerosene, which is a strong indicator of the levels of m-xylene. The presence of kerosene heater is associated with $e^{0.8} = 2.2\ \mu g/m^3$ increase of the levels of m-xylene.

The second variable in the model is the presence of new carpet. It is a significant indicator for the concentrations of m-xylene as the presence of new furniture is associated with an increase of the concentrations of m-xylene with $e^{0.7} = 2.0\ \mu g/m^3$.

Smoking inside is the next variable to enter the model and it isassociated with with $e^{0.72} = 2.05\ \mu g/m^3$ increase of the level of m-xylene.

Age of the house has also significant effect on m-xylene levels with $p = 0.035$.

According to the study there are two variable that have a significant influence on the levels of o,p-xylene and m-xylene for summer, which are new painting and new furniture. The presence of new furniture is associated with $e^{0.48} = 1.6\ \mu g/m^3$ increase of the level of o,p-xylene and with $e^{0.99} = 2.7\ \mu g/m^3$ increase of the level of m-xylene. New painting is also a significant predictor for those two variables as new painting of the house increases the level of p-xylene with $e^{0.42} = 1.5\ \mu g/m^3$ and the level of m-xylene with $e^{1.5} = 4.5\ \mu g/m^3$.

F. Indicators of styrene

Styrene is an aromatic hydrocarbon but with quite limited sources compared to others such as xylenes and toluene. The main origin of styrene indoors include plastics, paints, synthetic rubber, and resins.

The results of the multiple linear regression analysis of styrene are presented in the Table 6.7.

Table 6.7 Indicators of styrene

Dependent Variable	Model characteristics	Predicted Variables	B	β	Significance (p)
Winter Styrene	R = 0.40 R^2 = 0.16 F = 2.83	Kerosene New Carpet	1.22 0.64	0.26 0.24	0.000 0.008
Summer Styrene	R = 0.20 R^2 = 0.04 F = 1.28	New painting	0.15	0.06	0.016

According to the study, there are two variables that significantly influence the concentrations of styrene for winter data, which are kerosene and humidifier. The use of kerosene indicates an increase in the level of styrene with $e^{1.22} = 3.3\ \mu g/m^3$ and presence of a new carpet is associated with an increase of the level of styrene with $e^{0.64} = 1.2\ \mu g/m^3$.

For summer data, there is only one significant predictor of styrene, which is a new painting. New painting in the house contributes to the increase of the level of styrene with $e^{0.15} = 1.1\ \mu g/m^3$.

G. Indicators of chlorobenzene

Chlorobenzene belongs to chlorinated hydrocarbons with major sources of solvent and textile additives.

Table 6.8 shows the variables that significantly contribute to the concentrations of chlorobenzene.

Table 6.8 Indicators of chlorobenzene

Dependent Variable	Model characteristics	Predicted Variables	B	St Error	Significance (p)
Winter	R = 0.45	Kerosene	2.22	0.47	
Chlorobenzene	R^2 = 0.17	Attached			0.000
	F = 2.79	garage	0.5	0.19	0.000

For winter data there are two predictors of the concentration of chlorobenzene. Kerosene space heater is the most powerful indicator of chlorobenzene as the use of kerosene is associated with $e^{2.2}$ = 9.2 $\mu g/m^3$ increase of the level of chlorobenzene.

Garage attached to the house is the next variable entered the model. It has a positive relationship with chlorobenzene and it is associated with an increase of the level of chlorobenzene with $e^{0.5}$ = 1.6 $\mu g/m^3$.

There are no variables, which appeared to have significant effect on chlorobenzene during summer.

H. Indicators of 1,3-dichlorobenzene, 1,2-dichlorobenzene and 1,4-dichlorobenzene

The following three compounds 1,3- dichlorobenzene, 1,2- dichlorobenzene and 1,4- dichlorobenzene are halogenated hydrocarbons. Their major sources include consumer products, commercial products and pesticides.

There were no variables found to be significantly associated with 1,3-dichlorobenzene, 1,2 - dichlorobenzene and 1,4 - dichlorobenzene for winter and with 1,2 - dichlorobenzene and 1,4 - dichlorobenzene for summer.

Table 6.9 presents the multiple linear regression analysis of 1,3-Dichlorobenzene for summer.

The only one variable that has a significant relationship with 1,3 - dichlorobenzene is the new painting. A freshly painted house is associated with $e^{0.596}$ = 1.8 $\mu g/m^3$ increase of the concentrations of 1,3 - dichlorobenzene.

Table 6.9 Indicators of 1.3 - Dichlorobenzene

Dependent Variable	Model characteristics	Predicted Variables	B	St Error	Significance (p)
Summer 1,3-dichlorobenzene	R = 0.36 R^2 = 0.12 F = 13.08	New painting	0.60	0.29	0.000

6.8.4 Factors associated with indoor allergen levels of house dust mites

The results from the multiple linear regression analysis of house dust mites are presented in Table 7.0.

In order to improve the normal distribution of house dust mites data, some outliers needed to be deleted.

Table 7.0 Indicators of house dust mites in winter

Dependent Variable	Model characteristics	Predicted Variables	B	St Error	Significance (p)
Winter House dust mites	R = 0.31 R^2 = 0.1 F = 1.47	Number of people live in the child's room	0.24	0.24	0.003

There is only one predictor of house dust mites for winter data, which is the number of people who shared the child's bedroomt. The regression coefficient indicates that with every second person that lives in the child's bedroom the allergen level of house dust mites is associated with $e^{0.24}$ = 3 $\mu g/gm$ increase.

There are no variables that appeared to have a significant effect on the allergen level of house dust mites for summer.

6.8.5 Factors associated with indoor levels of particulate matter (PM_{10})

Multiple linear regression analysis of particulate matter (PM_{10}), winter, is displayed in Table 7.1.

For winter data, there are two predictors of the concentrations of particulate matter, smoking inside and presence of carpet. Smoking inside the house is associated with $e^{0.49} = 1.6\ \mu g/m^3$ increase of the concentrations of the particles. Presence of carpet is related to an increase of the indoor concentrations of particulate matter (PM_{10}) with $e^{0.34} = 1.4\ \mu g/m^3$.

Table 7.1 Indicators of particulate matter (PM_{10})

Dependent Variable	Model characteristics	Predicted Variables	B	St Error	Significance (p)
Winter	R = 0.25	Smoking			
Particulate	R^2 = 0.05	inside	0.49	0.21	0.02
Matter	F = 5.75	Carpet	0.34	0.17	0.048

There are no variables that showed to have significant association with the level of particulate matter for the summer data.

6.9 The public health impact

Since the domestic exposure to formaldehyde, benzene, toluene, and house dust mites predicted the likelihood of childhood asthma, it is useful to estimate the potential public health impact of the levels of indoor air pollutants. In order to assess the potential impact of the indoor air pollutants a population attributable risk proportion (PARP) was calculated (see Chapter 5). All estimates for the

PARP were calculated using odds ratios from the multivariate model. Table 7.2 displays the population attributable risk proportions.

Table 7.2 Population Attributable Risk Proportions (PARP)

Measures of exposure	PARP*	95% CI
Formaldehyde >100 µg/m^3	8.57	0.49 - 17.36
Benzene > 50 µg/m^3	3.57	0.01 - 7.54
Toluene > 50 µg/m^3	5.95	0.89 - 11.01
Dust mites > 1.0 µg/gm	42.86	23.65 - 62.06

- All values are percentages

The results in Table 7.2 suggest that approximately 8.6% of childhood asthma can be attributed to domestic exposure to formaldehyde.

According to the results for benzene (Table 7.2), of all asthmatic children, approximately 3.6% suffer from asthma as a consequence of exposure to benzene levels higher than 50 µg/m^3.

Exposure to toluene appeared to be also a significant predictor for asthma. The estimation of population attributable risk proportion indicates that almost 6% of childhood asthma can be attributed to indoor exposure to toluene with concentration higher than 50 µg/m^3.

It has been proposed that exposure to dust with concentrations of house dust mite allergen Der p 1 greater than 2 µg/gm is a risk factor for the development of asthma and that exposure do dust with an allergen concentration greater 10 µg/gm is a risk factor for acute attacks of asthma (Platts-Mills T, 1989), although Price (1990) proposed lower thresholds. The present study shows that 42.8% of

childhood asthma can be attributed to exposure to house dust mite with allergen level greater than 1 μg/gm (Table 7.2).

CHAPTER SEVEN

DISCUSSION AND CONCLUSION

7.1 Introduction

This Chapter discusses the findings of the study within three sections, namely, indoor environmental risk factors for asthma, house characteristics, and indoor environmental risk factors for respiratory symptoms. The final section of this Chapter describes the conclusions of the study findings and gives some recommendations for further research.

Before discussing the findings, the reliability of the questionnaire is assessed, and also the representativeness of the series of cases and controls is considered as this has a fundamental influence on the validity of the results.

7.2 Reliability assessment of the questionnaire

The questionnaire used in the present study was designed on the base of the standardised questionnaire of the American Thoracic Society. In order to assess the reliability of the questionnaire in Australia, which has a different climate and culture, a test-retest was conducted. The reliability assessment was conducted

on nine questions, which were considered to be the most important. The number of the children involved in the test-retest was 20. Statistical analyses used for assessing the reliability of the questionnaire were proportion of agreement (%), the McNamar test, and Kappa coefficient.

The reliability assessment of the questionnaire on respiratory symptoms is presented in Table 7.3

Table 7.3 Reliability assessment of the questionnaire used in the study

Questions	a	b	c	d	PA (%)	McNemar Test	Kappa Coefficient
During the last month, has your child had runny nose?	14	3	2	0	73.7	1.000	- 0.144
During the last month, has your child had cough?	16	1	2	0	84.2	1.000	- 0.075
During the last month, has your child had wheeze?	9	1	2	7	84.2	1.00	0.681
During the last month, has your child had hayfever?	15	1	1	2	89.5	0.250	0.604
During the last month, has your child had eczema?	17	1	0	1	94.7	1.000	0.641
During the last month, has your child had allergies?	8	3	5	3	57.9	0.726	0.105
Does anybody currently smoke inside the house – parents or other family members?	13	3	1	2	26.3	0.625	0.377
Does anybody currently smoke inside the house – visitors?	14	3	2	0	73.7	1.000	0.144
Do you use gas for cooking?	5	2	1	11	84.2	1.000	0.650

Number of study subjects (N) = 20; "a" and "d" are numbers of agreement; "b" and "c" are numbers of disagreement; "PA" is the proportion of agreement.

The results showed that seven questions have a proportion of agreement between 73.7% and 94.7% and only two questions have lower values of 26.3% and 57.9%.

The Kappa coefficients of those two questions are 38% and 10%, respectively, which values represent poor agreement.

The wide range of Kappa coefficients (- 0.144 to 0.681) found in this study may be due to instability of the Kappa coefficient under certain conditions, which are referred to as limited variation. According to Haas (1991), the limited variation occurs when there is a large proportion of agreement: greater than 85%. As can be seen from Table 7.3, six out of nine questions have a proportion of agreement greater than 84%. Thus, according to Scwartz (1994), the Kappa becomes unstable and inappropriate as a reliability measurement in case of a large proportion of agreement. Although the limitations of Kappa, there is no other alternatives for assessing reliability of a questionnaire.

7.3 Validity of research

In a case – control study the threats to validity are numerous and mainly arise from the potential for bias related to the selection of subjects and the collection of data. The following provides an overview of the potential various threats to the validity.

It is acknowledged that the selection of the case and the control groups could generate selection bias. The cases were identified through the Accident and Emergency Department at Princess Margaret Hospital for Children however according to statistics, 80% of the children within the Perth Metropolitan area attend the Accident and Emergency Department at Princess Margaret Hospital for children which could minimise the selection bias, generated through the selection process of the study subjects.

A further source of selection bias in this study may arise from refusal of cases or selected controls to participate in the study. Two strategies were employed throughout the data collection phase in order to minimize this possibility. First, to ensure maximum participation by control subjects the author prepared a

A further source of selection bias in this study may arise from refusal of cases or selected controls to participate in the study. Two strategies were employed throughout the data collection phase in order to minimize this possibility. First, to ensure maximum participation by control subjects the author prepared a personal invitation to the parents or guardians. Second letters of encouragement from the Health Department and Princess Margaret Hospital for Children supported the written invitation. If participation by the respondents was not forthcoming on the first contact, a second strategy of making telephone calls at different time in the day was employed.

The validity of the diagnosis of asthma may also have introduced a bias (observation or information) due to the young age of the study subjects and the difficulty differentiating wheezing illnesses in this age-group. However, had many cases not been asthmatic and many controls under diagnosed, it is unlikely that the study would have shown that atopy and family history of asthma increase the risk of asthma.

Further sources of information and selection bias could be introduced from the cover letter sent to the parents or guardians, which explains the nature of the study. Although detailed information of the study has not been provided, it could generate such a bias.

It is acknowlwdged, that selection of young children with mild asthma but not diagnosed with asthma could have been recruited as control subjects, it is a limitation of the study.

Due to time and resourse restrictions, single measurements of the temperature and the relative humidity have been performed, which is also a limitation of the study.

Because children may be unable to cooperate adequately with physiological testing and, for reasons of feasibility, epidemiological studies of childhood

asthma have tended to use questionnaires as the most widely used method for classifying subjects as affected (Tinkelman, 1993).

The questionnaire used in the present study was a standardised questionnaire based upon the questionnaire of the American Thoracic Society. It included questions on major respiratory symptoms and questions related to asthma but it is likely that the questionnaire does not cover all symptoms of this complex disease. Also, questionnaire responses may be a subject to recall or observation biases. Even with the use of a standardised questionnaire of respiratory symptoms, parents may apply different interpretations of the symptom questions in reporting their children's symptoms.

Confounding bias may also occur when an environmental factor (confounder), which is associated with the exposure of interest, is also associated with the development of asthma, independently of the exposure. Thus, the confounding variable may underestimate or overestimate the association between exposure and outcome. There are several statistical methods available to control confounding such as standardisation, the Mantel-Haenzel method, and the logistic regression analysis. The present study used logistic regression analysis, which provided adjusted estimates of the odds ratio. There are also other factors that were not measured in the present study but could distort the estimation of the exposure effects. In order to control the effect of the potential extraneous variables, multivariate analysis were used in the study.

In terms of the external validity, Western Australia has specific climate conditions, which may lead to limitation of the generalization of the study results to populations in other countries, and even to populations in other states in Australia.

Finally, the validity of the study could have been eroded as a direct consequence of the unreliability of the recorded data. To ensure reliability of the data, quality control measures were instituted by the author in the collection of the data.

Furthermore, the coding of the data was undertaken consistently by the author, with minimal misclassification.

7.4 Discussion of the findings

7.4.1 Risk factors for asthma

Asthma is a considerable health burden in western societies and there is evidence that it may increase in young children (Magnus, 1997). Although epidemiological studies have given insight into the risk factors that may be associated with the increased incidence of asthma, the aetiology of asthma remains unclear. Genetic factors appear to be important for determining the risk for asthma in an individual but cannot be responsible for the observed increased prevalence. Environmental exposure in early life that affect immune maturation appear to be key factors for the development of asthma. The indoor environment is a likely candidate since infants spend about 90% of the time indoors at a time when immune deviation usually occurs. Therefore, interactions between genetic and environmental factors are most likely to explain differences in prevalence worldwide. In this context, it is of paramount importance to establish the environmental factors that influence the development of asthma in predisposed individuals.

Most of the potential risk factors for childhood asthma considered in the present study have been studied before. According to the logistic regression model for winter data, atopic status was strongly associated with asthma with an odds ratio (OR = 3.29; 95% CI: 1.47 – 7.33) and this is in agreement with previous studies (Burrows, 1989; Claire Infante-Rivard, 1993). According to Marsh (1981) atopic individuals characteristically enhanced formation of specific IgE antibody after exposure to antigens. Although many studies have demonstrated a relationship between atopy and asthma, the mechanistic pathways, either casual or noncasual, that link atopy and asthma are not well defined. Nevertheless, atopy in children

does predict increased risk of asthma, and its presence or absence may be used as an empiric predictor (Tinkelman, 1993).

In the present study, family history of asthma also appeared to be an independent risk factor for asthma with odds ratio OR = 2.82 (95% CI 1.34 – 5.95) and this is generally consistent with previous findings. Leeder and colleagues (1976) evaluated a cohort of 200 children from birth to age five years and found that the incidence of asthma increased from 2.5 percent if neither parent had asthma to 5.4 percent if one parent had asthma. Similar findings were reported by Lebowitz (1984) in a study of 344 families from Tucson, Arizona. When neither parent had asthma, 6.5 percent of the children had physician-diagnosed asthma; when one or both parents had asthma, 19.7 percent and 63.6 percent of the children had asthma, respectively. Studies of the familial aggregation of asthma in general population samples indicate a strong familial influence on the prevalence of childhood asthma, but do not separate genetic from environmental effects.

Investigations to date do not provide consistent results concerning child's gender as a predictor of asthma. Rackemann and Edwards (1952) described the clinical course of 688 asthmatic children selected from a private practice and followed over 20 years. They found that boys and girls did not differ in the status of asthma. Gortmaker and colleagues (1982) had similar results. The present study found that boys are at higher risk for the development of asthma with odds ratio of OR = 2.55 (95% CI: 1.05 – 6.17) and this result is consistent with the study findings of Schenker (1983), Kaplan (1985) and Melia (1982). A difference in airway geometry in boys and girls is one explanation for the male excess. Taussig (1977) measured expiratory flow rates in 65 normal children and found lower flow rates in boys. This finding, together with other observations (Doershuk, 1974) made Tinkelman (1993) to suggest that boys tend to have smaller airways at a given lung size than girls.

Among the housing characteristics, the presence of air conditioning and fireplaces appeared as protective factors for asthma with odds ratios, OR = 0.28

(95% CI: 0.12 – 0.62) and OR = 0.32 (95% CI: 0.18 – 0.90), respectively. Air conditioning may improve the ventilation inside the house and consequently may reduce the exposure levels of indoor air pollutants. Also, the presence of an air conditioner can maintain a good and healthy indoor climate. The observed protective effect of fireplaces may be confounded by other underlying relationships or may not have any casual pathway.

The use of a humidifier has a marginally significant effect (p = 0.06) on asthma with an odds ratio of OR = 2.77 (95% CI: 0.95 – 10.51). A few studies have observed the effect of humidifier on respiratory symptoms and found that if a humidifier is not well maintained and cleaned, it can be a reservoir for infectious and allergenic agents such as bacteria and fungi (Burge, 1990; Solomon, 1990). Also, a humidifier may be a moisture source that subsequently leads to condensation and biologic growth on colder surfaces. According to Pollart and colleagues (1988) high humidity and moderate temperature are conditions favoring the growth of mites.

As it was explained in the Chapter 5, nitrogen dioxide was monitored in the child's bedroom and in the living room. The logistic regression models for both rooms are quite similar (Chapter 6) except that nitrogen dioxide appeared to have significant but negative association with asthma in the model for the child's bedroom. The Education Programs that the Asthma Foundation and the Health Department organise among the community, especially for families with children, who suffer from asthma, are more likely to explain these findings. These programs, along with the information regarding the triggers and the risk factors for asthma, also include recommendations to use electricity for cooking and heating, instead of gas appliances, especially unflued gas heaters. These educational programs are likely to explain the study findings that more controls (87%) than cases (83%) used gas for cooking and heating while families with asthmatic children use more electric appliances (62%) than those with non-asthmatic (56%). Also, seven percent of the controls reported to use kerosene

space heaters, whilst none of the asthmatic children seemed to be exposed to kerosene (0%).

The fact that nitrogen dioxide appeared only in the regression model for the child's bedroom, the poor ventilation in this room is likely to be one of the explanations. Fifty six percent of the families reported to have very good ventilation in the living room, compared to 32 percent in the child's bedroom. Furthermore, 7.3 percent of the participants indicated that they had very poor ventilation in the child's room, compared to 2.6 percent in the living room. In addition, higher nitrogen dioxide levels (>100 ppb) were measured in the child's bedroom among 63 percent of all families, compared to 41 percent who had such high levels in the living room. According to the World Health Organisation the recommended maximum one-hourly exposure level to NO_2 is 100 ppb, which was recently changed from 212 ppb (WHO, 1996).

The present study found that domestic exposure to formaldehyde during hot months, is a significant risk factor for asthma in children and this finding agrees with other studies (Quackenboss, 1989; Norbäck, 1995; Wieslander, 1997). Krzyzanowski and colleagues (1990) found that prevalence rates of asthma and chronic bronchitis in children were significantly greater for children exposed to formaldehyde levels above 60 ppb (69 $\mu g/m^3$) in the home. In a recent study of Franklin and colleagues (2000) it was reported that domestic exposure to formaldehyde might invoke an inflammatory response in the airways of healthy children. Formaldehyde concentrations in the study houses were reasonably low, with a total of seven samples exceeding 120 $\mu g/m^3$, which is the National Health and Medical Research Council (Australia) recommended guideline for maximum permissible level within domestic premises and schools (NHMRC, 1982). Despite the low formaldehyde exposure levels found in the present study, indoor formaldehyde appeared to be a significant risk factor for asthma in this study population with odds ratio OR = 1.02. For children exposed to formaldehyde at levels equivalent to 120 $\mu g/m^3$ (100 ppb), the likelihood of having asthma increases by 35%. Given that, the prevalence of atopy in the control group was

50%, (slightly higher than in other Australian population 41%) (Kendall, 1998) the effect of formaldehyde exposure is likely to be an underestimate. It is important to notice that formaldehyde results were not confounded for other factors considered to be potentially risk factors for asthma such as combustion sources, age, gender, family history of asthma, atopy, pets, family size, parent's educational level, and house dust mites.

Two experimental studies have shown that volatile organic compounds may affect the airways and induce inflammation (Koren, 1992; Harving, 1991). Two recent studies have demonstrated a significant relationship between asthma and exposure to volatile organic compounds (Norbäck, 1995; Weislander, 1997). These results are consistent with the findings of the present study that toluene and benzene are significant predictors of asthma with odds ratios of OR = 1.09 95% CI: 1.02 – 1.16) and OR = 1.07 (95% CI: 1.03 – 1.11), respectively. According to Lansari (1992) potential source of benzene is the use of contaminated water in showers. Generation of VOCs from gas and electric heating units, consumer products and from building materials has also been studied (Zweidinger, 1991; DeBertoli, 1986).

Since indoor air pollution has been identified as a critical problem affecting children's health worldwide there is a need for further information on adverse health effects from indoor environmental irritants. Entrance of air pollutants into the body is usually through the respiratory tract and environmental irritants such as formaldehyde and volatile organic compounds are capable of direct acute and chronic health effects within the respiratory tract itself, depending upon the pollutants and its deposition site (Brooks, 1992). Obviously, the respiratory tract is an important asset that requires protection. Future research should increase the understanding about which health effects occur after exposure to average pollutant concentrations found in the house, and which result from exposure to higher concentrations for short periods of time.

In the present study, exposure to house dust mite appeared to be a very strong predictor of asthma and this result is consistent with previous findings (Platts-Mills, 1992; Sporik, 1992). The World Health Organization has recognized domestic mite allergy as a universal health problem and it has become of great importance for future research to establish which environmental factors lead to an increase the amount of house dust mites.

The present study found that spending longer hours outside protects children from developing of asthma with ($p = 0.004$). Children exposed to fresh air with less allergens and pollutants are likely to have less probability of having asthma compared to those who spend most of their time indoors.

7.4.2 House characteristics associated with indoor air pollutants

The literature suggests (Maroni, 1995) that the sources of indoor air pollution include oil, gas, kerosene, coal, wood, tobacco products; building materials and furnishings, asbestos containing insulation, wet or a damp carpet, furniture made of certain pressed wood products; products for household cleaning and maintenance, personal care, or hobbies; central heating, cooling systems and humidification devices. The relative importance of any single source depends on how much of a given pollutant is emitted and how harmful those emissions could be. Furthermore, when there is a little infiltration, natural ventilation, or mechanical ventilation, the air exchange rate is low and pollutant levels can increase.

In the present study, indoor concentrations of formaldehyde were measured in the child's bedroom and in the living room on two occasions over 12 months, winter and summer. The study results showed that presence of gas heaters has a significant influence on formaldehyde levels and this result is consistent with the findings of Maroni and colleagues (1995). Presence of carpet also appeared to affect the levels of formaldehyde significantly. Carpet in a house can absorb

formaldehyde and later start releasing it in the air under particular conditions such as high temperature and low ventilation.

Other organic pollutants that were monitored in the study were volatile organic compounds (VOCs). According to the study findings, benzene as a volatile compound was significantly affected only by the ventilation rate inside, as good ventilation helps to reduce the indoor levels of benzene. The regression model showed that there were some more variables that might have affected the level of benzene but are not included in the model. One possible explanation is that indoor concentrations of benzene are more likely to be influenced from outdoor sources.

The second aromatic hydrocarbon, which was measured, was ethylbenzene. The present study found that the presence of a new carpet and new furniture significantly affect the levels of ethylbenzene and the results are consistent with the findings of the U.S Environmental Protection Agency (1987). The study also found that smoking inside influences the concentrations of ethylbenzene.

Furthermore the study found that the presence of new furniture and new painting significantly affect the indoor levels of m-xylene and p-xylene, which results are in agreement with the findings of U.S Environmental Protection Agency (1987).

The literature suggests that combustion appliances, which include kerosene, gas heaters, fireplaces, and gas stoves, are the main sources of aldehydes and hydrocarbons (U.S.EPA, 1987). The present study also found that these appliances are significantly associated with the levels of toluene, xylenes, styrene and chlorobenzene.

Weislander and colleagues (1997) stated that indoor painting is related to increased indoor concentration of volatile organic compounds, which is in agreement with the present study finding. Recently painted surfaces appeared to

have significant effect on the levels of volatile organic compounds and in particular, styrene, 1,3 – dichlorobenzene, m-xylene and o,p-xylene.

A study by Norbäck (1990) showed that the VOCs concentrations are higher at higher room temperatures. During summer, when the ventilation rate is low and the temperature is high, the emission rates of VOCs increase. This finding is consistent with the results of the present study, which found a significant, positive relationship between indoor temperature and levels of volatile organic compounds (in particular chlorobenzene, styrene and toluene).

The next indoor air pollutant monitored in the study was nitrogen dioxide. Generally NO_2 is emitted from indoor combustion sources, including tobacco smoke, gas appliances, kerosene heaters, and fireplaces (Maroni, 1995). The present study found that during winter the use of gas for heating significantly increases the levels of nitrigen dioxide which is in consistency with other study (Devalia, 1994). According to the study findings, during summer families who use air conditioning are exposed to lower levels of nitrogen dioxide. This result explains that households with better ventilation are more likely to have lower levels of pollutants.

Airborne particulate matter (PM) represents a complex mixture of organic and inorganic substances. Combustion sources, including gas appliances and tobacco smoke, are probably the major indoor generators of fine-mode particles. Sprays and cooking aerosols may also contribute to the total concentration (Maroni, 1995). These findings agree with the study results that smoking inside and presence of carpet significantly increase the levels of particulate matter indoors.

House dust mites are the most common potential indoor allergen and mites can be found in floors and tend to bury themselves deep in carpets, mattresses, and soft furnishings (Platts-Mills, 1992; Sporik, 1992). The study found that the number of people who shared the child's bedroom appeared to have a significantly positive relationship with the allergen levels of house dust mite.

7.4.3 House characteristics

Nowadays people in the western countries live in homes, which have been carpeted, heated, cooled, and humidified to make them energy efficient. Thus, the houses become an ideal habitat not only for domestic mites bit some other insects, molds and bacteria. Furthermore, with the modern construction techniques, indoor air pollution can be greater than outdoors.

According to the study results 55 percent of all families who participated in the study reported the use of gas appliances and more controls than cases were exposed to them. Furthermore, none of the families with asthmatic children used kerosene, while 7 percent in those of controls reported having kerosene space heaters. Thus, it is evident from the study results that cases try to avoid the use of gas for heating and cooking as 61 percent of the case subjects used electricity for cooking compared to 55 percent of the control subjects.

Although some studies report an association between using a humidifier and risk of asthma (Burge, 1990; Solomon, 1990; Infante-Rivard, 1993), there is still a belief among the public that some humidity is necessary to avoid respiratory illness in children. In this study, more cases (17%) compared to controls (10%) reported to have a humidifier in the house but the difference was not significant ($\chi^2 = 1.7$;df = 1; p = 0.19).

Ventilation modification is often used to correct or prevent indoor air quality problems. If too little outdoor air enters a home, pollutants can accumulate to levels that can pose health and comfort problems. Also houses, which have a relative humidity level below 60 percent, are likely to have very little house dust mite and mould growth. This low level of humidity can be achieved with good ventilation. Coastal regions in Australia have humid ambient climate and only good ventilation inside the house could maintain high indoor air quality. In the present study, only 40 percent of all studied families reported to have air

7.4.4 Characteristics of the study children

The mean age of case subjects was 24 months and 15 days and of controls 19 months and 18 days and a possible explanation of the age difference is that the childhood asthma is more likely to occur and develop at older age.

In the study the male: female sex ratios were 1.53:1 and 2.26:1 in cases and controls, respectively. Investigations to date do not provide consistent results concerning child's gender as a predictor of outcome. This study similar as others (Schenker, 1983; Kaplan, 1985; Melia, 1982) found that childhood asthma is more prevalent in boys than girls. Contrary, some other studies (Rackeman, 1952; Blair, 1977; Infante-Rivard, 1993) didn't find that boys were at increased risk of asthma.

Epidemiological studies indicate that asthma and atopy are linked (Weiss, 1985), although the relationship between atopy and asthma is quite complex. Burrows and colleagues (1976) used skin tests to assess the atopic status of the children, selected at random in Tucson. The results showed that skin test reactivity was strongly associated with the attacks of wheezing. Further analysis of data from the Tucson population showed that the prevalence of asthma is more strongly associated with level of IgE than skin-test reactivity (Burrows, 1989). In the present study, the atopic status of the children was assessed by skin prick tests and the difference in the atopic status between asthmatic and non-asthmatic children was significant (χ^2 = 10.6;df = 1; p = 0.001) as more cases were defined as atopic (72%) compared to controls (50%).

7.4.5 Indoor environmental risk factors for the respiratory symptoms: wheeze, hay fever, runny nose, and cough.

Wheeze is a classical sign of asthma and it is associated with asthma disorders. This could explain the study finding of the significant difference (p = 0.000) in the frequency of wheeze between asthmatic and non-asthmatic children (See

Chapter 6.3.2). Also, a significant seasonal variation ($p < 0.01$) in wheeze was found in the study.

In the logistic regression model for wheeze, age and gender of the study subjects appeared to be significant factors for this respiratory disorder with odds ratios of OR = 1.07 (95%CI: 1.02 – 1.12) and OR = 1.98 (95%CI: 1.01 – 3.89), respectively. Age and gender of the study subjects were also significant factors for asthma.

According to the study, high humidity significantly affects the wheeze in young children with odds ratio of OR = 1.04 (95% CI: 0.27-1.07). Problems of condensation and dampness in the house are a common cause of the complaint. There is widespread public concern that housing is a cause of respiratory ill health (McCarthy, 1985) and dampness is perceived as a public health issue (Martin, 1987).

Exposure to house dust mite and p-xylene had only a marginally significant effect on wheeze.

During summer, domestic exposure to formaldehyde and benzene appeared to be significantly associated with wheeze with odds ratios of OR = 1.02 (95% CI: 0.99 – 1.04) and OR = 1.02 (95% CI: 0.99 – 1.03), respectively, which results are similar to those for asthma. The similarity between the risk factors for asthma and wheeze confirms that wheeze is a symptom closely related to the asthma disorder.

Hayfever is an allergic condition and it has also been associated with asthma. This agrees with the study finding that more cases (28.4%) than controls (6.8%) reported to have hayfever and the difference was significant ($p \leq 0.001$). Domestic exposure to toluene and benzene significantly contributes to this symptom with odds ratios of OR = 1.02 (95% CI: 1.00-1.03) and OR = 1.05 (95% CI: 1.02 – 1.08) respectively. Toluene and benzene also appeared in the logistic regression analysis for asthma.

According to the study, indoor temperature is significantly associated with hayfever with odds ratio of OR = 1.36 (95% CI: 1.10 – 1.68). Higher temperature helps to release some indoor pollutants into the air and hence can increase their indoor concentrations. It is well known that house dust mites required particular conditions of temperature and humidity in order to grow, as the optimum conditions are 25^0C and 70% - 80%, respectively.

The presence of carpet seemed to be a very powerful indicator for hayfever with odds ratio of OR = 5.54 (95% CI: 1.12 – 27.32). Since carpet is a potential reservoir for house dust mites and many other bacteria, these may provoke hayfever, which is an allergic disorder.

Exposure to gas heaters is also a significant factor (OR = 1.98; 95% CI: 0.77 – 5.08) for hayfever, which relationship could be confouded by age, attendance of day care and some other confounding factors. Epidemiological studies suggest that children who are exposed to combustion contaminants from gas appliances have higher rates of respiratory symptoms and illness than other children (WHO, 1987). According to the World Health Organisation, only children who already have respiratory disorders are likely to be sensitive to the effects of nitrogen dioxide. Exposure levels can be greatly reduced by opening the windows, having an extractor fan, and conducting regular maintenance of gas appliances.

As hayfever is an allergic disorder, it is understandable why allergy to pets is the strongest indicator with the odds ratio of OR = 23.82 (95% CI: 3.93 – 206.76). Cat and dog allergens become airborne and are easily inhaled because they are carried on flakes of dry skin and dried saliva. Because of the small size of the flakes, they can remain airborne for hours, and high levels can therefore continue to exist for very long periods even after the pets have been removed. Regular washing of the pets, removing the carpet and thorough cleaning of dust-collecting surfaces may help to reduce the airborne pets allergens.

The next respiratory symptom, considered in the present study is the runny nose. This symptom is usually associated with colds but it also may originate from an allergy. The present study found that children who have first-degree relatives with asthma are at higher risk of runny nose. Also, exposure to volatile organic compounds appeared to contribute significantly to the symptoms of runny nose. The study found that domestic exposure to ethylbenzene and 1,4 – dichlorobenzene are significant risk factors for this respiratory symptom with odds ratios of OR = 1.20 (95%CI: 1.00 – 1.43) and OR = 1.02 (95%CI: 1.00 – 1.45), respectively. These two volatile organic compounds are recognised eye and respiratory tract irritants, so they could provoke runny nose in susceptible individuals (Tucker, 1988; Dreisbach, 1980; Turiel, 1985). Spending longer hours outdoors seems to protect children from developing a runny nose with odds ratio of OR = 0.28 (95% CI: 0.08 – 0.97). According to the study, spending more than 2 hours a day outdoors is a protective factor for asthma as well.

Cough is the last studied respiratory symptom in children. The study found that more asthmatics (98%) than non-asthmatic subjects (73%) reported having a cough. According to the study, attending a day care centre significantly increases the likelihood of having a cough with the odds ratio of OR = 3.35 (95% CI: 1.20 – 9.34).

As it was mentioned previously, the domestic exposure to benzene is a significant risk factor for asthma, wheeze and hayfever in young children. The present study found that this pollutant significantly contributes to having a cough with odds ratio of OR = 1.04 (95% CI: 1.14 – 4.60). Since benzene is a well known irritant, exposure to benzene may results in provoking a cough in children.

The present study found that children who are defined as atopic are at significantly greater risk of having cough with odds ratio of OR = 2.3 (95% CI: 1.14 – 4.60) compared to those who did not show a positive reaction to common allergens. It has been acknowledged that the atopic children are more vulnerable to the effects of exposure to indoor contaminants.

The presence of air conditioning seems to protect children significantly from asthma as well from having a cough with OR = 0.52 (95% CI: 0.27 – 1.00). If air conditioning is well maintained it could bring more fresh air inside and decrease the level of indoor contamination.

Exposure to particulate matter and house dust mites have only marginally significant effects on cough with p = 0.06 and p = 0.056, respectively.

7.5 Conclusions and recommendations

In the last several years, scientific evidence has indicated that the air within homes and other buildings can be more seriously polluted than outdoor air in even the largest and most industrialized cities. Nowadays people spend approximately 90% of their time indoors, thus for many people the health risks may be greater due to exposure to air pollutants indoors than outdoors. The locations of highest concern are those involving prolonged, continuing exposure, which are the home, the school, and the workplace. People who may be exposed to indoor air pollutants for the longest period of time are often children, elderly people, and the chronically ill.

Children require special protection because they are more vulnerable to the effects of environmental hazards. They receive greater exposure per unit of body weight than adults, and they are more susceptible to their effects because of the immature and developing systems (Maroni, 1995).

Today children live in an environment that is vastly different from that of a few generations ago. Economic development, increasing urbanization and industrialization have increased the risk of exposure to indoor environmental hazards. While pollutant levels from individual sources may not pose a significant health risk by themselves, most homes have more than one source that contributes to indoor air contamination. These include combustion sources such

as oil, gas, kerosene, coal, wood, and tobacco smoke; building materials and furnishings, wet or damp carpet, furniture made of certain pressed wood products, products for cleaning and maintenance, personal care, or hobbies, central heating and cooling system; and outdoor sources such as radon, pesticides, and outdoor air pollution. Thus, there can be a serious risk from the cumulative effects of contaminants from these sources.

According to the study finding, domestic exposure to formaldehyde and volatile organic compounds (benzene and toluene) increase the risk of asthma in young children. Due to extensive use in numerous manufacturing processes and building materials, formaldehyde is probably the most recognised indoor volatile organic compound. The predominant route of exposure to formaldehyde in the home is through inhalation, so it primarily affects the airways. Thus, in order to avoid exposure to higher levels of formaldehyde, which may lead to adverse health effects, people need to minimize all products that are releasing formaldehyde in the indoor air. Carpet and chipboards are products that absorb formaldehyde and may also start to release this pollutant into the air under particular conditions. Overall levels of formaldehyde can be lower if more fresh air goes into the home by opening doors and windows and installing an exhaust fan. Low levels of humidity can also help to reduce indoor formaldehyde levels.

Among the other indoor environmental factors, that appeared to be predictors of asthma, is the allergen levels of house dust mite. The presence of air conditioning at home and spending longer hours outdoors have a significant protective factor for asthma.

The results of the study confirm the role of susceptibility factors in asthma and show that indoor environmental factors contribute as risk factors for asthma in early childhood. Since the quality of the indoor environment is potentially modifiable there might be opportunities for intervention to reduce asthma symptoms. Furthermore, the observation that exposure to formaldehyde, benzene, and toluene in early childhood is associated with asthma suggests the

possibility that irritants in indoor air might be involved in the initiation phase of asthma.

The World Health Organization European Centre for Environment and Health has recognised the need to set the priority research in environmental epidemiology. An International Workshop held in 1993 identified the following health outcomes as the most important for assessment:

1. Incidence and development of various states of asthma;
2. Incidence of disease of the lower respiratory system in children, especially prior to age six; and
3. Development and exacerbation of chronic respiratory disease and disorders that obstruct the respiratory passage.

The workshop has pointed out that diseases of the respiratory system are of primary concern when the health effects of exposure to indoor and outdoor air are concerned.

It is always better to prevent an illness rather than use medicines to treat symptoms once the illness has developed. This is especially true for asthma, where inflammation of the airways develops. A healthy indoor environment with a low allergen level and low concentrations of indoor air pollutants such as formaldehyde, volatile organic compounds, carbon dioxide may prevent the development of allergies and airway inflammation in the first place.

Usually the most effective way to improve indoor air quality is to eliminate the sources of pollutants or to reduce their emission.

Another approach to lowering the indoor levels of air pollutants in the house is to increase the amount of outdoor air coming indoors. Good healthy indoor air quality needs a good background level of ventilation in the house at all times with extractor fans in bathroom, kitchen and laundry areas. Opening windows and doors or running air conditioner increase the outdoor ventilation rate. Kitchen or

bathroom fans that exhaust outdoors remove contaminants directly from the room where the fan is located and increase the outdoor air ventilation rate. During winter the house needs to be heated in order to reduce the condensation and maintain adequate ventilation. Also it is important to reduce all places where allergen levels are possibly high. This may require changes the indoor environment as removing the carpet, changes to furnishings, keeping pets outside and any sources, which could increase the relative humidity.

The next important step is to educate the general public about asthma and indoor air quality. This includes promoting awareness and education regarding indoor air quality and the benefit of cleaner and healthy indoor environment. In addition, to provide guidelines to susceptible individuals to help them to reduce the risk of adverse health effects related to indoor air pollution.

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Appendices

Appendix A

FORM OF CONSENT

I,.....

Given names Surname

have read the information explaining the study entitled **"Indoor environmental risk factors for childhood respiratory symptoms and asthma"**

I agree to

allow.....

(full name of participant and relationship of participant to signatory)

.....

to participate in the study.

I understand my child may withdraw from the study at any stage and withdrawal will not interfere with routine care.

I agree that research data gathered from the results of the study may be published, provided that names are not used.

Dated.....day of.....19

PARENT OR GUARDIAN'S SIGNATURE.....

I, ... have explained the above to the (Investigator's full name)

signatories who stated that he/she understood the same.

SIGNATURE.....

Appendix B

INFORMATION SHEET FOR PARENTS

Dear Parent/Guardian,

We would like to invite you to participate in a study to investigate some indoor environmental factors affecting childhood respiratory symptoms and asthma. We are looking for asthmatic babies and young children aged between 6 months and 3 years old, who have admitted Princess Margaret Hospital with asthma attack.

The research project which we are carrying out in conjunction with the Respiratory Medicine Department at Princess Margaret Hospital and the Health Department of Western Australia aims to improve our knowledge about the possible link between substances which may be present in the indoor air and the development or aggravation of asthma among young children. The type of substances that we are interested in come from sources such as gas cooking or heating and vapors from new furniture and carpets.

The research project has been divided into two stages described below.

The first stage involves completing a questionnaire, which will give us information about your child's health history and status and his/her home environment. The completion of the questionnaire will take you about 5 minutes.

The second stage involves indoor air monitoring and medical assessment of your child.

Indoor Air Monitoring

The air will be measured in your home twice per year, once in the summer and once in the winter. Air samples will be collected from the living room and the child's bedroom. A researcher will contact you to make a visit in your home at a time convenient for you. Each visit to make the measurements should take no more than 15-20 minutes.

Child Medical Assessment

The assessment will include a skin prick test to determine the reactivity to some common allergens, which may be related to respiratory symptoms. These tests are safe and do not cause discomfort apart from slight itching that goes away after few minutes.

We would be most grateful if you would be prepared to take part in both stages and indicate your willingness by completing both the consent section at the end of the information sheet and the questionnaire, and return them in the envelope provided.

In both stages the information you provide will be kept confidential and will only be used for research purposes. The results will be presented in an aggregated form, so those individual participants will not be identified.

The medical assessment will not involve any costs to you and the results of these tests will be made available to you, as will the results of the air measurements.

Your involvement in this study is completely voluntary and you are free to withdraw at any time.

Your time to take part in this study is most appreciated and should you have any questions or concerns about the study please contact me at Curtin University 9266 2817 or home 9354 5333.

Thank you for your assistance.

Yours sincerely

Mrs. Krassi Rumchev
PhD Researcher
School of Public Health
Curtin University

Appendix C

curtin

University of Technology
Western Australia

QUESTIONNAIRE

Name of the child _____

_____

Date of birth _____

Address _____

_____

Telephone number _____

Date questionnaire completed _____

CHILD HEALTH QUESTIONNAIRE

This questionnaire will ask you mainly about your child's health history and status. Be assured that your answers will remain strictly confidential.

Please answer by placing a tick in the most appropriate box.

1. Sex of child
   - a) male ☐
   - b) female ☐

2. Person completing the questionnaire
   - a) child's mother ☐
   - b) child's father ☐
   - c) guardian ☐
   - d) other ☐

Specify relationship _____

3. What is the highest qualification of

	Year 10	Year 12	TAFE	University
a) the mother?	☐	☐	☐	☐
b) the father?	☐	☐	☐	☐

4. Occupation of the mother _____

5. Occupation of the father _____

6. Does this child attend child day care or nursery school?

Yes	No
☐	☐

7. If your answer is "Yes" how many hours does this child spend in the day care or in the nursery school per week? _____

8. Please, answer the following questions by placing a tick on "Yes or "No":

	Yes	No
a) During the last 6 months has this child had a cough:		
1) with cold?	☐	☐
2) occasionally apart from colds?	☐	☐
3) most days or nights?	☐	☐
4) no	☐	☐
b) Does this child's chest ever sound wheezy or whistling:		
1) with cold?	☐	☐
2) occasionally apart from colds?	☐	☐
3) most days or nights?	☐	☐
4) no, please go to question 9	☐	☐
c) Has your child ever had an attack of wheezing that has caused him/her to be short of breath?	☐	☐
d) If "Yes" to 8c) has he/she had 3 or more such episodes per week within the past 6 months?	☐	☐

9. Has a doctor ever said that this child has any allergies to

	Yes	No
a) pollen?	☐	☐
b) dust?	☐	☐
c) chemicals?	☐	☐
d) cockroach?	☐	☐
e) pets?	☐	☐
f) none?	☐	☐

10. Has this child's biological mother ever had know

	Yes	No	Don't
a) asthma?	☐	☐	☐
b) eczema?	☐	☐	☐
c) hayfever?	☐	☐	☐

11. Has this child's biological father ever had know

	Yes	No	Don't
a) asthma?	☐	☐	☐
b) eczema?	☐	☐	☐
c) hayfever?	☐	☐	☐

12. Has any of this child's brothers or sisters ever had know

	Yes	No	Don't
a) asthma?	☐	☐	☐
b) eczema?	☐	☐	☐
c) hayfever?	☐	☐	☐

13. During the last 3 months, has this child had any of the following symptoms?

	No	Occasionally	Frequently
a) running or stuffy nose	☐	☐	☐
b) trouble breathing	☐	☐	☐
c) hay fever	☐	☐	☐
d) allergies	☐	☐	☐

14. If "Yes", how long do they usually last ?

	Hours	Days	Month
a) running or stuffy nose	☐	☐	☐
b) trouble breathing	☐	☐	☐
c) hay fever	☐	☐	☐
d) allergies	☐	☐	☐

15. Has a doctor ever said that this child had asthma?

Yes	No
☐	☐

16. If your answer is "Yes", do asthma attacks occur more frequently or more severely during any particular season?

a) spring	☐
b) summer	☐
c) autumn	☐
d) winter	☐
e) no seasonal difference	☐

DWELLING QUESTIONNAIRE

The questions in this section relate to your child's home environment. Please answer by placing a tick in the most appropriate box.

	Yes	No
1. Smoking inside the house		
a) parents	☐	☐
b) visitors	☐	☐
c) nobody	☐	☐
2. Gas Heating		
a) flued	☐	☐
b) unflued	☐	☐
3. Open Fire Place	☐	☐
4. Closed Wood Fire	☐	☐
5. Kerosene Space Heater	☐	☐
6. Central Air Conditioning	☐	☐
7. Air Conditioning in Child's Room	☐	☐
8. Humidifier in Child's Room	☐	☐
9. Gas Cooking Appliances	☐	☐
10. Electric Cooking	☐	☐
11. Garage Attached to the Home	☐	☐
12. Pets or Birds (inside)	☐	☐

13. What kind of floor coverings do you have?

	in child's bedroom	in living room
a) carpet	☐	☐
b) ceramic	☐	☐
c) linoleum	☐	☐
d) concrete	☐	☐
e) slate (stone)	☐	☐
f) parquet	☐	☐
g) other	☐	☐

14. During the last 3 months, have the following changes taken place?

	in child's bedroom	in living room
a) new carpeting	☐	☐
b) walls painted	☐	☐
c) new furniture	☐	☐
d) new wall covering	☐	☐

15. How would you describe the general ventilation?

	in child's bedroom	in living room
a) very good	☐	☐
b) good	☐	☐
c) poor	☐	☐

16. How old is your house?

a) Less than 5 years ☐

b) Between 5 and 10 years ☐

c) Greater than 10 years ☐

17. How many people live in the house? ☐

18. How many bedrooms do you have?

a) one bedroom ☐

b) two bedrooms ☐

c) three bedrooms ☐

d) four bedrooms ☐

e) five bedrooms or more ☐

19. How many people share this child's bedroom?

a) own bedroom ☐

b) 1 person ☐

c) 2 persons ☐

d) 3 or more ☐

Thank you for your assistance

Appendix D

School of Public Health

QUESTIONNAIRE

Name of the child_____

Date questionnaire completed _____

This questionnaire will ask you mainly about your child's health status and his/her home environment.

Please, be assured that your answers will remain strictly confidential.

Please answer each question by placing a tick in the most appropriate box.

1. During the last month, has your child had any of the following symptoms?

	Yes	No
a) runny or stuffy nose?	☐	☐
b) watery eyes	☐	☐
c) cough	☐	☐
d) wheeze	☐	☐
e) hay fever	☐	☐
f) eczema	☐	☐
g) allergies	☐	☐

2. Is your child currently taking any medication? ☐ ☐

If "Yes", please specify _____

2. Does anybody currently smoke inside the house?

	Yes	No
a) parents	☐	☐
b) other family members	☐	☐
b) visitors	☐	☐

3. During the last month, have the following changes taken place?

	Yes	No
a) new carpeting		
1) in child's bedroom	☐	☐
2) in living room	☐	☐
b) walls painted		
1) in child's bedroom	☐	☐
2) in living room	☐	☐
c) new furniture	☐	☐
1) in child's bedroom	☐	☐
2) in living room	☐	☐
d) new wall covering		
1) in child's bedroom	☐	☐
2) in living room	☐	☐

4. What do you use for cooking?

a) gas cooking appliances	☐	☐
b) electric cooking appliances	☐	☐

5. How would you describe the general ventilation?

	in child's bedroom	in living room
a) very good	☐	☐
b) good	☐	☐
c) poor	☐	☐

6. Do you keep any pets inside the house?

Yes	No
☐	☐

Thank you for your assistance

Appendix E

Definition of terms

Association - statistical dependence between two or more events, characteristics, or other variables (Last, 1988)

Bias- deviation of results or references from the truth, or processes leading to such deviation (Last, 1988);

Effect modifier - A factor that modifies the effect of a putative factor under study (Last, 1988);

Exposure - Proximity and/or contact with a source of a disease agent in such a manner that effective transmission of the agent or harmful effects of the agent may occur (Last, 1988).

Hazard - A factor or exposure that may adversely affect health (Last, 1988).

Odds ratio - The number of people with disease who were exposed to a risk factor (Ie) over those with disease who were not exposed (Io) divided by those without disease who were exposed (Ne) over those without who were not exposed (No), or OR=(Ie/Io)/(Ne/No) (Swinton, 1998);

Risk factor - An aspect of personal behavior or lifestyle, an environmental exposure, or an inborn or inherited characteristic, which on the basis of epidemiological evidence is known to be associated with health-related condition(s) considered important to prevent (Last, 1988);

Reliability - It concerns the extent that repeat measurements made by it under constant conditions will give the same result (Moser, 1986);

Validity - It concerns the extent to which an instrument measures what it is intended to measure (Rothney, 1996);

Prevalence - The proportion of the population with a disease, disorder, or abnormality. Cumulative prevalence is the total number of those who have had the disorder within a given time (Toelle, 1992);

Incidence - The number of individuals who develop an abnormality within a given time (usually a year) expressed as a percentage of the population (Toelle, 1992);

Morbidity - The degree to which quality of life is impaired (Toelle, 1992);

Airway responsiveness – The response of the airways to varying provoking stimuli (Toelle, 1992);

Airway hyperresponsiveness – Airways that narrow too easily or too much in response to a provoking stimulus. In persistent asthma, the airways are hyperresponsive to many different provoking stimuli. Objective parameters are required to assess airway hyperresponsiveness (Toelle, 1992);

Atopy – The propensity, usually genetic, for developing IgE-mediated responses to common environmental allergens (Toelle, 1992);

Exacerbate – to aggravate or make asthma worse. "Exacerbate" replaces the words "cause", "induce".

Exacerbation – any worsening of asthma. Onset can be acute and sudden, or gradual over several days. "Exacerbation" replaces the words "attack" and episode".